STABLE MIXED CARBOXYLIC ACID DIMERS

BY

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Abstract

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Carboxylic acids are known to exist predominantly as dimers. Mixed dimers between different carboxylic acids are known in the gas and liquid phases, but generally revert to separate homodimers upon solidification. Following a chance discovery of an apparent stable mixed carboxylic acid dimer between acetic and phenylacetic acids, a series of substituted phenylacetic acids were prepared in high purities and converted to mixed dimers with acetic acid for study. Some, but not all substituted acids studied, appeared to form stable mixed dimers, based upon melting point and Infrared analyses. Infrared analyses of the mixed dimers showed slight but significant differences from their parent acids, interpreted as hydrogen bonding between the acetic acid carbonyl and phenylacetic hydroxyl hydrogen. The physical data strongly suggest that these stable dimers observed are indeed pure molecular compounds. Attempts to generate single crystals by recrystallization for proof of structure by X-ray diffraction analysis resulted in regeneration of homo dimers.

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Dedication

This thesis is dedicated to Soma, my wife,
who is constantly helping me to have a beautiful life
and to my son Rittick, and to Riya, my daughter,
who give me immense joy and always make my day better.

INTRODUCTION

Carboxylic acids have long been known to exist primarily as dimers [1]. This is true in all phases: solid [2,3,4], liquid [5] and gas [6,7,8]. Some studies have shown the existence of mixed dimers, i.e., dimers formed from two different carboxylic acids, but little information is available [9].

In solution, mixed dimers formed readily from two different carboxylic acids. These have generally been present as statistical mixtures with the non-mixed dimers of the acids from which they formed, roughly 50% mixed dimer and 25% each of the parent (non-mixed) dimers (from equimolar amounts of acids)[10]. This represents an equilibrium state, and equilibration is assumed to be rapid (unlike anhydrides, which have no direct means of equilibration).

In the gas phase, the existence of mixed dimers has been shown by a variety of physical methods. Since these are generated from the liquid phase, they also generally exist as statistical mixtures. One example of a pure mixed dimer, the trifluoroacetic acid/formic acid dimer, was reported and studied by infrared spectrometry [10]. In this case increased strength of hydrogen bonding, apparently due to the substantial difference in electro-negativity between the two parent acids, is assumed to be the driving force for formation of the mixed dimer. Most mixtures containing mixed dimers in the liquid phase revert to the parent acids upon solidification/crystallization. For example, naphthaleneacetic acid may be recovered from acetic acid unchanged [11]. This suggests that there is no real

driving force other than entropy behind the formation of most mixed dimers, and that the energies associated with forming crystals outweigh those of the entropies involved in forming the mixed dimers.

In a few cases, however, solid mixed dimers were reported. A solid prepared from 4-aminobenzoic acid and 3,5-dintrobenzoic acid was shown by X-ray crystallography to contain a mixture of homo and hetero (mixed) dimers as well as linear chains [12,13]. The system of acetic acid and trimesic acid (benzene-1,3,5-tricarboxylic acid) forms a 1:2 complex (one mole acetic acid to two moles trimesic acid) which has been analyzed by single crystal X-ray diffraction, and shown to be comprised of an asymmetric repeating unit containing a mixture of trimesic-trimesic dimer linkages and trimesic-acetic dimer linkages[14]. In one special case, the mixed dimer from trifluoroacetic acid and acetic acid was obtained in pure form by low-temperature crystallization from the mixed acids, and its structure was determined [15]. Other examples involved mixed dimers in which the acids were chiral, mirror images of each other differing only in minor substituents. Here the driving force appeared to be the energy of crystallization, the mixed dimers (referred to as quasi-racemates) associating more readily than either individual dimer [16]. This finding was developed into a general method for correlating chiral configuration, depending upon whether the mixture forms a molecular compound or solid solution [17]. Existence of definite compounds was determined by X- ray crystallography [18] infrared spectroscopy [19] or most-simply by melting point behavior.

Given the above historical information, a chance discovery of an apparently stable mixed dimer was made. Radioactive phenylacetic acid -^{14}C is prepared, and used in one method of producing radioactive Potassium Cyanide [20]. The intermediate phenylacetic acid is seldom pure, and a few attempts were made to purify it by recrystallization. Since acetic acid is used to recrystallize naphthylacetic acid [21], it appeared a logical choice to try. A small amount of radioactive phenylacetic acid was dissolved in about ten volumes of acetic acid, and recrystallization was attempted; no crystals resulted. Recovery of the phenylacetic acid by evaporation of the acetic acid, even above the boiling point of acetic acid, did not regenerate phenylacetic acid, but instead gave a larger mass of crystalline material of lower but very sharp melting point. Further analysis showed that the increase in mass corresponded exactly to one mole of acetic acid per mole of phenylacetic acid. Since the melting point was sharp, and the molar ratio exactly one-to-one, the material was clearly a molecular compound, presumably a mixed dimer.

Given this discovery, questions arose as to why this dimer was stable, when similar acids had not shown this behavior. It was decided that further research was needed, and the plans of the research project were submitted for approval as partial fulfillment of the requirements of the degree of Master of Science.

RESEARCH DESIGN AND METHODOLOGY

The first objective of this study was to reproduce the initial discovery by melt crystallization of equimolar quantities of acetic and phenylacetic acids (Scheme I) and verify the melting behavior of this system.

If successful, the next stage would be to produce a series of related phenyl substituted compounds with the intent of studying stability and possibly identifying, though various physical tests, any unique features associated with these compounds. One physical test considered was IR, particularly with the idea of observing and quantifying changes in hydrogen bonding; quantitative differences between members of an appropriately substituted series would lead to a Hammett plot which might allow interpretation of the factors allowing stable mixed dimers. Conclusive determination of atomic position and molecular structure through X-ray crystallography was also considered a desirable possibility. For the Hammett plot, the following series was chosen: unsubstituted; 3- and 4-methyl, 3- and 4-methoxy, 3- and 4-fluoro, 3- and 4-chloro, 3- and 4-bromo, 3- and 4-iodo, and 3- and 4-nitro. It was hoped that one of the bromo or iodo acids would form dimer crystals suitable for X-ray analysis by the classic heavy-atom technique.

The first requirement of this line of study would be a source of high purity phenylacetic acids. These acids are commercially available from a variety of suppliers of laboratory chemicals in purities of 95% to 98%. Purification of these available acids by recrystallization was considered, but many of the acids desired are of relatively low

melting point. In particular, the isomeric purity of the substituted acids was unknown, and it was not certain that recrystallization would fully remove undesired isomers if present. Distillation was even less encouraging, as isomers often differ in boiling point by only a few degrees. It was decided that specialized syntheses tailored for high purities would be advisable.

Various methods for preparation of the necessary phenylacetic acids were considered. Hydrolysis of commercially available phenylacetonitriles [21] was rejected since, similar to the commercially available acids, the presence of isomers could not be ruled out, and such isomers, if present, would be difficult to reliably remove. Carbene insertion from diazoacetic acid derivatives was useless [22] as mixed isomers would be formed from substituted benzene derivatives. Conversion of benzyl halides, either via carbonation of grignard derivatives or more simply via reaction with cyanide ion and subsequent hydrolysis, remained a possible option, though still dependent upon obtaining the starting benzyl halides isomerically pure [21]. Particular attention was given to the Willgerodt reaction [23, 24] as the starting acetophenones are mostly available in reasonably pure form, and the intermediate thiomorpholides are highly crystalline and easily purified by recrystallization. Of these methods, the Willgerodt reaction was considered most likely to provide the purest acids and was thus selected as the primary method (Scheme II). Since nitro groups are incompatible with the Willgerodt reaction [23] the benzyl halide via nitrite route was chosen for this pair of compounds (Scheme III). This route was also chosen for the 3-iodo compounds, as 3-iodoacetophenone was not readily available.

For preparation of the mixed dimers, a bulk melting point method was chosen, as this would allow repeated melting point determinations on the same sample. Also, by holding a stirred silicone oil-heating bath at gradually increasing temperatures for prolonged periods during melting, highly accurate melting point ranges could be determined. A sample size of roughly three grams of each phenylacetic acid was selected as large enough to permit accurate weighing and to allow accurately measurable equimolar quantities of acetic acid to be added. A standard 14ml borosilicate screw-cap vial with polyethylene seal were chosen as a convenient vessel for dimer synthesis and melting point determination.

Infrared analyses of the solid dimers were planned to be performed as standard KBr pellets; analyses of the starting phenylacetic acids was planned for comparison with the expectation that some differences in carbonyl or hydroxyl behavior would be detected. Since, in the cases of certain quasi-racemates, some differences between the individual and mixed acids were noted in the fingerprint region, it was hoped that the mixed acetic/phenylacetic system might show similar differences.

X-ray analysis was viewed as an ultimate proof of mixed dimer structure, if possible. Most previous studies upon quasiracemates performed powder X-ray analyses upon a range of compositions varying from 100% of one chiral acid through 100% of another chiral acid, along with similar X-ray spectra of each acid's racemate [25, 26]. This technique did not appear applicable to the acetic/phenylacetic system, however. One study did manage to produce quasiracemate crystals in which one component contained a

bromine atom; this system was analyzed by the classical single crystal/heavy atom X-ray technique and yielded very good data confirming conclusively the mixed dimer structure [18]. If single crystals of mixed acetic/phenylacetic dimers could be produced, X-ray analysis probably would yield conclusive results either confirming or refuting the postulated mixed dimer structure.

ANALYSIS

A series of phenylacetic acids was prepared. The synthetic routes selected behaved as expected, without complications. The acids were of acceptable purities as evidenced by their melting points, in general higher and sharper than reported for their commercial counterparts (Table-II). Subsequently these acids were used to prepare 1:1 complexes with acetic acid for study (Table-I). The original discovery of a stable compound with sharp melting point formed from mixing equimolar quantities of acetic acid and phenylacetic acid was confirmed.

Similar equimolar mixtures were made from acetic and substituted phenylacetic acids; some gave relatively narrow melting point ranges, while others did not (Table-II).
Literature states that "only a pure substance, or a mixture having the composition of the eutectic, melts sharply at a definite temperature"[27]. Eutectics have a considerable range of compositions, with one component sometimes present at only a few percent [27]. The existence of a series of equimolar mixtures with sharp melting points strongly suggests pure substances; a large series of precisely equimolar eutectics would be an extreme

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coincidence, as a eutectic "rarely corresponds to the exact composition of a simple chemical compound"[28]. Thus the mixtures in this series found to have relatively narrow melting ranges are likely to be true compounds.

The literature discusses systems in which "two components form a compound possessing a congruent melting point"[27]. This is defined as a system "capable of existing as a solid compound in equilibrium with a liquid of the same composition". Further discussion states "if the compound is not completely stable but tends to decompose (dissociate) into its components in the liquid phase, the melting point will be lowered by the products of decomposition"[27]. Melting point depression from impurities is usually accompanied by a certain broadening of the melting point range; a sharp melting point range is generally accepted as an indication of purity [29]. For the systems in this study, equilibration between mixed dimers and non-mixed dimers would be decomposition equivalent to dissociation, regenerating to some extent the original components, which formed the new compound. Some broadening of melting points would be expected to result from such equilibration.   Broadening of the melting point ranges for the mixtures in this study which appeared to give discrete compounds leads to some rough conclusions about the composition of the liquid phases with which these crystals are in equilibrium. Most reagent chemicals are supplied at purities of 98% or better. Those supplied as 98% material usually have melting point ranges of one or two degrees Centigrade, while those

Scheme I: **Preparation of mixed dimers from Phenylacetic Acid / Acetic Acid**
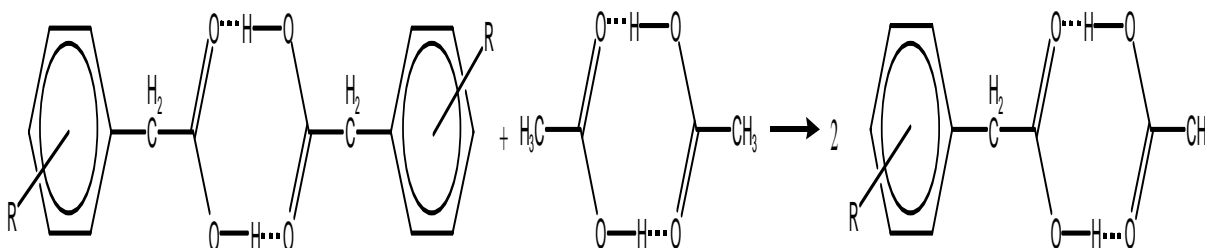
Where, R =H, 3-CH$_3$, 4-CH$_3$, 3-OCH$_3$, 4-OCH$_3$, 3-F, 4-F, 3-Cl, 4-Cl, 3-Br, 4-Br, 3-I, 4-I, 3-NO$_2$, 4- NO$_2$

Scheme II: **Synthesis of substituted Phenylacetic Acid by Willgerodt reaction**
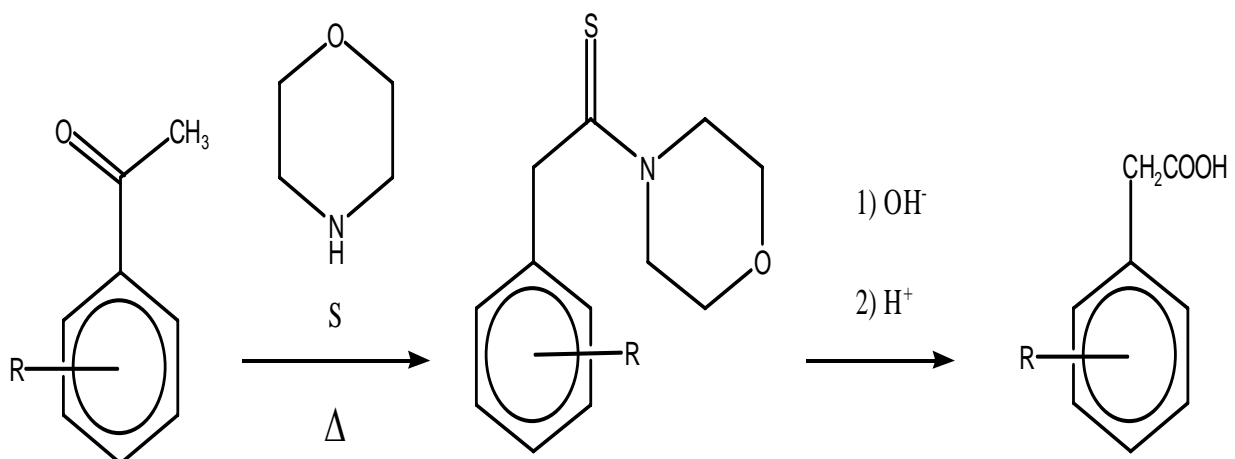
Where, R = H, 3-CH₃, 4-CH₃, 3-OCH₃, 4-OCH₃, 3-F, 4-F, 3-Cl, 4-Cl, 3-Br, 4-Br, 4-I

Scheme III: Synthesis of substituted Phenylacetic Acid from benzyl halide
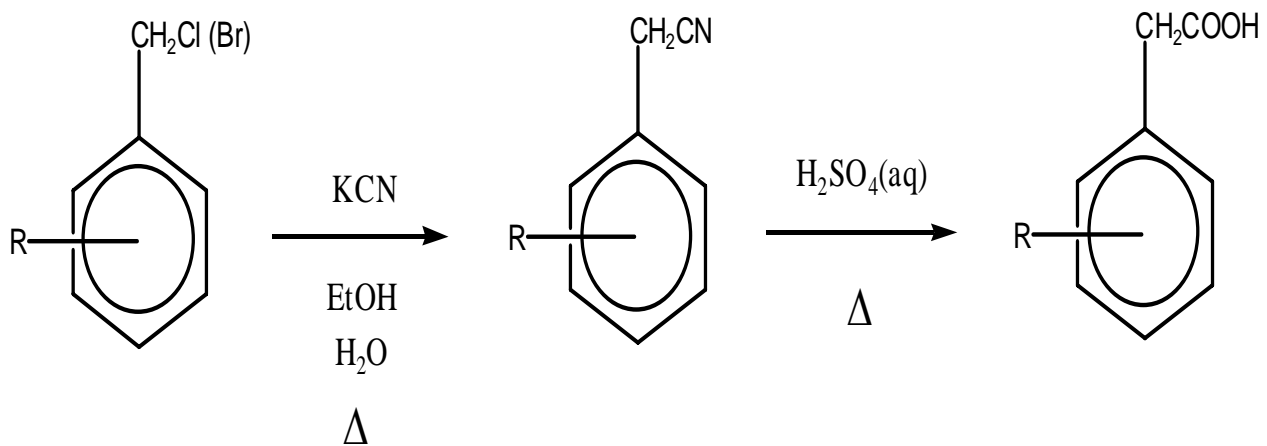
Where, R = 3-I, 3-NO₂, 4-NO₂

TABLE I

Weight of Phenylacetic Acid & substituted Phenylacetic Acids taken to form mixed dimers with equimolar Acetic Acid (AcOH)

Structural Formula: $R-C_6H_4-CH_2COOH$

Compound	F.Wt.	Sample + Vial (g)	Empty Vial (g)	Net Wt. Taken (g)	mmol	AcOH Added (ml)
R=H	136.15	18.6262	15.4612	3.165	23.25	1.33
R= 3 -CH$_3$	150.17	17.8597	14.3225	3.5372	23.55	1.348
R= 4 - CH$_3$	150.17	17.9206	14.3892	3.5314	23.52	1.346
R= 3-OCH$_3$	166.17	17.9722	14.4652	3.507	21.1	1.21
R= 4 - OCH$_3$	166.17	17.8483	14.3571	3.4912	21.01	1.203
R= 3 –NO$_2$	181.15	15.3988	14.4327	0.9661	5.33	0.305
R= 4 – NO$_2$	181.15	18.3562	14.3454	4.0108	22.14	1.267
R= 3 -F	154.14	17.6303	14.2615	3.3688	21.86	1.251
R= 4 - F	154.14	17.8949	14.4397	3.4552	22.42	1.283
R= 3 -Cl	170.59	18.3358	14.4203	3.9155	22.95	1.314
R= 4 - Cl	170.59	18.3320	14.3988	3.9332	23.06	1.32
R= 3 -Br	215.04	17.8580	14.4717	3.3863	15.75	0.902
R= 4 - Br	215.04	17.6408	14.4998	3.141	14.61	0.836
R= 3 -I	262.04	16.6923	14.2268	2.4655	9.41	0.5387
R= 4 - I	262.04	15.4954	14.4841	1.0113	3.86	0.221

TABLE II

Determination of melting point of mixed dimers formed from substituted Phenylacetic Acids with equimolar Acetic Acid
Structural Formula: $R-C_6H_4-CH_2COOH/ CH_3COOH$

Compound	MP of Parent compound (Lit. Value)	MP of Synthesized Parent compound (Observed)	Physical State of Acid Mixture at 20°C	Bulk MP Range For Mixed Dimers (Observed)
R = H	76°C - 78°C[*]	77.5°C - 78°C	Solid	40°C - 43°C
R= 3 -CH$_3$	64°C - 66°C[	65°C – 66°C	Solid	38°C - 41°C 37°C - 40°C
R= 4 -CH$_3$	88°C - 92°C	91°C -92°C	Solid	55°C - 58°C 55°C - 58°C
R= 3-OCH$_3$	65°C - 69°C[*]	65°C – 66°C	Solid	47°C - 49°C 47°C - 49°C
R= 4-OCH$_3$	84°C - 86°C[*]	85°C – 86°C	Solid	54°C - 58°C 54°C - 58°C
R= 3 –NO$_2$	117°C-120°C[*]	118°C - 120°C	Solid-Liquid	X
R= 4–NO$_2$	150°C - 155°C [*]	153°C – 155°C	Solid-Liquid	X
R= 3 -F	42°C- 44°C[*]	42°C – 44°C	Liquid	X
R= 4 - F	81°C - 83°C[*]	82°C – 83°C	Solid	40°C - 44°C
R= 3 -Cl	76°C - 79°C[*]	78°C – 79°C	Solid	46°C - 49°C 46°C - 49°C
R= 4 - Cl	102°C -105°C [*]	104°C – 105°C	Solid	56°C - 70°C
R= 3 -Br	98°C - 102°C [*]	101°C - 102°C	Solid	70°C - 74°C 70°C - 74°C
R= 4–Br	114°C - 117°C [*]	116°C – 117°C	Solid	56°C - 80°C 56°C - 80°C
R= 3 -I	127°C - 131°C [*]	129°C – 131°C	Solid	X
R= 4 -I	136°C - 140°C	138°C – 140°C	Solid	68°C – (>) 120°C

[X denotes melting point not taken, due to liquid present at room temperature]

[* denotes values obtained from Aldrich Catalogue 2007-2008]

of 99% or higher usually report ranges of at most one degree Centigrade. For the parent system, that from acetic acid and phenylacetic acid, the melting point range was two degrees Centigrade, and no acetic acid could be distilled from the mixture; both these facts suggest that at most only a small amount of acetic acid, possibly two percent or less, was present in the liquid phase. Those systems having melting point ranges of three or four degrees Centigrade presumably have greater percentages of the acetic and substituted phenylacetic acids, but probably less than five percent each and certainly well below the statistical twenty-five percent each expected based upon entropy alone. The 4-chloro- and 4-bromophenylacetic acids formed mixed systems that looked like homogeneous crystals but gave broad melting point ranges; these systems likely are closer to the statistical twenty-five percent of each starting acid in the liquid phase. As observed from melting point behavior alone, it is not possible to distinguish between the situation where the solid phase is pure and the liquid phase is a mixture or the situation where the solid phase has formed as a mixture that matches the liquid phase.

Both nitrophenylacetic acids produced mixed systems, which did not initially solidify fully at room temperature. Either their melting point ranges were so broad as to extend below room temperature or, more likely, the nitrophenylacetic acids crystallized alone, leaving primarily acetic acid behind as a liquid phase. The 3- and 4-iodophenylacetic acids (melting points 129^0C -131^0C and 138^0C -140^0C respectively) gave mixed systems

which, while solid at room temperature, exhibited melting over a very broad range, and yielded a distillate of acetic acid before melting was complete; it is possible that these systems may contain some amount of iodophenylacetic acids in the solid phase.

Nitro groups are the most polar substituents in the series, and it may be that their polarity leads to increased association between nitrophenylacetic acid molecules at the expense of mixed dimer formation. Iodo groups, while only slightly more polar than the other halogen substituents, are considerably more polarizable, and thus Van der Waals forces could influence crystallization in favor of non-mixed dimers. Hyperconjugation of the 4-halo groups in order to achieve greater polarizability than the 3-halo groups is unlikely; in this case it may simply be that the 4-chloro- and 4-bromophenylacetic acids, having higher melting points and greater symmetry, crystallize with greater lattice energy than do the respective 3-chloro- and 3-bromophenylacetic acids, and that this is sufficient to favor the dimer in one case but not the other. All the other member of the series appears to have formed stable mixed dimers, with stability increasing as polarity of the substituents decreases.

Infrared spectra of all solid mixed compounds were taken alongside the acids from which they were made [Table–III & Table-IV]. Acetic acid itself (prepared as a KBr pellet for ease of comparison, despite being a liquid) gave a relatively simple spectrum. The main peak of the carbonyl stretch was observed at 1716 cm^{-1}, assigned to the dimer, with a small shoulder at about 1755 cm^{-1} assigned as monomer. A peak at 1410 cm^{-1} is assigned as C-O-H bending, and the peak at 1294 cm^{-1} (showing a broad shoulder at lower

wavenumbers) is assigned as C-O stretching. The O-H stretch typically observed around 3000cm^{-1} was so broad as to be unobserved. Similarly, C-H bending of the methyl group was too weak to be detected. The spectra of the series of phenylacetic acids were as expected for carboxylic acid dimers: strong, broad bonded O-H stretches around 3000

cm^{-1} with aromatic and aliphatic C-H stretches superimposed, strong sharp hydrogen-bonded carbonyl stretches at about 1700 cm^{-1} sharp, but weaker C-O-H bending bands around 1410 cm^{-1}, and C-O stretching bands around 1300 cm^{-1}, and a variety of other peaks below 1600 cm^{-1} related to the methylene group, aromatic ring and substituents. Curiously, spectra of the mixed dimers were almost superimposable with the phenylacetic acids from which they were made. It was expected that at least minor differences in hydrogen bonding, recognizable as differences in the bonded carbonyl and C-O stretches and/or C-O-H bendings, would be observed between the dimers and source acids. Virtually no changes in vibrational energies could be detected as a result of forming the mixed dimers; in general all differences were less than 1 cm^{-1}, likely within experimental error. Each dimer spectrum closely matched its parent phenylacetic acid spectrum regardless of whether the dimer had a sharp melting point range or not. This similarity between the parent acids and mixed dimers is so striking that, in the absence of the melting point evidence, it would appear on first inspection that only the parent acids had been analyzed. A recent study of formic, acetic, propionic and butyric acid dimers included a discussion of bonding changes as a result of dimerization and why differences are slight [30]. Closer inspection of the spectra did yield two subtle but notable differences.

TABLE – III

Major IR Frequencies of Mixed Dimers Formed Between Substituted Phenylacetic Acid & Equimolar of Acetic Acid

Structural Formula: $R-C_6H_4-CH_2COOH/ CH_3COOH$

Mixed Dimer	C=O---H Str. (cm^{-1})	O-H Bend. (cm^{-1})	C-O Str. (cm^{-1})	O-H Str. (cm^{-1})
R = H	1700.04 s	1407.89 m	1243.95 sh	2500-3100 b
R= 3 -CH$_3$	1698.76	1409.79 m	1262.21 w	2500-3100 b
R= 4 - CH$_3$	1698.77 s	1411.32 m	1256.70 m, sh	2500-3100 b
R= 3-OCH$_3$	1697.46 s	1434.78 m	1297.51 m	2500-3100 b
R= 4-OCH$_3$	1694.19 sh	1406.52 m, sh	1317.06 m, sh	2500-3100 b
R= 3 –NO$_2$	1708.73 s	1410.64 w, sh	1243.14 m	2500-3100 b
R= 4–NO$_2$	1712.06 s	1406.53 w, sh	1304.89 m, sh	2500-3100 b
R= 4 - F	1700.52 s	1408.71 m	1231.05 s	2500-3200 b
R= 3 -Cl	1700.82 s	1430.10 m	1247.4 m, sh	2500-3100 b
R= 4 - Cl	1697.56 s	1405.71 m, sh	1255.39 m, sh	2500-3100 b
R= 3 -Br	1697.69 s	1409.03 m	1243.73 m, sh	2500-3100 b
R= 4–Br	1700.36 s	1404.46 m, sh	1253.57 m, sh	2500-3100 b
R= 3 -I	1698.42 s, sh	1419.34 m, sh	1227.63 m, sh	2500-3100 b
R= 4 -I	1667.23 s	1404.96 m	1233.65 m	2500-3100 b

Key:
1. Str. = Stretching Frequency, Bend. = Bending Frequency
2. s = strong, m = medium, w = weak, sh = shoulder, b = broad

TABLE – IV

Major IR Frequencies of Acetic Acid & Substituted Phenylacetic Acid

Structural Formula: $R-C_6H_4-CH_2COOH$

Free Acid	C=O---H Str. (cm^{-1})	O-H Bend. (cm^{-1})	C-O Str. (cm^{-1})	O-H Str. (cm^{-1})
CH_3COOH	1716.42 m	1409.92 w	1294.36 w, sh	none
R = H	1701.24 s, sh	1407.63 m	1242.92 m, sh	2500-3200 b
R= 3 -CH$_3$	1702.57 m, sh	1409.61 m	1261.26 m	2500-3200 b
R= 4 - CH$_3$	1701.35 s, sh	1411.46 m	1256.76 m, sh	2500-3200 b
R= 3-OCH$_3$	1697.44 s	1408.91m	1267.00 m	2500 - 3000
R= 4-OCH$_3$	1710.42 1694.05	1429.01w	1244.12 s	2500-3200 b
R= 3 –NO$_2$	1708.29 s	1399.94 w	1240.09 m	2500-3200 b
R= 4–NO$_2$	1697.50 sh	1429.96 w, sh	1253.01 m	2500-3200 b
R= 4 - F	1700.79 s, sh	1408.28 m, sh	1229.30 m	2500-3200 b
R= 3 -Cl	1691.26 sh	1408.39 m	1246.34 m, sh	2500-3200 b
R= 4 - Cl	1697.20 s	1405.45 m. sh	1253.06 w	2500-3200 b
R= 3 -Br	1695.12 s	1410.91 m, sh	1240.56 m, sh	2500-3200 b
R= 4–Br	1698.88 s	1404.48 m, sh	1253.59 w, sh	2500-3200 b
R= 3 -I	1698.44 s	1408.57 w, sh	1243.04 w, sh	2500-3200 b
R= 4 -I	1698.49 s	1405.16 m	1234.30 m	2500-3200 b

Key:
1. Str. = Stretching Frequency, Bend. = Bending Frequency
2. s = strong, m = medium, w = weak,   sh = shoulder, b = broad

Firstly, the carbonyl stretch of acetic acid was not present in any of the dimer scans. This could be due to acetic acid, which is a small molecule and thus difficult to polarize, having weak infrared absorptions. If this is so, acetic acid could absorb so weakly in the infrared that its absorptions are overwhelmed by the phenylacetic acid components of the mixtures (a quantitative study, difficult to do using KBr pellets, would be needed to rule this out). However, a moderately strong spectrum was obtained from an amount of acetic acid somewhat less than the amounts of the other materials studied, so it is difficult to believe that the presence of an equimolar amount of acetic acid in the samples would be irrelevant. It appears that the acetic acid present has interacted with the phenylacetic acids in the samples to produce materials in which the carbonyl stretch of acetic acid has been altered and no longer occurs at the same energy. Specifically, the carbonyl stretch of the acetic acid incorporated into the mixed dimer samples has been reduced by about 15 cm^{-1}. This indicates that phenylacetic acids undergo hydrogen bonding to the acetic acid carbonyl more strongly than another acetic acid monomer does, with corresponding weakening of the acetic acid carbonyl double bond character and lowering of its stretching frequency relative to pure acetic acid. Stronger hydrogen bonding in the mixed dimer implies that the mixed dimer is more stable than the individual acetic and phenylacetic acids, although exact energy differences cannot be calculated based upon one bond alone. If the energy difference were sufficiently large, mixed dimers would be greatly favored in the liquid phase; this, coupled with thermodynamic or even kinetic effects in crystallization would be sufficient to produce pure mixed dimer crystals.

The second difference between the mixed dimers and parent phenylacetic acids, noticeable in the unsubstituted, 3- and 4-methyl, 4-fluoro and 3-chloro pairs, was that the carbonyl peak of the dimers was smoother and sharper than that of the corresponding parent acids. These dimers had the narrowest melting point ranges of the series, and appear based upon this IR evidence to have more consistent crystal environments in the vicinity of their carbonyl groups than do their parent phenylacetic acids. This is possible, as some acids under certain conditions have configurations other than dimers, such as linear hydrogen bonded chains. Traces of such other associated forms could be present in the parent acids but not in the mixed dimers. Absence of these spectral irregularities in these mixed dimers, regardless of their source, is strong evidence that these mixed dimers do indeed represent true compounds. It also suggests that they are pure in the solid state, broadened melting point being an effect of the solid-liquid interface and not caused by non-uniformity within the solid phase.

It is unfortunate that experiments to produce pure single crystals of dimers by recrystallization did not produce favorable results. The 3-bromo mixed dimer had a relatively sharp melting point range, and looked a favorable candidate for determination of atomic structure by the classical heavy-atom X-ray diffraction technique. When it did not yield mixed dimer crystals, recrystallization was attempted upon the unsubstitued mixed dimer, as it seemed the most stable of the series; it unfortunately did not yield mixed dimer crystals, either. Successful recrystallization and X-ray analysis of atomic positions in at least one member of this series would conclusively prove whether or not these molecular compounds truly exist as mixed dimers.

EXPERIMENTAL

Part I: Synthesis of Phenylacetic and Substituted Phenylacetic Acids

Phenylacetothiomorpholide

120.2g Acetophenone (1.00 mole), 51.2g Sulfur powder (1.6 mole) and 122g Morpholine (1.4 mole) was placed in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and poured into 500mL of 2N Hydrochloric acid. 300mL Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered and evaporated to dryness on the rotary evaporator to produce a brownish-yellow semi crystalline mass.

The above material was extracted twice with 600mL of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 600mL. On cooling thick orange crystals were deposited; these were washed twice with 60mL of Ethanol and air-dried, yield: 110g, (fw 221.4, 0.49 mole), mp

63^0C -64^0C. A second crop of crystals was obtained by concentrating the mother liquor

and washings at boiling to about 200mL and, allowed to cool; this after washing and

drying weighed 51g, (0.23 mole), for a combined yield of 161 grams, 72.7%.

Phenylacetic Acid

70g Phenylacetothiomorpholide (0.31 mole) and 500mL 10% Sodium Hydroxide in

Ethanol were placed in a 1000mL round bottom flask fitted with a magnetic stir bar and a

reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred

at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by

evaporation on a rotary evaporator, and the mixture was diluted with water to about

500mL. The resulting solution was filtered to remove a small amount of tarry material,

acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride,

and extracted four times with 200mL of Dichloromethane. The extracts were combined,

dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator,

and vacuum dried to yield masses of near-white crystals. These were recrystallized from

600mL Petroleum ether to yield large clear crystalline plates, which were washed twice

with 20mL Petroleum ether and vacuum dried, yield: 22.1g (fw 136.2, 0.16 mole), 51%,

mp 77.5^0C -78^0C. (These crystals were judged adequate for the study and a second crop

was not collected.)

3-Methyl-phenylacetothiomorpholide

25g 3-Methyl acetophenone (0.18 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) was placed in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and poured into 300 mL of 2N Hydrochloric acid. 200mL of Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce a brownish-yellow semi crystalline mass.

The above material was extracted twice with 300mL of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250mL. On cooling lemon yellow crystals were deposited; these were washed twice with 30mL of Ethanol, and air-dried, yield: 18.8g (fw 235.4, 0.080 mole), mp 74^0C -75^0C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80mL, and allowed to cool; this after washing and drying weighed 7.6g (0.32 mole), for a combined yield of 26.4 grams, 60%.

3-Methyl-phenylacetic Acid

23.5g 3-Methyl phenylacetothiomorpholide (0.10 mole) and 200 mL Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on a rotary evaporator, and the mixture was diluted with water to about 200mL. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride and extracted four times with 100mL of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 200mL of Petroleum ether to yield clear crystals, which were washed twice with 20mL of Petroleum ether, and vacuum dried, yield: 8.1g (fw 150.2, 0.054 mole), 54%, mp 65^0C - 66^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

4-Methyl-phenylacetothiomorpholide

25g 4-Methyl acetophenone (0.18 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) was placed in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at

180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about

60^0C, and was poured into 300mL of 2N Hydrochloric acid. 200mL Dichloromethane

was added; the mixture was shaken to equilibrate the phases, and then transferred to a

separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was

extracted for a second time with 100mL of Dichloromethane. The organic phases were

combined, dried, filtered, evaporated to dryness on the rotary evaporator, and vacuum

dried to produce a brownish-yellow semi crystalline mass.

The above material was extracted twice with 300mL of boiling Ethanol, and the

combined extracts were filtered while warm, and concentrated at boiling to

approximately 250mL. On cooling yellowish-white crystals were deposited; these were

washed twice with 30mL of Ethanol and air-dried, yield: 15.1g (fw 235.4, 0.064 mole),

mp 86^0C –87^0C. A second crop of crystals was obtained by concentrating the mother

liquor and washings at boiling to about 80mL and allowing to cool; this after washing

and drying weighed 8.9g (0.38 mole), for a combined yield of 24.0 grams, 56%.

4-Methyl-phenylacetic Acid

23.5g 4-Methyl phenylacetothiomorpholide (0.10 mole) and 200 mL Sodium Hydroxide

in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and

a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred

at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by

evaporation on the rotary evaporator, and the mixture was diluted with water to about

200mL. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride, and extracted four times with 100mL of Methylene Chloride. The extracts were combined, dried with Magnesium sulfate, filtered, and evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 200mL of Petroleum ether to yield large clear crystals, which were washed twice with 20mL Petroleum ether, and vacuum dried, yield: 7.6g (fw 150.2, 0.050 mole), 50%, mp 91^0C -92^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

3-Methoxy-phenylacetothiomorpholide

25g 3-Methoxy acetophenone (0.166 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) were placed in a 250ml round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and was poured into 300mL of 2N Hydrochloric acid. 200mL of Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred into a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce a brownish mostly crystalline mass.

The above material was extracted twice with 300mL of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250mL. On cooling stocky lemon-yellow crystals were deposited; these were washed twice with 30mL of Ethanol, and air dried, yield: 14.4g (fw 251.4, 0.057 mole), mp 71^0C -72^0C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80mL, and allowing to cool; this after washing and drying weighed 8.6g (0.034 mole), for a combined yield of 23.0 grams, 55%.

3-Methoxy-phenylacetic Acid

22g 3-Methoxy phenylacetothiomorpholide (0.087 mole) and 200 mL Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was diluted with water to about 200mL. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride and extracted four times with 100mL of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 200mL of 90% Ethanol to yield clear colorless crystals that were washed twice with 20mL of 90% Ethanol and vacuum dried, yield: 8.1g (fw 150.2, 0.054 mole), 54%, mp

65^0C -66^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

4-Methoxy-phenylacetothiomorpholide

25g 4-Methoxy acetophenone (0.166 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) were placed in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and was poured into 300mL of 2N Hydrochloric acid. 200ml Dichloromethane were added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce a brownish mostly crystalline mass.

The above material was extracted twice with 300mL boiling Ethanol and the combined extracts filtered while warm and concentrated at boiling to approximately 250mL. On cooling stocky strongly-yellow crystals were deposited; these were washed twice with 30mL Ethanol and air dried, yield: 15.1g (fw 251.4, 0.060 mole), mp 71^0C -72^0C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80mL and allowing to cool; this after washing and drying weighed 10.4g (0.033 mole), for a combined yield of 25.5 grams, 61%.

4-Methoxy-phenylacetic Acid

22g 4-Methoxy phenylacetothiomorpholide (0.087 mole) and 200 mL Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed on the rotovap and the mixture diluted with water to about 200mL. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH=1 with concentrated Hydrochloric acid, saturated with Sodium Chloride and, extracted four times with 100mL of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 200mL of 90% Ethanol to yield clear colorless crystals, which were washed twice with 20mL of 90% Ethanol, and vacuum dried, yield: 6.7g (fw 150.2, 0.044 mole), 51%, mp 65^0C - 66^0C. (These crystals were judged adequate for the study and a second crop was not collected.)

3-Fluoro-phenylacetonitrile

25g 3-Fluorobenzyl bromide (fw 189.02, 0.132 mole), 17.2g Potassium Cyanide (fw 65.12, 0.053 mole), 150mL Ethanol and 30mL Water were added to a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was

heated in an oil bath at 110^0C -120^0C and stirred at reflux 18 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on a rotary evaporator, and the mixture was acidified cautiously with 1:1 Hydrochloric Acid. The oily product was extracted three times with 100mL of Dichloromethane; the extracts were dried with Magnesium Sulfate, filtered, and evaporated to dryness on the rotary evaporator to yield brownish oil. This crude product was carried forward to hydrolysis without purification.

3-Fluoro-phenylacetic Acid

The above crude 3-Fluorophenylacetonitrile was treated with 80mL of 20% Sulfuric Acid in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated in an oil bath at 150^0C -160^0C, and stirred at reflux for 18 hours, then allowed to cool. The mixture was diluted to approximately 300mL with water, saturated with Sodium Chloride, then extracted three times with 100mL of Dichloromethane. The combined extracts were dried over Magnesium Sulfate, filtered, and evaporated to dryness on the rotary evaporator. The resulting thick oil was dissolved in 300mL of Pentane, and concentrated to 150mL at boiling. The solution was stoppered, and allowed to cool slowly in an insulated container overnight. The resulting crystals were washed twice with 10mL of Pentane, and vacuum dried, yield: 6.8g (fw 154.14, 0.044 mole), 33%, mp 42^0C-44^0C (A second crop of crystals was not obtained despite concentrating the solution further. (Attempts to recrystallize the product from Petroleum Ether were unsuccessful.)

4-Fluoro-phenylacetothiomorpholide

25g 4-Fluoro-acetophenone (fw 138.14, 0.181 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) was placed in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and was poured into 300mL of 2N Hydrochloric acid. 200mL Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce mostly a brownish crystalline mass.

The above material was extracted twice with 300mL of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250mL. On cooling stocky lemon-yellow crystals were deposited; these were washed twice with 30mL of Ethanol, and air dried, yield: 16.0g (fw 239.32, 0.060 mole), mp 40-41C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80mL, and allowed to cool; this after washing and drying weighed 8.3g (0.033 mole), for a combined yield of 25.5 grams (101mole) 56%.

4-Fluoro-phenylacetic Acid

25g 4-Fluoro phenylacetothiomorpholide (0.104 mole) and 200 mL Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was diluted with water to about 200mL. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride, and extracted four times with 100mL of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 150mL of Petroleum Ether to yield clear colorless crystals, which were washed twice with 15mL of Petroleum Ether, and vacuum dried, yield: 7.0g (fw 154.14, 0.045 mole), 51%, mp 82^0C -83^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

3-Chlorophenylacetothiomorpholide

25g 3-Chloroacetophenone (fw 154.59, 0.162 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) was placed in a 250mL round bottom flask fitted with a

magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and poured into 300mL of 2N Hydrochloric acid. 200mL of Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce mostly a brownish crystalline mass.

The above material was extracted twice with 300mL of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250mL. On cooling, stocky yellow crystals were deposited; these were washed twice with 30mL of Ethanol, and air dried, yield: 13.2g (fw 255.77, 0.052 mole), mp 54^0C -55^0C. A second crop of crystals was obtained by concentrating the combined mother liquor and washings at boiling to about 80mL, and allowed to cool; this after washing and drying weighed 12.8g (0.050 mole), for a combined yield of 26.0 grams (0.101mole) 62%.

3-Chlorophenylacetic Acid

25g 3-Chlorophenylacetothiomorpholide (0.104 mole) and 200 mL Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred

at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was diluted with water to about 200mL. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH =1 with concentrated Hydrochloric acid, saturated with Sodium Chloride, and extracted four times with 100mL of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 250mL of Petroleum Ether to yield clear colorless crystals, which were washed twice with 20mL of Petroleum Ether, and vacuum dried, yield: 9.2g (fw 170.59, 0.054 mole), 52%, mp 78.5^0C -79^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

4-Chlorophenylacetothiomorpholide

25g 4-Chloroacetophenone (fw 154.59, 0.162 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) was placed in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and poured into 300mL of 2N Hydrochloric acid. 200mL of Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered and evaporated to dryness on the rotary evaporator to produce a brownish mostly crystalline mass.

The above material was extracted twice with 300mL of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250mL. On cooling thick yellowish-orange crystals were deposited; these were washed twice with 30ml of Ethanol, and air-dried, yield: 15.7g (fw 255.77, 0.061 mole), mp 68^0C -69^0C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80mL, and allowed to cool; this after washing and drying weighed 11.1g (0.043 mole), for a combined yield of 26.8 grams (0.105mole) 64%.

4-Chlorophenylacetic Acid

25g 4-Chlorophenylacetothiomorpholide (0.104 mole) and 200mL of Sodium Hydroxide in Ethanol were placed in a 500 mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on a rotary evaporator, and the mixture was diluted with water to about 200mL. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride, and extracted four times with 100mL of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 250mL of Petroleum Ether to yield clear colorless crystals, which were washed twice

with 20mL of Petroleum Ether and vacuum dried, yield: 10.6g (fw 170.59, 0.054 mole), 62%, mp 104^0C -105^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

3-Bromophenylacetothiomorpholide

25g 3-Bromoacetophenone (fw 199.04, 0.162 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) was placed in a 250mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and was poured into 300mL of 2N Hydrochloric acid. 200mL Dichloromethane were added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100mL of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce a brownish mostly crystalline mass.

The above material was extracted twice with 300mL of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250mL. On cooling thick yellowish-orange crystals were deposited; these were washed twice with 30ml of Ethanol and air-dried, yield: 14.5g (fw 300.22, 0.048 mole), mp 80^0C -81^0C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80mL, and allowed to cool; this after

washing and drying weighed 12.9g (0.043 mole), for a combined yield of 27.4 grams (0.091mole) 56%.

3-Bromophenylacetic Acid

25g 3-Bromophenylacetothiomorpholide (0.083 mole) and 200 ml Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C-140^0C, and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was diluted with water to about 200ml. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride, and extracted four times with 100ml of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 250ml of Petroleum Ether to yield clear colorless crystals, which were washed twice with 20ml of Petroleum Ether, and then vacuum dried, yield: 11.9g (fw 215.04, 0.055 mole), 66%, mp, 101^0C-102^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

4-Bromophenylacetothiomorpholide

25g 4-Bromoacetophenone (fw 199.04, 0.162 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) were placed in a 250ml round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and was poured into 300mL of 2N Hydrochloric acid. 200ml of Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100ml of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce a brownish mostly crystalline mass.

The above material was extracted twice with 300ml of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250ml. On cooling stocky orange crystals were deposited; these were washed twice with 30ml of Ethanol, and air dried, yield: 19.3g (fw 300.22, 0.064 mole), mp 116^0C -117^0C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80ml, and allowed to cool; this after washing and drying weighed 5.9g (0.020 mole), for a combined yield of 25.2 grams (0.084mole), 56%.

4-Bromophenylacetic Acid

25g 4-Bromophenylacetothiomorpholide (0.083 mole) and 200 ml Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was diluted with water to about 200ml. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride, and was extracted four times with 100ml of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 250ml of Petroleum Ether to yield clear colorless crystals, which were washed twice with 20ml of Petroleum Ether, and vacuum dried, yield: 8.6g (fw 215.04, 0.040 mole), 66%, mp, 116^0C -117^0C. (These crystals were judged adequate for the study, and a second crop was not collected.)

3-Iodophenylacetonitrile

10g 3-Iodobenzyl bromide (fw 296.93, 0.033 mole), 4.3g Potassium Cyanide (fw 65.12, 0.066 mole), 50ml Ethanol and 10ml Water were added to a 250ml round bottom flask

fitted with a magnetic stir bar and a reflux condenser. The mixture was heated in an oil bath at 110^0C-120^0C, and stirred at reflux 18 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was acidified cautiously with 1:1 Hydrochloric Acid. The oily product was extracted three times with 50ml of Dichloromethane; the extracts were dried with Magnesium Sulfate, filtered, and evaporated to dryness on the rotary evaporator to yield brownish oil. This crude product was carried forward to hydrolysis without purification.

3-Iodophenylacetic Acid

The above crude 3-Fluorophenylacetonitrile was treated with 80ml of 20% Sulfuric Acid in a 250ml round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated in an oil bath at 150^0C-$160^{\,0}$C, and stirred at reflux for 18 hours, then allowed to cool. The mixture was diluted to 100ml with water, saturated with Sodium Chloride, then extracted three times with 50ml of Dichloromethane. The combined extracts were dried over Magnesium Sulfate, filtered, and evaporated on a rotary evaporator. The resulting thick oil was dissolved in 150ml of Petroleum Ether, and concentrated to 70ml at boiling, then allowed to cool. The resulting crystals were washed twice with 6ml of Petroleum Ether, and vacuum dried, yield: 3.4g (fw 262.04, 0.013 mole), 39%. A second crop of crystals was obtained by concentrating the solution at boiling to approximately 20ml, but the product was tinged brown and not fully

crystalline. The melting point of the first crop was 125^0C-130^0C; recrystallization from 95% Ethanol raised this to 129^0C -131^0C.

4-Iodophenylacetothiomorpholide

25g 4-Iodoacetophenone (fw 199.04, 0.101 mole), 9.3g Sulfur powder (0.3 mole) and 23g Morpholine (0.26 mole) were placed in a 250ml round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 180^0C -190^0C, and stirred at reflux for six hours. The thick mixture was cooled to about 60^0C, and was poured into 300mL of 2N Hydrochloric acid. 200ml of Dichloromethane was added; the mixture was shaken to equilibrate the phases, and then transferred to a separatory funnel. The Dichloromethane layer was collected, and the aqueous phase was extracted for a second time with 100ml of Dichloromethane. The organic phases were combined, dried, filtered, and evaporated to dryness on the rotary evaporator to produce a brownish mostly crystalline mass.

The above material was extracted twice with 300ml of boiling Ethanol, and the combined extracts were filtered while warm, and concentrated at boiling to approximately 250ml. On cooling stocky yellow crystals were deposited; these were washed twice with 30ml of Ethanol, and air dried, yield: 12.3g (fw 347.23, 0.035 mole), mp 123^0C -125^0C. A second crop of crystals was obtained by concentrating the mother liquor and washings at boiling to about 80ml, and allowed to cool; this after washing and drying weighed 3.5g (0.010 mole), for a combined yield of 15.8 grams (0.0.45mole) 56%.

4-Iodophenylacetic Acid

15g Iodophenylacetothiomorpholide (0.043 mole) and 200 ml of Sodium Hydroxide in Ethanol were placed in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated with an oil bath at 130^0C -140^0C, and stirred at reflux for 10 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was diluted with water to about 200ml. The resulting solution was filtered to remove a small amount of tarry material, acidified to pH1 with concentrated Hydrochloric acid, saturated with Sodium Chloride, and extracted four times with 100ml of Dichloromethane. The extracts were combined, dried with Magnesium sulfate, filtered, evaporated to dryness on the rotary evaporator, and vacuum dried to yield masses of near-white crystals. These were recrystallized from 300ml of Petroleum Ether to yield small almost-colorless crystals, which were washed twice with 20ml of Petroleum Ether, and vacuum dried, yield: 5.7g (fw 262.04, 0.022 mole), 51%, mp 133^0C-138^0C. Recrystallization from 95% of Ethanol raised the melting point to 138^0C-140^0C.

3-Nitrophenylacetonitrile

10g 3-Nitrobenzyl bromide (fw 216.03, 0.046 mole), 6.03g Potassium Cyanide (fw 65.12, 0.092 mole), 80ml Ethanol and 14ml Water were added to a 250ml round bottom flask

fitted with a magnetic stir bar and a reflux condenser. The mixture was heated in an oil bath at 110^0C-120^0C, and stirred at reflux 18 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was acidified cautiously with 1:1 Hydrochloric Acid. The oily product was extracted three times with 50ml of Dichloromethane; the extracts were dried with Magnesium Sulfate, filtered, and evaporated to dryness on the rotary evaporator to yield a brownish semisolid mass. This crude product was carried forward to hydrolysis without purification.

3-Nitrophenylacetic Acid

The above crude 3-Nitrophenylacetonitrile was treated with 100ml of 20% Sulfuric Acid in a 250ml round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated in an oil bath at 150^0C -160^0C, and stirred at reflux for 18 hours, then allowed to cool. The mixture was diluted to 100ml with water, saturated with Sodium Chloride, and then extracted three times with 50ml of Dichloromethane. The combined extracts were dried over Magnesium Sulfate, filtered, and evaporated on the rotary evaporator. The resulting thick oil was dissolved in 150ml of 90% Ethanol, and concentrated to 70ml at boiling, then allowed to cool. The resulting crystals were washed twice with 8ml of 90% Ethanol, and vacuum dried, yield: 5.0g (fw 181.15, 0.027 mole), 60%, mp 113^0C-119^0C. A second recrystallization from 95% of Ethanol raised the melting point to 118^0C -120^0C.

4-Nitrophenylacetonitrile

25g 4-Nitrobenzyl bromide (fw 216.03, 0.115 mole), 15g Potassium Cyanide (fw 65.12, 0.23 mole), 125ml Ethanol and 25ml Water were added to a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated in an oil bath at 110^0C-120^0C, and stirred at reflux for18 hours, then allowed to cool. Most of the Ethanol was removed by evaporation on the rotary evaporator, and the mixture was acidified cautiously with 1:1 Hydrochloric Acid. The oily product was extracted three times with 50ml of Dichloromethane; the extracts were dried with Magnesium Sulfate, filtered, and evaporated to dryness on the rotary evaporator to yield a brownish solid. This crude product was carried forward to hydrolysis without purification.

4-Nitrophenylacetic Acid

The above crude 4-Nitrophenylacetonitrile was treated with 200ml of 20% Sulfuric Acid in a 500mL round bottom flask fitted with a magnetic stir bar and a reflux condenser. The mixture was heated in an oil bath at 150^0C -160^0C, and stirred at reflux for 18 hours, then allowed to cool. The mixture was diluted to 200ml with water, saturated with Sodium Chloride, and then extracted four times with 200ml of Dichloromethane. The combined extracts were dried over Magnesium Sulfate, filtered, and evaporated on the rotary evaporator. The resulting solid was dissolved in 450ml of 90% Ethanol, and

concentrated to 150ml at boiling, then allowed to cool. The resulting crystals were washed twice with 20ml of 90% Ethanol, and vacuum dried, yield: 14.6g (fw 181.15, 0.013 mole), 70%, mp 153^0C-155^0C. A second crop of crystals was not sought.

Part II: Preparations of Mixed Dimers

Samples were prepared in 14ml vials with screw caps containing polyethylene enclosures. Samples were approximately 3-5g in size. Melting points were checked by immersing the vial in an oil bath, and raising the temperature approximately 2^0C /min until melting was complete. Once an approximate melting point was established, the vial was allowed to cool below the point at which melting was observed and the sample was allowed to solidify. Heating was resumed at approximately 0.1^0C to 0.2^0C /min until the start of melting was observed, then raising the temperature more slowly, as needed, until melting was complete. The sample was again allowed to cool below the solidification point, and a third determination made at as slow a heating rate as possible.

Acetic Acid / Phenylacetic Acid Mixed Dimer

3.1650g Phenylacetic acid (fw 136.15, 23.25 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.396g Acetic Acid (fw 60.05, 23.25 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a range

45

of 41^0C - 43^0C. Attempted recrystallization of this material from petroleum ether (35^0C - 60^0C boiling point range) regenerated crystalline phenylacetic acid. A fresh sample of dimer was prepared, and recrystallized from Pentane (bp 35^0C-36^0C); phenylacetic acid was regenerated.

Acetic Acid / 3-Methylphenylacetic Acid Mixed Dimer

3.5372g 3-Methylphenylacetic acid (fw 150.17, 23.55 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.414g Acetic Acid (fw 60.05, 23.55 mmole) was added and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave ranges of 38^0C - 41^0C and 37^0C - 40^0C.

Acetic Acid / 4-Methylphenylacetic Acid Mixed Dimer

3.5314g 4-Methylphenylacetic acid (fw 150.17, 23.52 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.412g Acetic Acid (fw 60.05, 23.51 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a range of 55^0C -58^0C.

Acetic Acid / 3-Methoxyphenylacetic Acid Mixed Dimer

3.507g 3-Methoxyphenylacetic acid (fw 166.17, 21.1 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.269g Acetic Acid (fw 60.05, 21.1 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a range of 47^0C - 49^0C.

Acetic Acid / 4-Methoxyphenylacetic Acid Mixed Dimer

3.49127g 4-Methoxyphenylacetic acid (fw 166.17, 21.01 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.262g Acetic Acid (fw 60.05, 21.01 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a range of 54^0C -58^0C.

Acetic Acid / 3-Fluorophenylacetic Acid Mixed Dimer

3.3688g 3-Fluorophenylacetic acid (fw 154.14, 21.86 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.312g Acetic Acid (fw 60.05, 21.85

mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly; no solidification occurred. The sample was stored at 2^0C overnight without solidification. Storage overnight at -30^0C did produce a solid mass, which remained solid at 2^0C, but liquefied near room temperature.

Acetic Acid / 4-Fluorophenylacetic Acid Mixed Dimer

3.4552g 4-Fluorophenylacetic acid (fw 154.14, 22.42 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.346g Acetic Acid (fw 60.05, 22.41 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid.

Acetic Acid / 3-Chlorophenylacetic Acid Mixed Dimer

3.9155g 3-Chlorophenylacetic acid (fw 170.59, 22.95 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.378g Acetic Acid (fw 60.05, 22.95 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a range of 46^0C - 49^0C.

Acetic Acid / 4-Chlorophenylacetic Acid Mixed Dimer

3.9332g 4-Chlorophenylacetic acid (fw 170.59, 23.06 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.385g Acetic Acid (fw 60.05, 23.06 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a range of 46^0C - 49^0C

Acetic Acid / 3-Bromophenylacetic Acid Mixed Dimer

3.3863g 3-Bromophenylacetic acid (fw 215.04, 15.75 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 0.946g Acetic Acid (fw 60.05, 15.76 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a range of 70^0C -74^0C. Attempted recrystallization of this material from Petroleum Ether (35^0C - 60^0C boiling point range) regenerated crystalline 3-Bromophenylacetic acid. A fresh sample of dimer was prepared, and recrstyallized from Pentane (bp, 35^0C-36^0C); again, 3-Bromophenylacetic acid was regenerated.

Acetic Acid /4-Bromophenylacetic Acid Mixed Dimer

3.1410g 4-Bromophenylacetic acid (fw 215.04, 14.61 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 0.877g Acetic Acid (fw 60.05, 14.60 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. Two slow melting point determinations gave a broad range of 56^0C - 80^0C.

Acetic Acid / 3-Iodophenylacetic Acid Mixed Dimer

2.4655g 3-Iodophenylacetic acid (fw 262.04, 9.41 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 0.565g Acetic Acid (fw 60.05, 9.41 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. It was not possible to determine a melting point range for this compound; liquification began almost immediately upon heating, and was not complete before acetic acid began boiling from the mixture (Acetic Acid, bp, 117^0C-118^0C).

Acetic Acid / 4-Iodophenylacetic Acid Mixed Dimer

1.0113g 4-Iodophenylacetic acid (fw 262.04, 3.86 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 0.232g Acetic Acid (fw 60.05, 3.86 mmole) was added, and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. The resulting solid appeared crystalline and homogeneous, with no sign of liquid acetic acid. It was not possible to determine a melting point range for this compound; liquification began almost immediately upon heating, and was not complete before acetic acid began boiling from the mix (Acetic Acid, bp, 117^0C -118^0C).

Acetic Acid / 3-Nitrophenylacetic Acid Mixed Dimer

0.9661g 3-Nitrophenylacetic acid (fw 181.15, 5.33 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 0.312g Acetic Acid (fw 60.05, 5.33 mmole) was added and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. A homogenous solid did not result; solid (presumably 3-Nitrophenylacetic acid) and liquid (presumably Acetic Acid containing some 3-Nitrophenylacetic Acid) phases were present.

Acetic Acid / 4-Nitrophenylacetic Acid Mixed Dimer

4.0108g 4-Nitrophenylacetic acid (fw 181.15, 22.14 mmole) was placed in a 14ml screw cap vial with polyethylene closure insert. 1.329g Acetic Acid (fw 60.05, 22.13 mmole) was added and the cap sealed. The mixture was warmed until the contents were melted, and then allowed to cool slowly. A homogenous solid did not result; solid (presumably 4-Nitrophenylacetic acid) and liquid (presumably Acetic Acid containing some 4-Nitrophenylacetic Acid) phases were present.

CONCLUSION

A series of phenylacetic acids was treated with equimolar quantities of acetic acid, and the mixtures equilibrated by melting. All members of the series showed a shifting of the acetic acid carbonyl infrared absorption to lower energy, interpreted as hydrogen bonding between the acetic acid carbonyl and phenylacetic acid carboxyl proton. This hydrogen bonding appears energetically favored over hydrogen bonding between like molecules of the parent acids. No shifts of infrared absorptions of the phenylacetic acids upon mixed dimer formation, suitable for construction of a Hammett plot, were found. Many members of the series, specifically the less polar or polarizable members, appear to have crystallized in the pure state. These pure crystalline materials are true molecular compounds based upon their relatively sharp melting point ranges and the smoothness of their carbonyl infrared absorptions relative their to parent acids. It is believed that the mixed dimers, being energetically favored, dominate in the liquid phase, and crystallize

from that phase pure. Absolute proof of these compounds being mixed dimers awaits development of methods to prepare them as pure single crystals for X-ray diffraction analysis.

BIBLIOGRAPHY

1. Silverstein, R. M.; Bassler, G. C. *Spectrometric Identification of Organic Compounds, 2nd ed.*; John Wiley & Sons: California, **1967**; p 122-123

2. Flakus, H. T.; Chelmecki, M. *Spectrochimica Acta, Part A*. **2002**, 58, 1867-1880

3. Anilkumar, H.G.; Yathirajan, H. S.; Narasimhamurthy, T.; Vijay, T.; Rathore, R. S. *Acta Crystallographica,* **2005**, E61, σ2704-σ2705

4. Cox, P. J.; Hickey, G. *Acta Crystallographica,* **2004**, E60, σ771-σ773

5. Shipman, S. T.; Douglass, P. C.; Yoo, H. S.; Hinkle, C. E.; Mierzejewski, E. L.; Pate, B. H. *Physical Chemistry Chemical Physics*, **2007**, 9, 4572-4586

6. Nandi, C. K.; Samanta, A. K.; Chakraborty, T. *Chemical Physics Letters*, **2005**, 416, 261-267

7. Faubel, M.; Kisters, T. *Nature*, **1989**, 339, 527-529

8. Nandi, C. K.; Chakraborty, T. *Journal of Chemical Physics,* **2005**, 123, 124310-124317

9. Bures, M.; Bezus, *Collection of Czechoslovak Chemical Communications,* **1994**, 59, 1251-1260

10. Keller, J. W. *Journal of Physical Chemistry A*, **2004**, 108, 4610-4618

11. Vogel, A. I. *Textbook of Practical Organic Chemistry, 3rd edition*, Longman Group Limited, London, **1956**, p 925

12. Dannenberg, J.J. *Chem. Mater,* **1990**, 2, 635-636

13. Pedireddi, V. R.; PrakashaReddy, J. *Tetrahedron Letters*, **2002**, 43, 4927-4930

14. Vishweshwar, P.; Beauchamp, D. A.; Zaworotko, M. J. *Crystal Growth & Design,* **2006**, 6, 2429-2431

15. Schilling, M.; Bartmann, K.; Mootz, D. J. *Journal of Fluorine Chemistry,* **1995**, 73, 225-228

16. Gronowitz, S.; Larsson, S. *Arkiv For Kemi*, **1955**, 8, 567-577

17. Fredga, A. *Tetrahedron*, **1960**, 8, 126-144

18. Karle, I.L.; Karle, J. *Journal of the American Chemical Society*, **1966**, 88, 24-27

19. Rosenberg, A.; Schotte, L.; *Arkiv For Kemi*, **1955**, 8, 143-151

20. Murray, A.; Williams, D. L. *Orrganic Syntheses With Isotopes*, Interscience Publishers, Inc., New York, **1958**, p 72

21. Vogel, A. I. *Textbook of Practical Organic Chemistry, 3rd edition*, Longman Group Limited, London, **1956**, p 751

22. Anciaux, A. J.; Domonceau, A.; Noels, A. F.; Hubert, A. J.; Warin, R.; Teyssie, P. *Journal of Organic Chemistry*, **1980**, 46, 873-876

23. Spielman, M. A.; Carmack, M. *Organic Reactions, Volume 3*, Edited by Roger Adams, John Wiley & Sons, New York, **1946**, p 83

24. Schwenk, E.; Bloch, E. *Journal of the American Chemical Society*, **1942**, 64, 3051-3052

25. Pettersson, K.; *Arkiv For Kemi*, **1954**, 7, 347-353

26. Gronowitz, S. *Arkiv For Kemi*, **1957**, 11, 361-371

27. Vogel, A. I. *Textbook of Practical Organic Chemistry, 3rd edition*, Longman Group Limited, London, **1956**, p 29

28. Vogel, A. I. *Textbook of Practical Organic Chemistry, 3rd edition*, Longman Group Limited, London, **1956**, p 25

29. Vogel, A. I. *Textbook of Practical Organic Chemistry, 4th edition*, Longman Group Limited, London, **1978**, p 223

30. Chen, J.; Brooks, C. L., III; Scheraga, H. A. *Journal of Physical Chemistry B*, **2008**, 112, 242-249

APPENDIX

APPENDIX: A
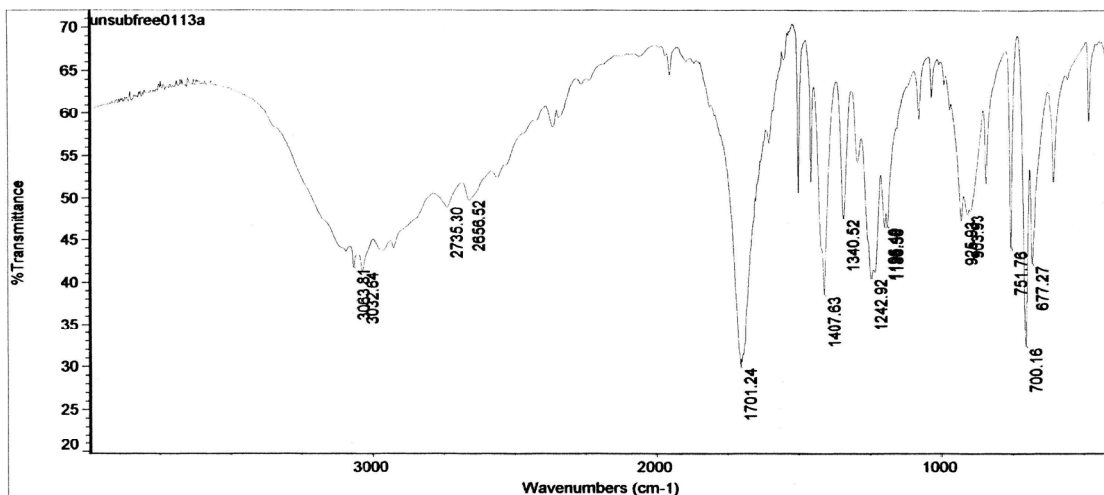
IR Spectrum of Acetic Acid
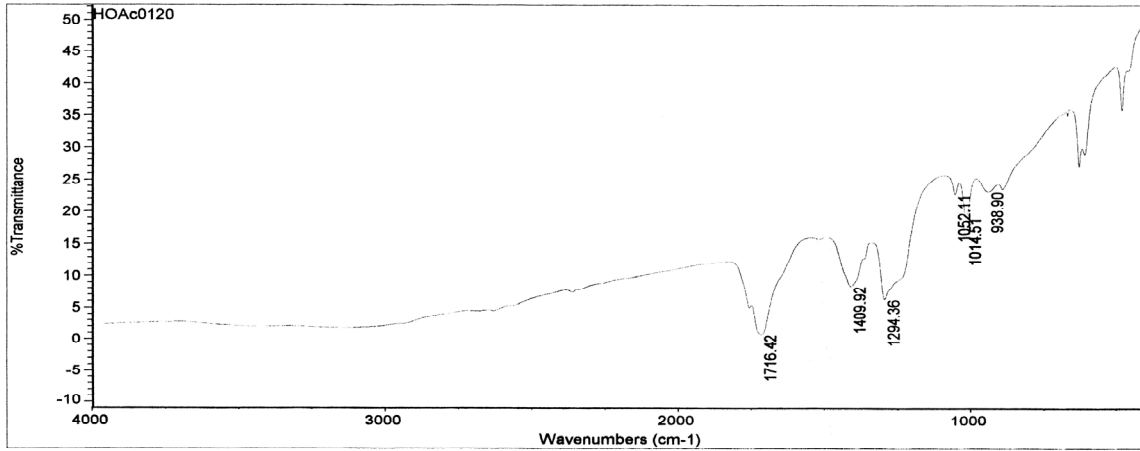
Tue Jan 20 14:20:29 2009
FIND PEAKS:
    Spectrum: HOAc0120
    Region: 4000.00   400.00
    Absolute threshold: 25.503
    Sensitivity: 50

Peak List:

POSITION	INTENSITY
1716.42	0.658
1294.36	6.253
1409.92	8.317
1014.51	19.092
1052.11	22.723
938.90	23.118

IR Spectrum of Phenylacetic Acid

Tue Jan 13 15:29:46 2009
FIND PEAKS:
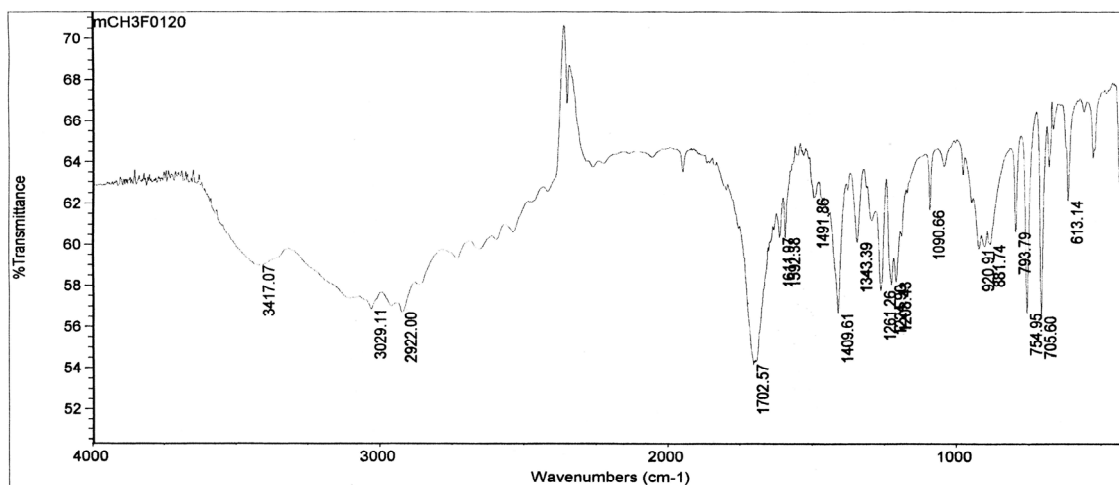Spectrum: unsubfree0113a
Region: 3999.84   399.21
Absolute threshold: 50.121
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1701.24	29.812
700.16	32.167
1407.63	38.355
1242.92	40.467
3032.64	41.193
3063.81	41.659
677.27	41.965
751.76	43.674
1186.36	46.334
1196.49	46.366
925.93	47.188
1340.52	47.387
903.93	48.041
2735.3	48.922
2656.52	49.751

APPENDIX: B

IR Spectrum of 3-CH$_3$-Phenylacetic Acid

Tue Jan 20 14:54:05 2009
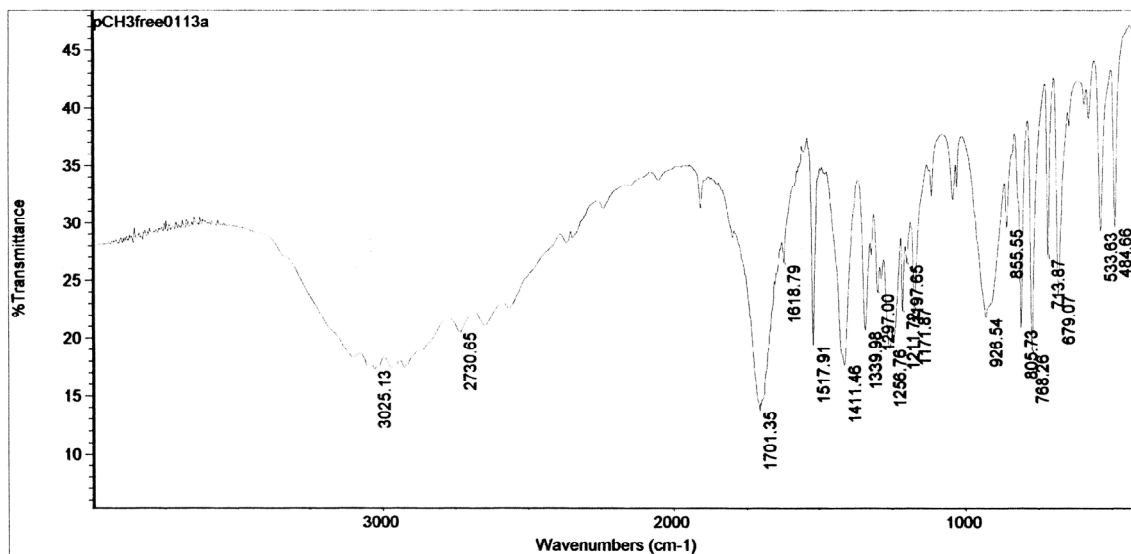FIND PEAKS:
Spectrum: mCH3F0120
Region: 4000.00   400.00
Absolute threshold: 62.401
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1702.57	54.171
705.60	56.521
1409.61	56.704
2922.00	56.721
754.95	56.685
3029.11	56.878
1261.26	57.778
1224.90	58.067
1208.43	58.206
3417.07	58.959
920.91	59.816
881.74	60.024
1343.39	60.1236
1611.97	60.367
1592.38	60.369
793.79	60.646
1090.66	61.690
613.14	62.150
1491.86	62.280

IR Spectrum of 4-CH₃-Phenylacetic Acid

Tue Jan 13 15:49:22 2009
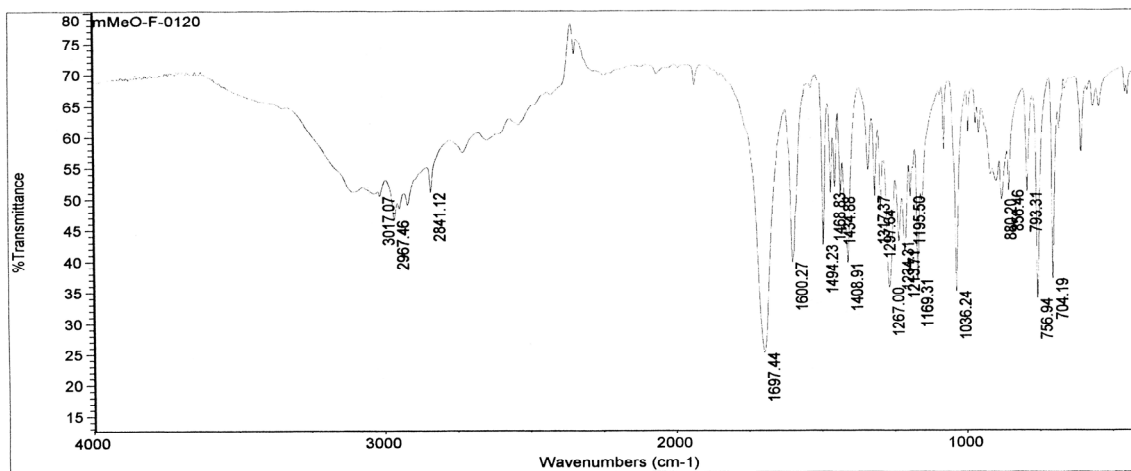FIND PEAKS:
Spectrum: pCH3free0113a
Region: 3999.84   399.21
Absolute threshold: 30.386
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1701.35	13.621
3025.13	17.212
1411.46	17.664
768.26	18.568
1256.76	19.015
1517.91	19.368
2730.65	20.496
1339.98	20.601
805.73	20.714
926.54	21.770
1211.72	22.278
1171.87	22.627
679.07	23.730
1297.00	23.867
1197.65	26.329
1618.79	26.341
713.87	26.816
533.63	29.168
855.55	29.434
484.66	29.558

IR Spectrum of 3-MeO -Phenylacetic Acid
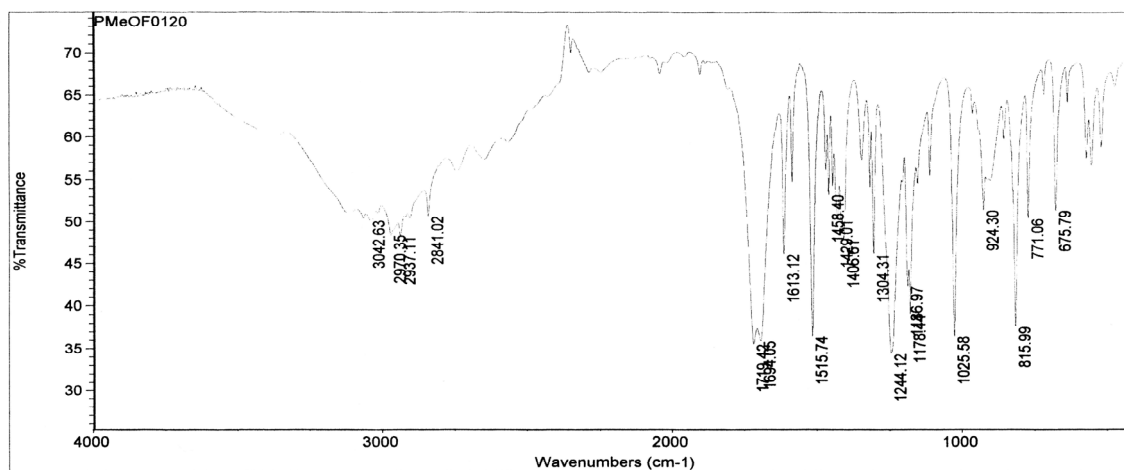

Tue Jan 20 16:03:52 2009
FIND PEAKS:
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    Region: 4000.00   400.00
    Absolute threshold: 51.647
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1697.44	25.077
756.94	33.858
1036.24	35.038
1267.00	35.647
704.19	37.081
1169.31	37.052
1600.27	39.789
1408.91	39.683
1213.71	41.713
1494.23	42.545
1234.31	43.102
2967.46	46.541
1297.64	48.237
880.20	49.902
1195.50	50.339
1434.88	50.358
1317.37	50.441
3017.07	50.482
2841.12	51.108
1468.83	50.977
856.46	51.315
793.31	51.084

IR Spectrum of 4-MeO -Phenylacetic Acid

Tue Jan 20 15:17:20 2009
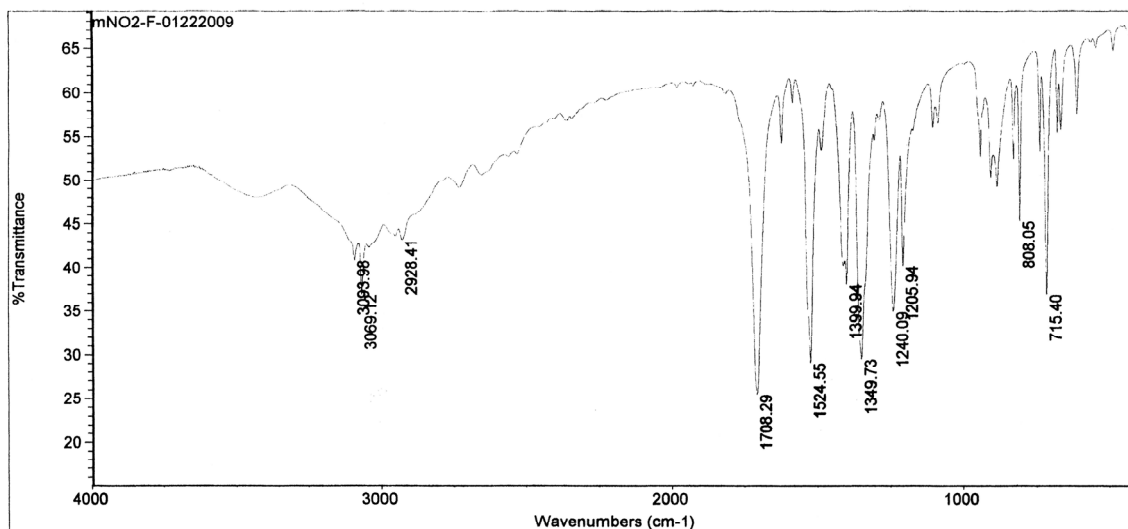FIND PEAKS:
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    Spectrum:          PMeOF0120
    Region:            4000.00        400.00
    Absolute threshold: 53.808
    Sensitivity:        50
```

PEAK LIST:

POSITION	INTENSITY
1244.12	34.407
1719.42	35.522
1694.05	35.899
1515.74	36.449
1025.58	36.472
815.99	37.630
1178.44	39.017
1186.97	42.277
1304.31	46.161
1613.12	46.111
1406.61	47.852
2937.11	48.223
2970.35	48.403
3042.63	50.172
1429.01	50.251
771.06	50.402
2841.02	50.666
924.30	51.418
675.79	51.321
1458.40	53.263

IR Spectrum of 3-NO$_2$-Phenylacetic Acid

mNO2-F-01222009

Thu Jan 22 14:36:03 2009
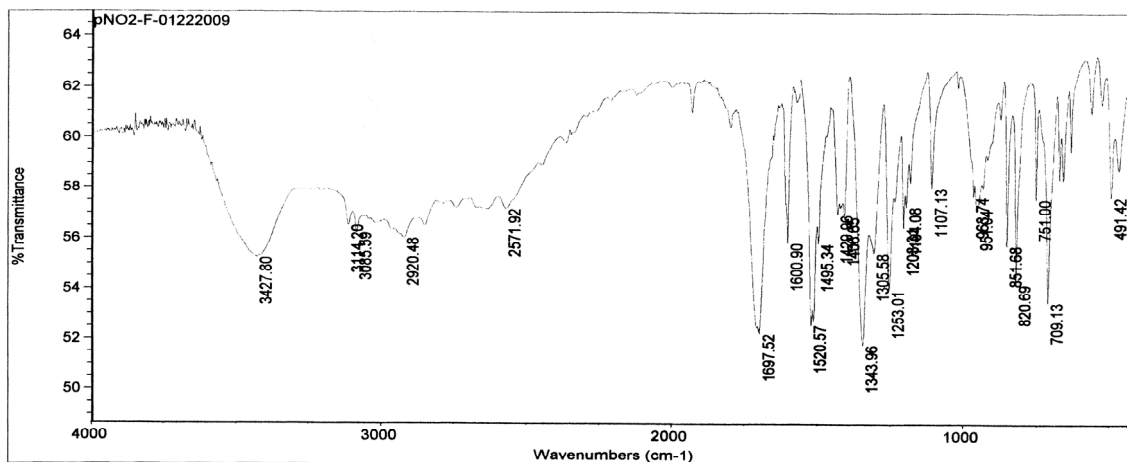FIND PEAKS:
    Spectrum: mNO2-F-01222009
    Region: 4000.00   400.00
    Absolute threshold: 46.493
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1708.29	25.449
1524.55	29.049
1349.73	29.506
1204.09	34.931
715.40	36.942
3069.12	36.896
1399.94	38.086
1205.94	40.201
3093.98	40.816
2928.41	43.177
808.05	45.300

IR Spectrum of 4-NO$_2$-Phenylacetic Acid

Thu Jan 22 15:01:31 2009
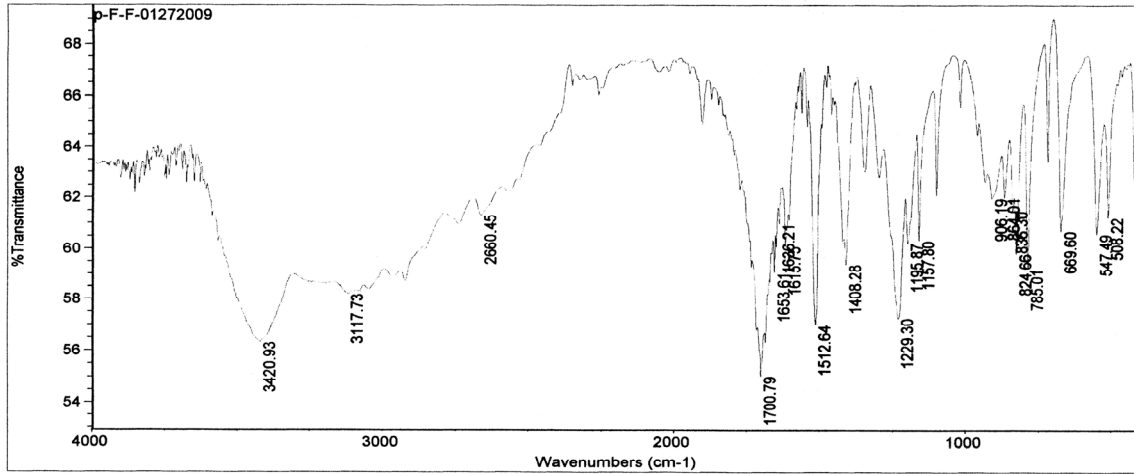FIND PEAKS:
    Spectrum: pNO2-F-01222009
    Region: 4000.00   400.00
    Absolute threshold: 58.129
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1343.96	51.799
1697.52	52.230
1520.57	52.572
709.13	53.493
1253.01	53.980
820.69	54.211
3427.80	55.241
1305.58	55.458
1600.90	55.860
1495.34	55.837
851.68	55.754
2920.48	56.011
3085.59	56.234
1203.31	56.486
3114.20	56.530
1406.65	56.883
1429.96	56.989
2571.92	57.186
951.04	57.214
1194.08	57.292
491.42	57.682
963.74	57.696
751.00	57.616
1107.13	58.027

IR Spectrum of 4-F -Phenylacetic Acid

Tue Jan 27 17:02:04 2009
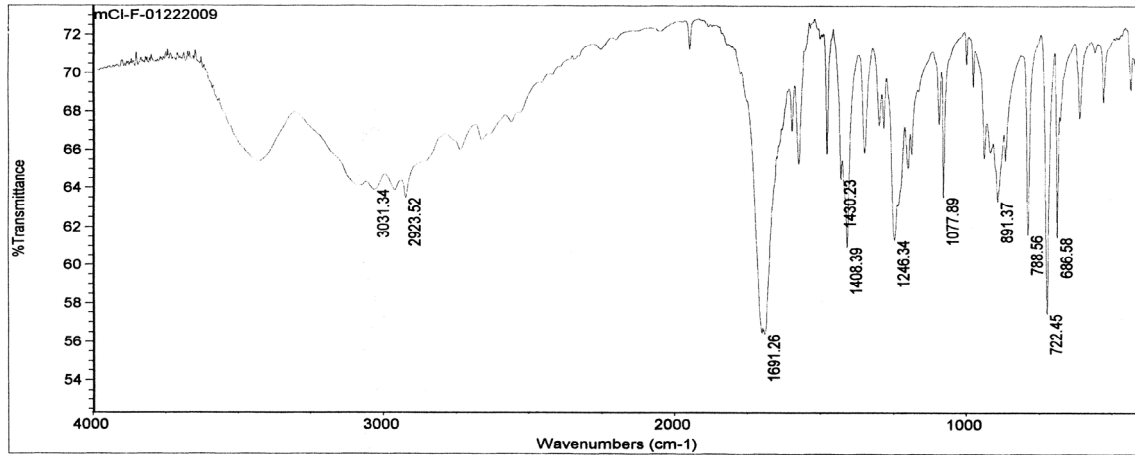FIND PEAKS:
Spectrum: p-F-F-01272009
Region: 4000.00   400.00
Absolute threshold: 62.019
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
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3420.93	56.324
1512.64	56.987
1229.30	57.261
3117.73	56.196
1653.61	59.070
786.01	59.226
1408.28	59.390
824.66	59.810
1615.75	60.108
1195.87	60.238
1157.80	60.339
547.49	60.594
669.60	60.717
1636.21	60.989
508.22	61.237
2660.45	61.322
836.30	61.487
906.19	61.979
864.01	62.011

IR Spectrum of 3-Cl-Phenylacetic Acid

Thu Jan 22 15:27:26 2009
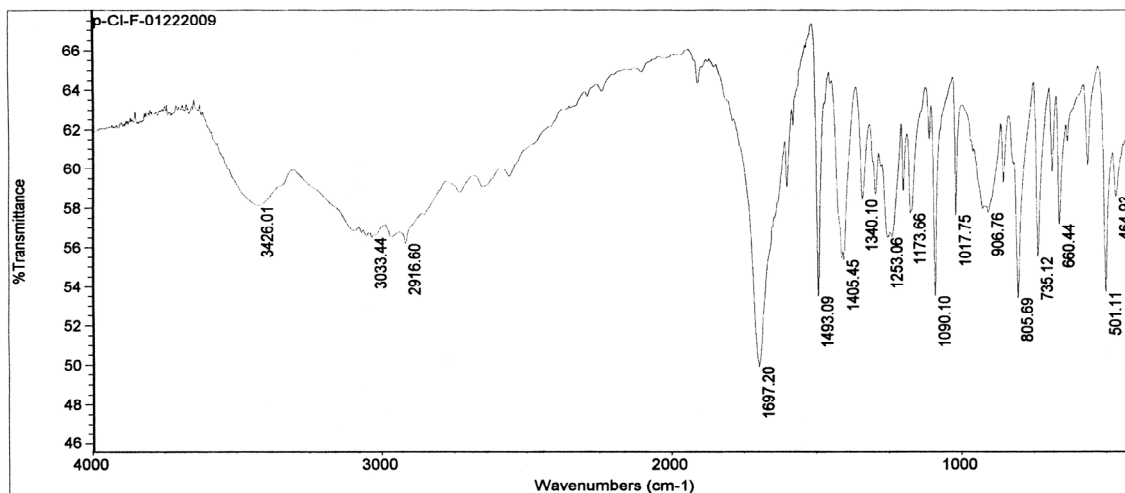FIND PEAKS:
    Spectrum: mCl-F-01222009
    Region: 4000.00   400.00
    Absolute threshold: 64.631
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1691.26	56.398
722.45	57.449
1408.39	60.952
1246.34	61.335
686.58	61.484
788.56	61.607
891.37	63.320
2923.52	63.474
1077.89	63.542
3031.34	63.905
1430.23	64.454

IR Spectrum of 4-Cl-Phenylacetic Acid

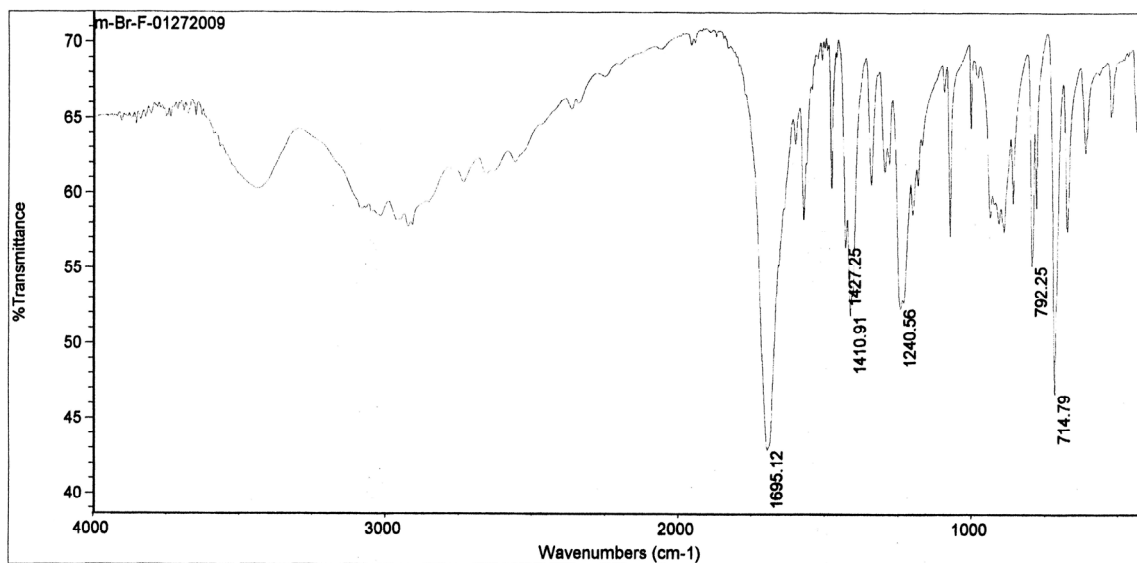p-Cl-F-01222009

Thu Jan 22 15:55:47 2009
FIND PEAKS:
Spectrum: p-Cl-F-01222009
Region: 4000.00   400.00
Absolute threshold: 58.630
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1697.20	49.910
805.69	53.413
1493.09	53.496
1090.10	53.523
501.11	53.722
1405.45	55.362
735.12	55.513
2916.60	56.201
3033.44	56.508
1253.06	56.516
660.44	57.198
1017.75	57.641
906.76	57.790
1173.66	57.738
3426.01	58.115
1340.10	58.433
464.93	58.614

IR Spectrum of 3-Br -Phenylacetic Acid

m-Br-F-01272009

Tue Jan 27 15:15:16 2009
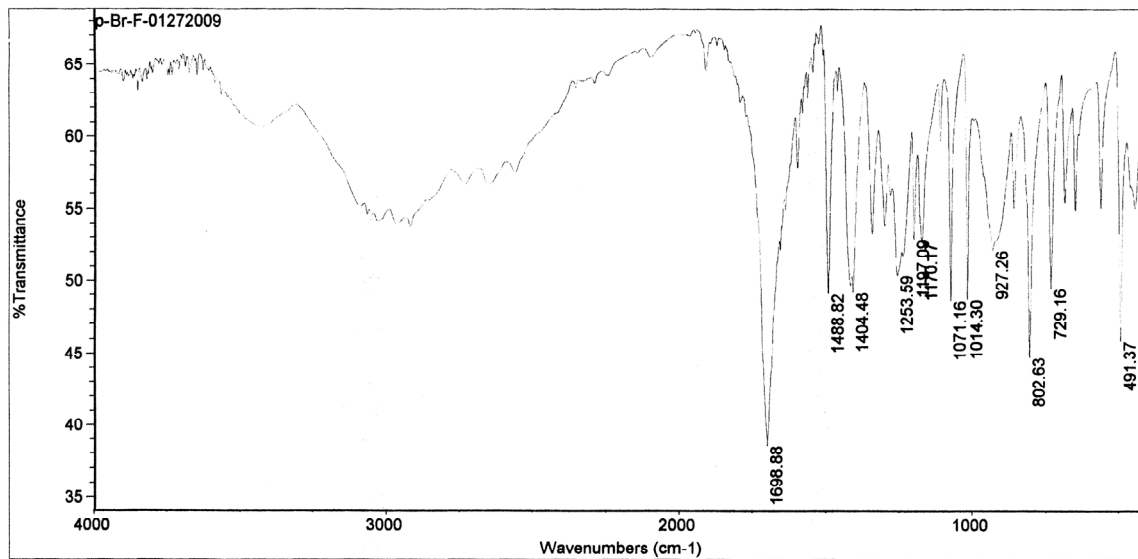FIND PEAKS:
      Spectrum: m-Br-F-01272009
      Region: 4000.00   400.00
      Absolute threshold: 56.916
      Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1695.12	42.879
714.79	46.659
1410.91	51.885
1240.56	52.331
792.25	55.146
1427.25	56.411

IR Spectrum of 4-Br -Phenylacetic Acid

Tue Jan 27 15:40:21 2009
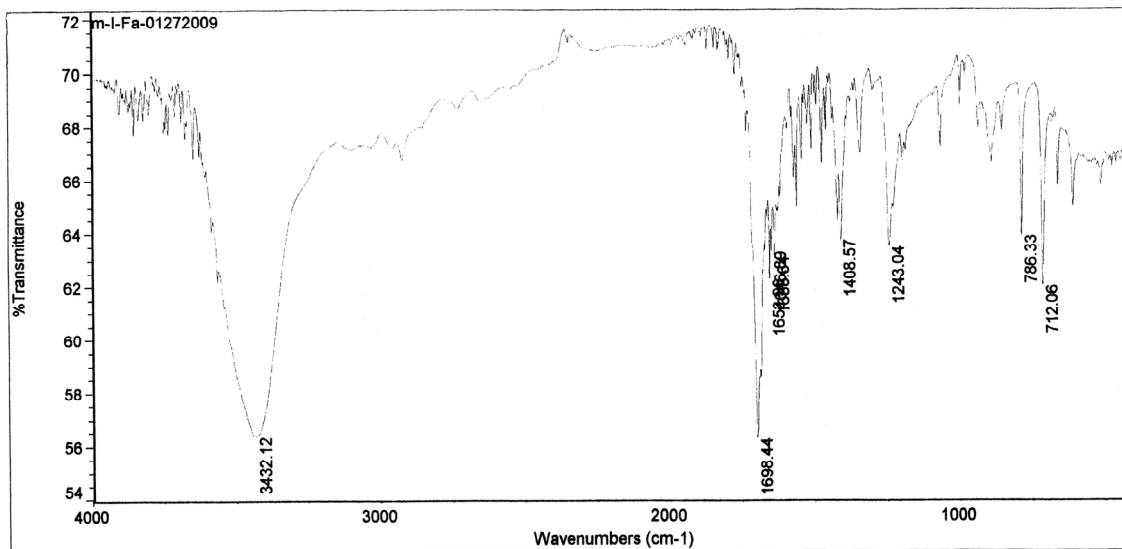FIND PEAKS:
Spectrum: p-Br-F-01272009
Region: 4000.00   400.00
Absolute threshold: 53.136
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1698.88	38.531
802.63	44.735
491.37	45.858
1014.30	48.679
1071.16	48.641
1488.82	49.104
1404.48	49.183
729.16	49.473
1253.59	50.402
927.26	52.165
1170.17	52.694
1197.09	52.887

IR Spectrum of 3-I -Phenylacetic Acid

Tue Jan 27 16:15:05 2009
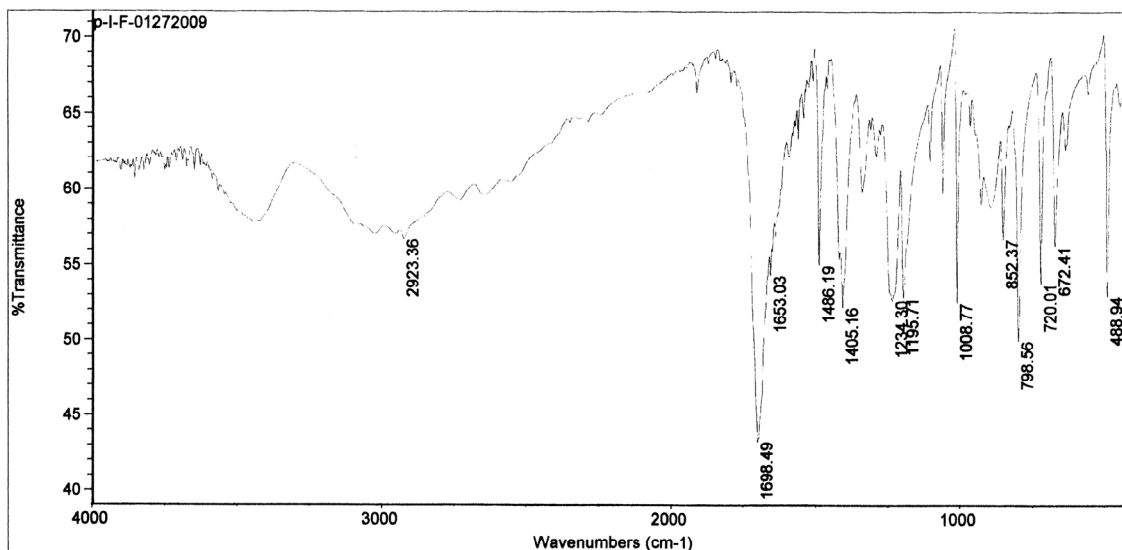FIND PEAKS:
    Spectrum: m-l-Fa-01272009
    Region: 4000.00   400.00
    Absolute threshold: 64.044
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1698.44	56.268
3432.12	56.366
712.06	62.030
1652.96	62.270
1635.64	63.133
1646.89	63.306
1243.04	63.499

IR Spectrum of 4-I -Phenylacetic Acid

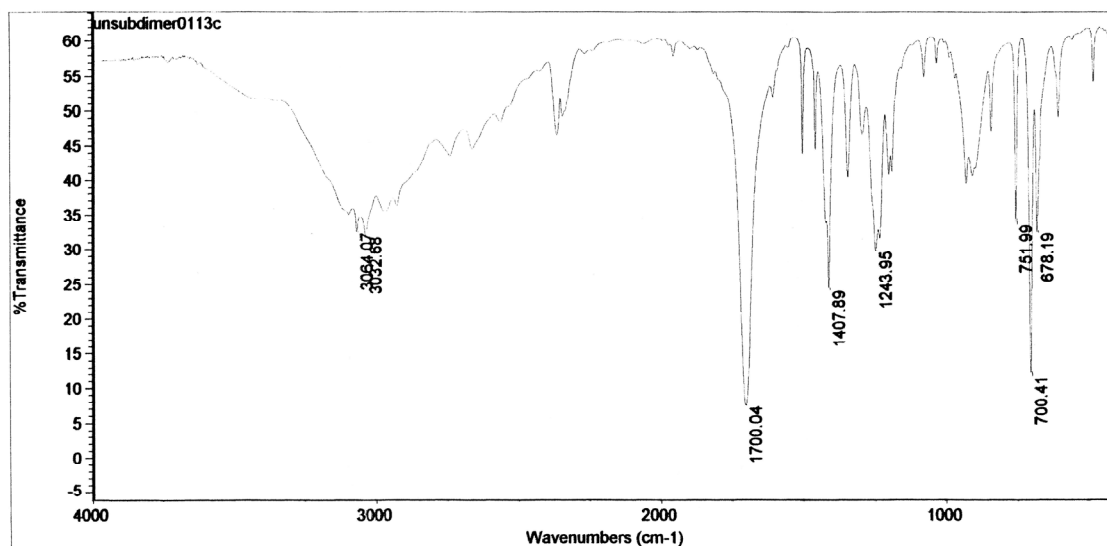Tue Jan 27 16:43:17 2009
FIND PEAKS:
    Spectrum: p-I-F-01272009
    Region: 4000.00   400.00
    Absolute threshold: 56.991
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1698.49	43.213
798.56	49.964
1405.16	52.200
1008.77	52.473
1234.30	52.669
1195.71	52.851
488.94	52.947
720.01	53.844
1653.03	54.315
1486.19	54.983
672.41	56.279
2923.36	56.694
852.37	56.724

APPENDIX: C

IR Spectrum of Dimer of Phenylacetic Acid/Acetic Acid

unsubdimer0113c

Peak labels on spectrum: 3064.07, 3032.68, 1700.04, 1407.89, 1243.95, 751.99, 700.41, 678.19

Tue Jan 13 15:19:30 2009
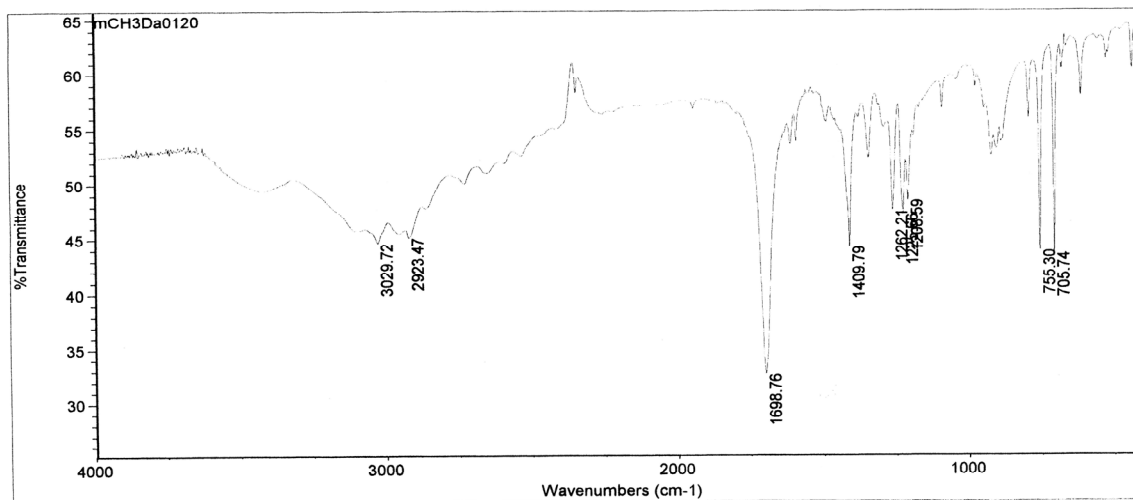FIND PEAKS:
    Spectrum: unsubdimer0113c
    Region: 4000.00   400.00
    Absolute threshold: 34.746
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1700.04	7.369
700.41	11.659
1407.89	24.173
1243.95	29.741
3032.68	31.831
3064.07	32.401
678.19	32.383
751.99	33.570

IR Spectrum of Dimer of 3-CH$_3$-Phenylacetic Acid/Acetic Acid

PEAK LIST:

POSITION	INTENSITY
1698.76	32.652
705.74	43.637
1409.79	44.244
755.30	43.881
3029.72	44.624
2923.47	45.106
1225.66	47.25
1262.21	47.627
1208.59	48.511

IR Spectrum of Dimer of 4-CH₃ -Phenylacetic Acid/Acetic Acid
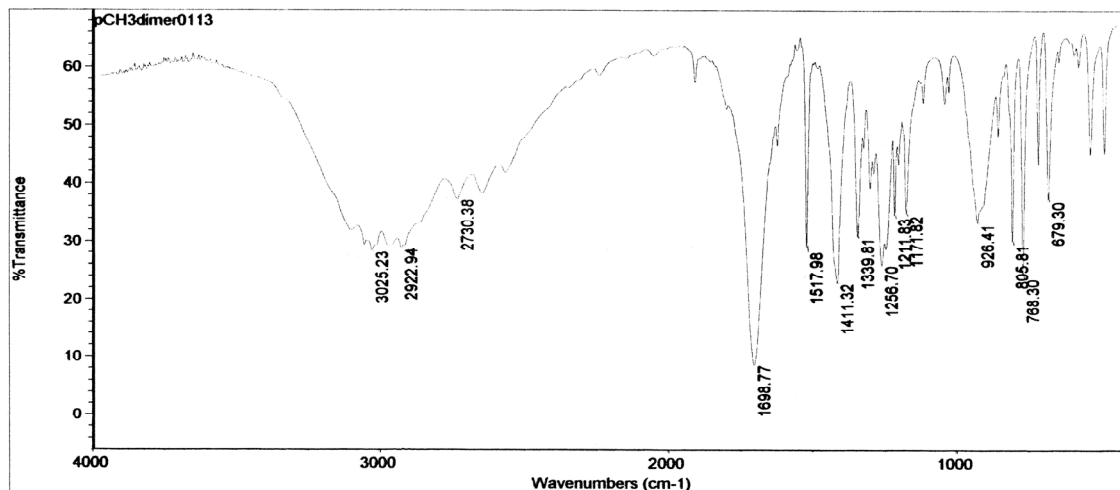
pCH3dimer0113

Tue Jan 13 15:55:50 2009
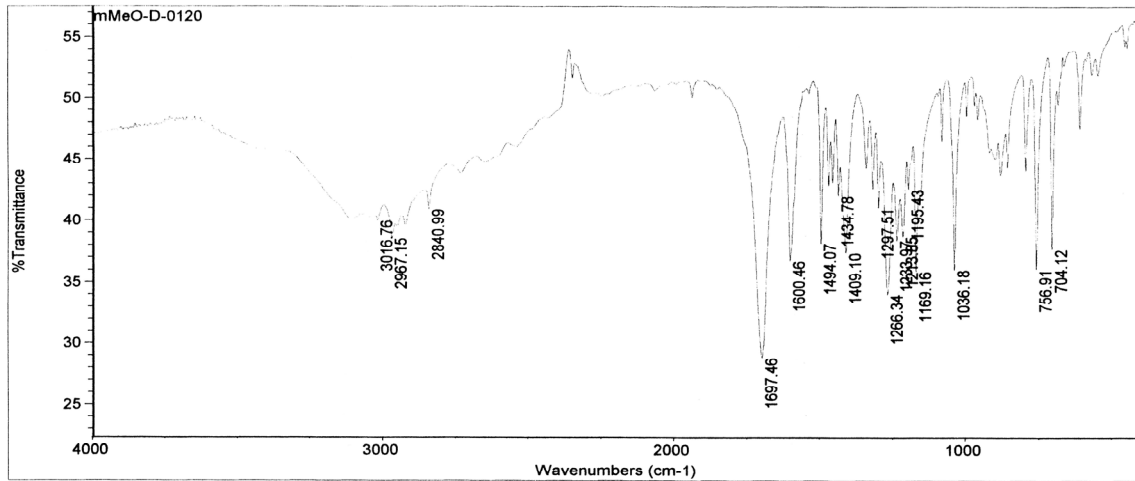FIND PEAKS:
    Spectrum: pCH3dimer0113
    Region: 4000.00   400.00
    Absolute threshold: 37.983
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1698.77	8.529
1411.32	22.799
768.30	23.574
1256.70	25.849
3025.23	28.170
1517.98	28.160
2922.94	28.642
805.81	29.449
1339.81	30.649
926.41	33.151
1211.83	34.080
1171.82	34.492
679.30	36.880
2730.38	37.184

IR Spectrum of Dimer of 3-MeO -Phenylacetic Acid/Acetic Acid

Tue Jan 20 15:50:56 2009
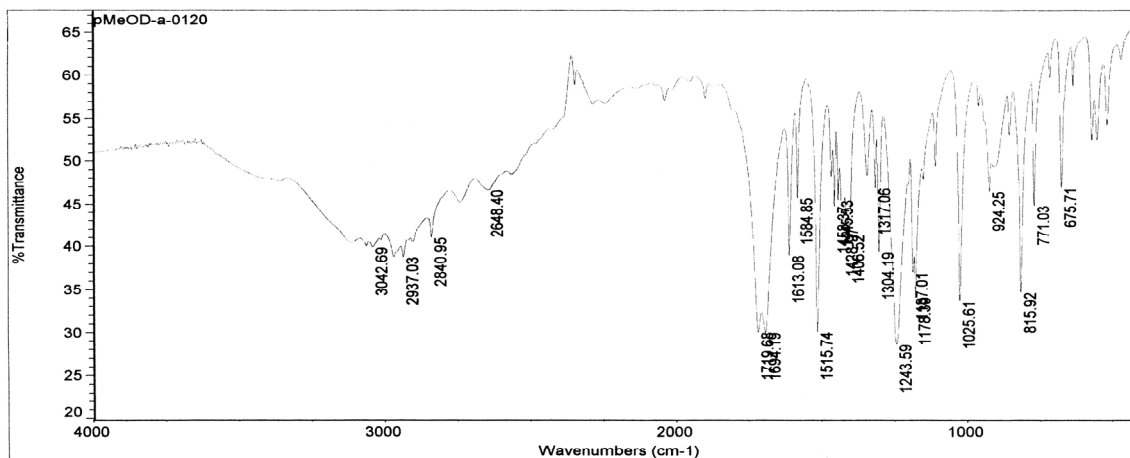FIND PEAKS:
    Spectrum: mMeO-D-0120
    Region: 4000.00   400.00
    Absolute threshold: 42.601
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1697.46	28.779
1266.34	34.026
1169.16	36.896
1036.18	36.022
756.91	36.096
1600.46	36.740
1409.10	37.383
704.12	37.704
1494.07	38.148
1233.97	38.391
2967.15	38.562
1213.85	38.741
3016.76	40.013
2840.99	40.915
1297.51	41.032
1434.78	42.031
1195.43	42.561

IR Spectrum of Dimer of 4-MeO -Phenylacetic Acid/Acetic Acid

PEAK LIST:

POSITION	INTENSITY
1243.59	28.574
1719.88	30.014
1515.74	30.046
1694.19	29.999
1025.61	33.678
1178.39	34.057
815.92	34.684
1187.01	37.008
2937.03	38.735
1613.08	38.951
1304.19	39.365
3042.69	39.866
2840.95	40.991
1406.52	41.318
1428.97	42.154
1458.37	44.760
771.03	44.833
1584.85	45.745
1445.53	45.504
924.25	46.494
2648.40	46.631
1317.06	46.900
675.71	46.982

IR Spectrum of Dimer of 3-NO₂ -Phenylacetic Acid/Acetic Acid
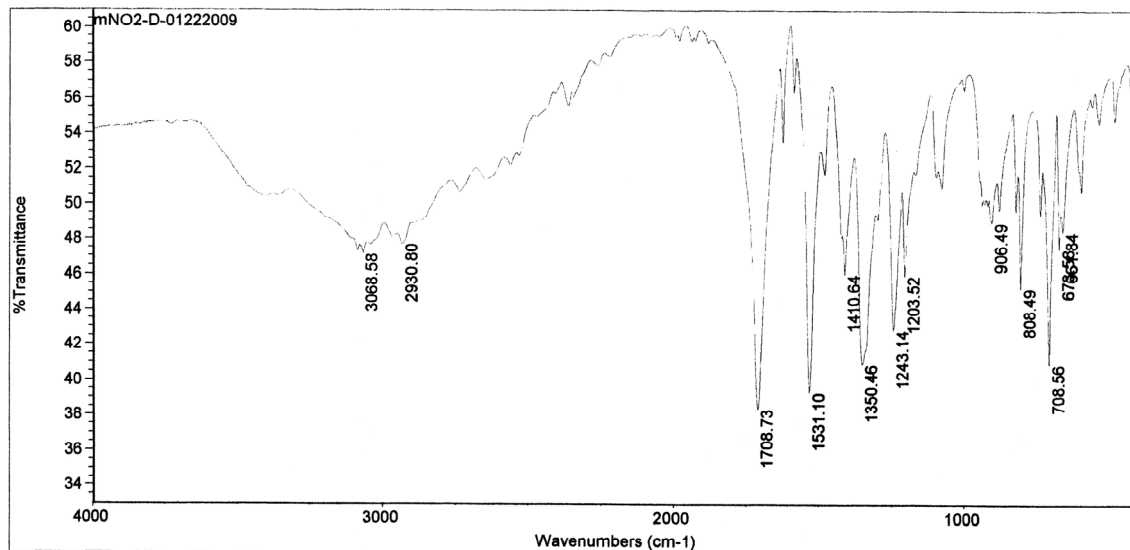
PEAK LIST:

POSITION	INTENSITY
1708.73	38.345
1531.10	39.302
1350.46	40.938
708.56	40.944
1243.14	42.847
808.49	45.259
1203.52	45.965
1410.64	46.059
3068.58	47.126
673.58	47.459
2930.80	47.689
661.84	48.433
906.49	48.969

IR Spectrum of Dimer of 4-NO₂ -Phenylacetic Acid/Acetic Acid

Thu Jan 22 14:48:28 2009
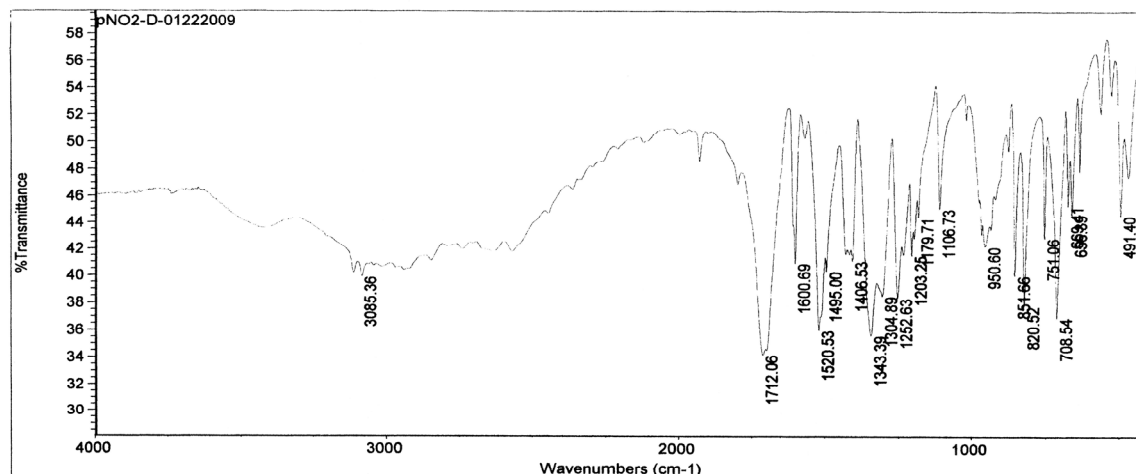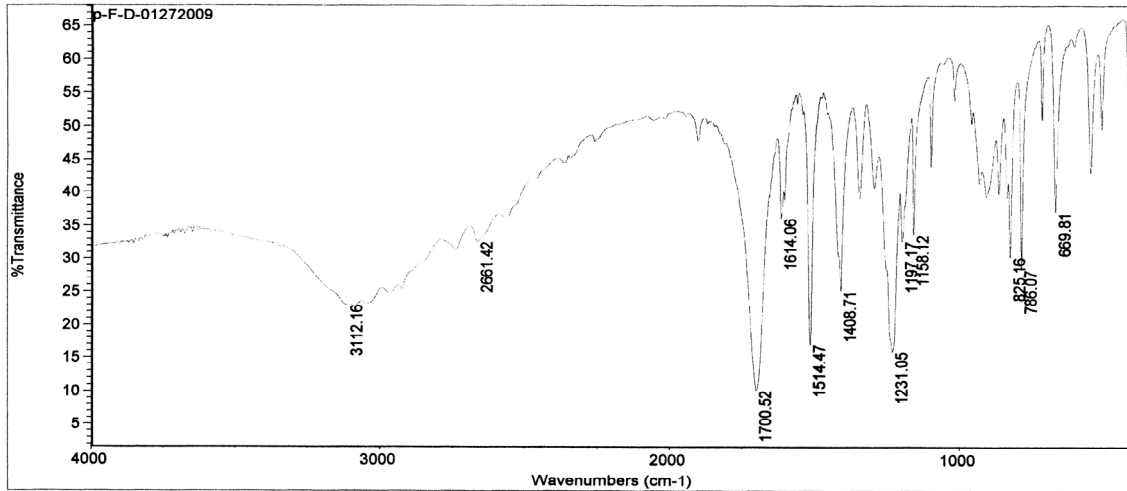FIND PEAKS:
Spectrum: pNO2-D-01222009
Region: 4000.00   400.00
Absolute threshold: 46.444
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1712.06	34.161
1343.39	35.597
1520.53	36.007
708.54	36.937
820.52	37.774
1252.63	38.354
1304.89	38.492
3085.36	39.908
851.66	40.036
1495.00	40.335
1600.69	40.924
1406.53	41.108
1203.25	41.529
950.60	42.227
751.06	42.871
1179.71	44.434
491.40	44.567
656.39	44.646
1106.73	45.076
669.41	45.304

IR Spectrum of Dimer of 4-F -Phenylacetic Acid/Acetic Acid

p-F-D-01272009

Tue Jan 27 16:52:23 2009
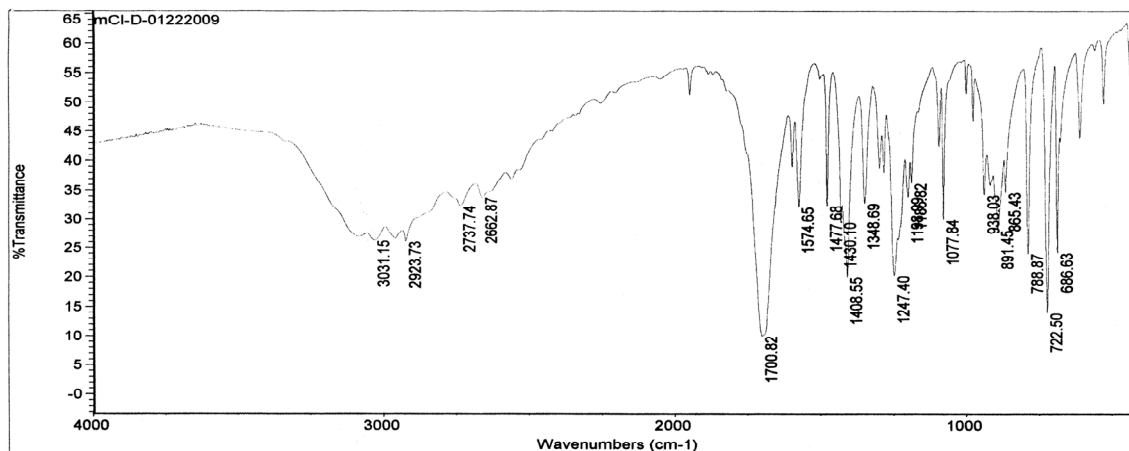FIND PEAKS:
    Spectrum: p-F-D-01272009
    Region: 4000.00   400.00
    Absolute threshold: 38.149
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1700.52	10.135
1231.05	15.918
1514.47	16.996
3112.16	23.000
1408.71	25.260
786.07	28.432
825.16	30.324
2661.42	32.669
1197.17	32.737
1158.12	33.738
1614.06	36.167
669.81	37.155

IR Spectrum of Dimer of 3-Cl -Phenylacetic Acid/Acetic Acid

Thu Jan 22 15:14:27 2009
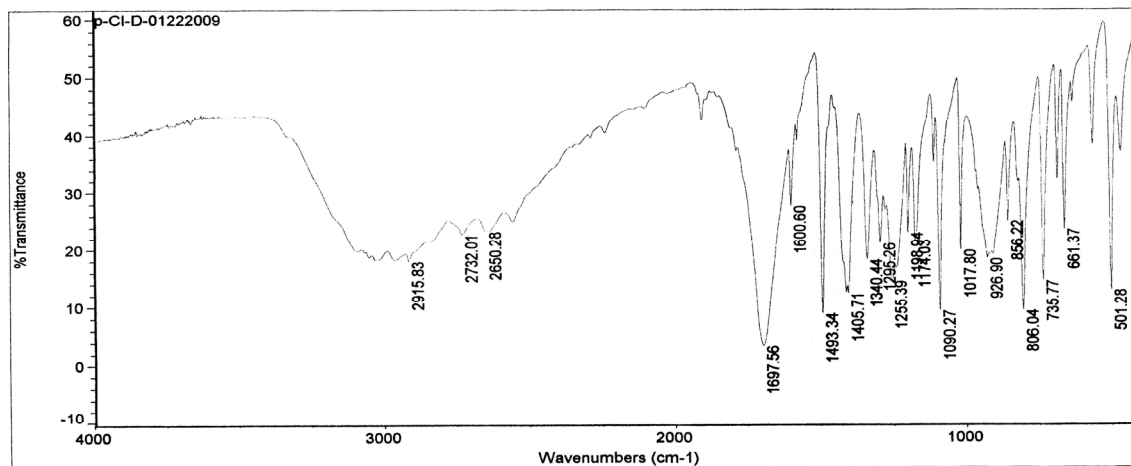FIND PEAKS:
    Spectrum: mCl-D-01222009
    Region: 4000.00   400.00
    Absolute threshold: 36.673
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1700.82	9.970
722.50	14.032
1408.55	20.003
1247.40	20.218
788.87	24.102
686.63	24.240
2923.73	26.100
3031.15	26.283
891.45	28.185
1430.10	29.577
1077.84	30.108
2737.74	32.304
1574.65	32.118
1477.68	32.431
1348.69	32.804
2662.87	33.808
1198.99	33.867
938.03	34.355
865.43	34.775
1186.82	36.318

IR Spectrum of Dimer of 4-Cl -Phenylacetic Acid/Acetic Acid

Thu Jan 22 15:40:00 2009
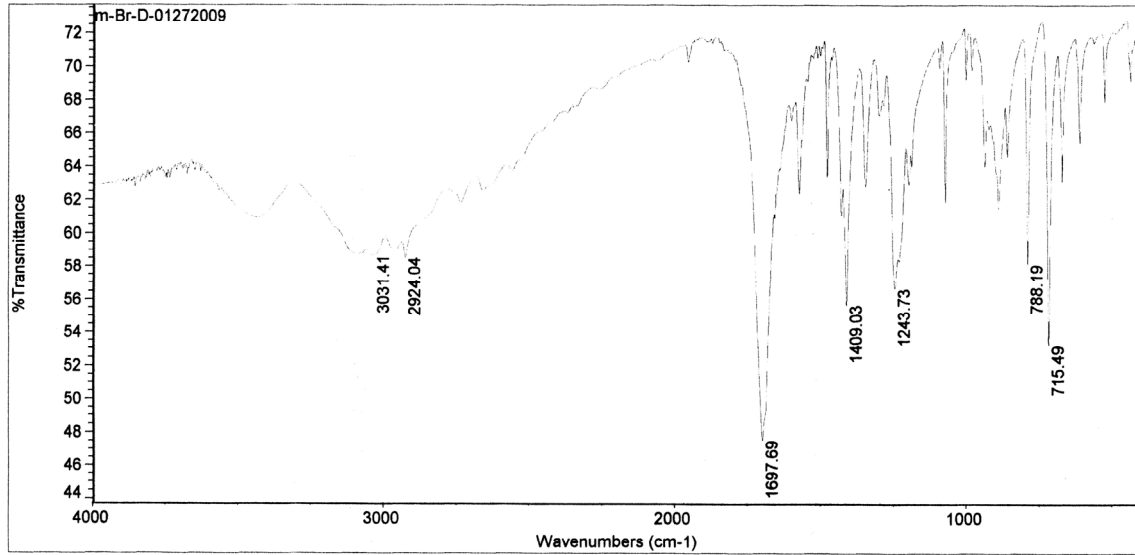FIND PEAKS:
    Spectrum: p-Cl-D-01222009
    Region: 4000.00   400.00
    Absolute threshold: 31.438
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1697.56	3.402
1493.34	8.888
806.04	9.462
1090.27	9.317
1405.71	12.444
501.28	12.926
1255.39	14.554
735.77	14.606
2915.83	18.017
1340.44	18.300
926.90	18.469
1017.80	19.961
1295.26	21.194
1174.03	21.740
2732.01	22.787
2650.28	23.270
1198.94	23.075
661.37	23.656
856.22	25.162
1600.60	27.761

IR Spectrum of Dimer of 3-Br -Phenylacetic Acid/Acetic Acid

Tue Jan 27 15:04:27 2009
FIND PEAKS:
Spectrum: m-Br-D-01272009
Region: 4000.00   400.00
Absolute threshold: 60.163
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1697.69	47.536
715.49	53.215
1409.03	55.674
1243.73	56.666
788.19	58.141
2924.04	58.513
3031.41	58.656

IR Spectrum of Dimer of 4-Br -Phenylacetic Acid/Acetic Acid

Tue Jan 27 15:26:04 2009
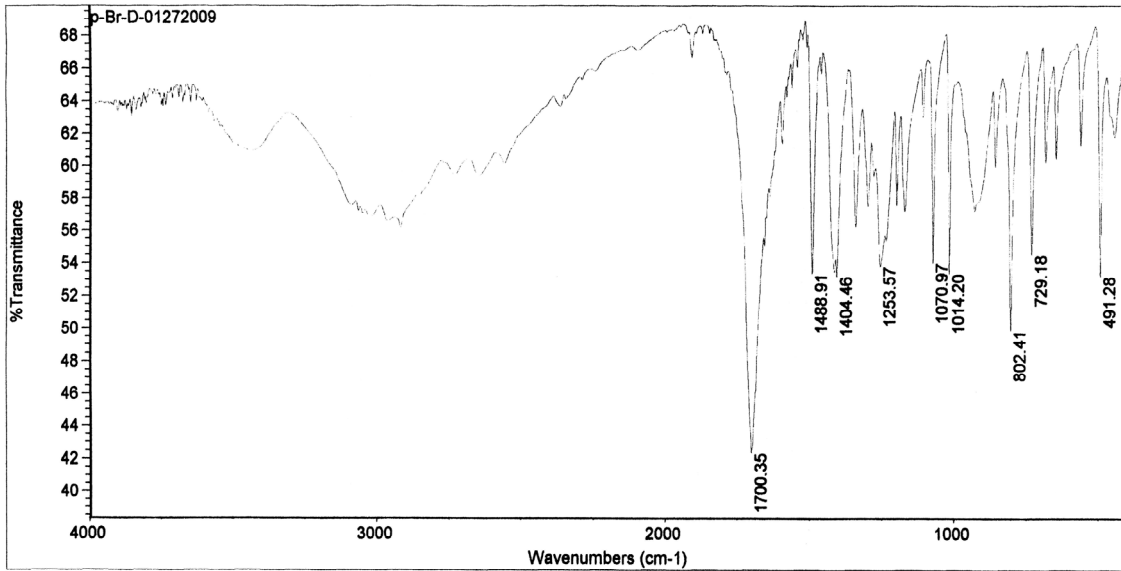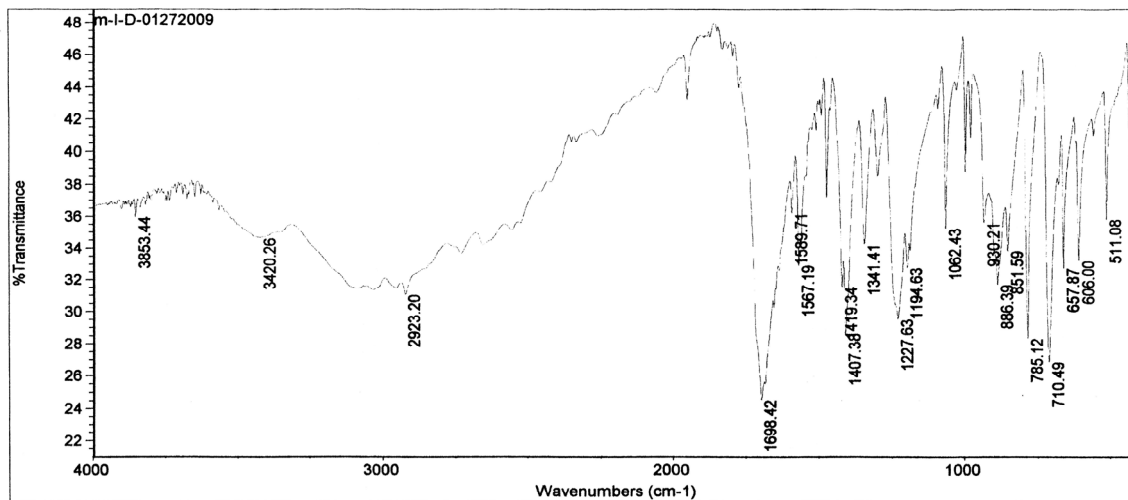FIND PEAKS:
   Spectrum: p-Br-D-01272009
   Region: 4000.00   400.00
   Absolute threshold: 55.630
   Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1700.35	42.322
802.41	49.919
1404.46	53.232
491.28	53.219
1488.91	53.417
1014.20	53.400
1253.57	53.822
1070.97	54.033
729.18	54.540

IR Spectrum of Dimer of 3-I -Phenylacetic Acid/Acetic Acid

Tue Jan 27 15:53:22 2009
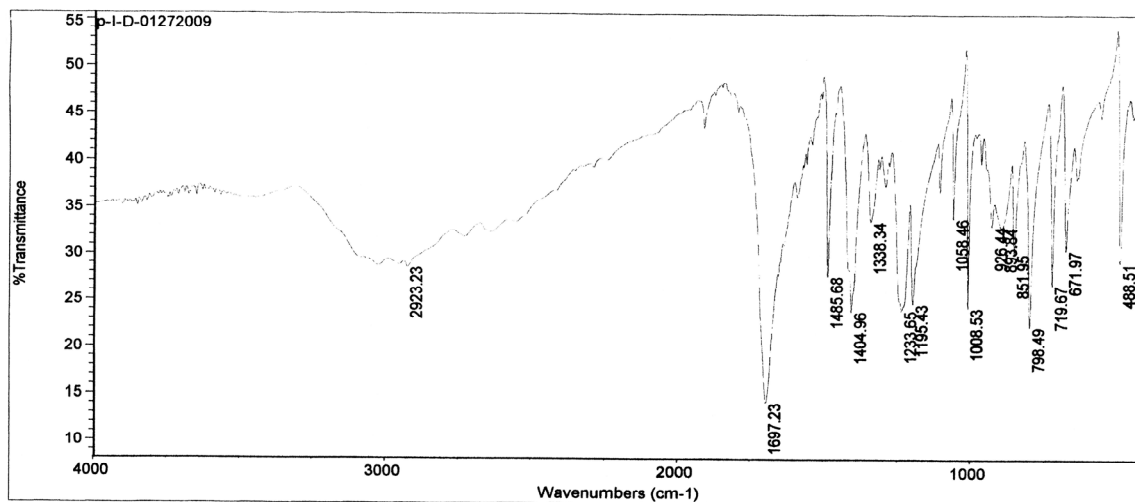FIND PEAKS:
    Spectrum: m-l-D-01272009
    Region: 4000.00   400.00
    Absolute threshold: 36.265
    Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1698.42	24.531
710.49	26.845
785.12	28.343
1407.38	28.625
1227.63	29.521
2923.20	31.035
1419.34	31.525
886.39	31.668
657.87	32.728
1194.63	32.771
1567.19	32.911
606.00	33.224
851.59	33.825
1341.41	34.246
3420.26	34.628
1062.43	35.242
930.21	35.621
511.08	35.812
3853.44	35.957
1589.71	36.198

IR Spectrum of Dimer of 4-I -Phenylacetic Acid/Acetic Acid

Tue Jan 27 16:24:39 2009
FIND PEAKS:
Spectrum: p-I-D-01272009
Region: 4000.00   400.00
Absolute threshold: 34.177
Sensitivity: 50

PEAK LIST:

POSITION	INTENSITY
1697.23	14.154
798.49	22.178
1233.65	24.005
1404.96	23.894
1008.53	24.318
1195.43	24.719
719.67	26.738
1485.68	27.694
2923.23	28.545
488.51	29.215
851.95	30.149
671.97	30.539
893.84	33.021
926.44	33.186
1338.34	33.563
1058.46	33.967