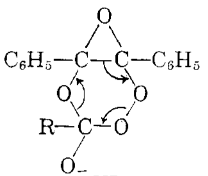
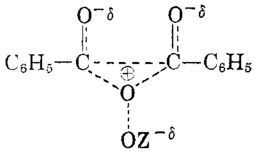
as much mixed acid as ethyl ester product. Unfortunately, the composition of the acid and ester products, with respect to benzoic and anisic moieties was not reported,[40] and, until we have had the opportunity to investigate this matter further, little can be said.

Furthermore it seems possible that two other factors could alter the structure of the transition state; (i) the nature of the solvent medium, and (ii) the nature of the leaving group Z. For example, where $Z = \underset{\overset{\|}{O}}{RCO^-}$, an alternative to V is


VI


VII

the transition state VI in which a neighboring group effect is operating. Apparently the solvent medium also plays a role in choosing between the alternatives. A poorly ionizing solvent like ether would tend to resist separation of the carboxylic acid anion and thereby enhance the neighboring group relationship. A solvent of low dielectric such as ether or chloroform may favor the occurrence of cleavage in concert with bond making and the transition state for such a mechanism might possibly be that represented by VII. Edwards and co-workers,[41] most recently, and Bartlett[42] have accepted as reasonable an analogous transition state for epoxidations by means of perbenzoic acid (Z = benzoyl).

Acknowledgment.—H. K. is obliged to the National Science Foundation for support of this project under grant NSF-G6037.

[41] D. R. Campbell, J. O. Edwards, J. Maclachlan and K. Polgar, *J. Am. Chem. Soc.*, **80**, 5308 (1959).

[42] P. D. Bartlett, *Record Chem. Prog.*, **11**, 47 (1950).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MARYLAND, COLLEGE PARK, MD.]

The Synthesis of α-Methoxyarylacetic Acids from the Base-catalyzed Condensation of Arylaldehydes with Bromoform and Methanol. Studies of Aldehyde Reactivities

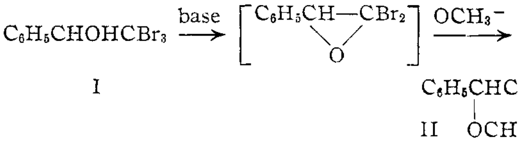
BY WILKINS REEVE AND EDWARD L. COMPERE, JR.[1]

RECEIVED JANUARY 6, 1961

Certain arylaldehydes undergo a base-catalyzed reaction with bromoform in methanol solution to form α-methoxyarylacetates. This reaction has been studied with 23 aldehydes and one ketone, and it is concluded that the effect of ring substituents in this reaction is much like their effect in the Perkin reaction. Yields of approximately 75% of theory are obtained with the chlorobenzaldehydes, but *p*-hydroxybenzaldehyde and *p*-dimethylaminobenzaldehyde do not react. Many of the α-methoxyarylacetic acids form insoluble sodium *acid* salts, and the structural features necessary for this to occur are discussed. Many of the acids are potent plant growth regulators.

In an earlier publication,[2] a one-step synthetic method of preparing α-methoxyarylacetate esters and salts by the base-catalyzed condensation of an aryl aldehyde with chloroform or bromoform in methanol solution was described, and data were presented for seven substituted benzaldehydes to illustrate the utility of the method. The object of the present work was to study an extensive series of aromatic aldehydes to determine the relationship between structure and reactivity of the aldehyde in this reaction. The α-methoxyarylacetic acids are especially interesting because of two unusual characteristics. First, many of them have the ability to form relatively insoluble, crystalline, sodium acid salts, containing equimolecular amounts of the acid combined with its sodium salt, and at least one of these acid salts is useful in analytical chemistry[2,3]; second, they are potent plant growth regulators and, unlike most arylacetic acids, they are translocated readily throughout the plant and some of them have the property of even being exuded through the roots into the soil.[4]

The α-methoxyarylacetate salts synthesized in this work were all prepared by what amounted to a standard procedure; 0.5 mole of potassium hydroxide in methanol was slowly added over a three-hour period to a mixture of 0.1 mole of the aldehyde and 0.12 mole of bromoform maintained at a temperature near 5°. The reaction consisted of the bromoform condensing with the carbonyl group to form first a tribromomethylcarbinol (I), which then was converted successively into a postulated epoxide and an ester (II) of the desired acid.[2]



The tribromomethylphenylcarbinol has been prepared in 15% yield by Howard from benzaldehyde and bromoform with potassium hydroxide,[5] and the ester II has been demonstrated to be an intermediate when the haloform employed was chloroform.[2] Since the over-all yield of the methoxy acid, resulting from the hydrolysis of the ester and its isolation in the form of its sodium acid salt, is 40% it is obviously advantageous to carry out the reaction as described here so that the tribromocarbinol is not isolated. *m*-Chlorobenzal-

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[1] Bakelite Fellow, 1957–1958.

[2] W. Reeve and C. W. Woods, *J. Am. Chem. Soc.*, **82**, 4062 (1960).

[3] W. Reeve and I. Christoffel, *Anal. Chem.*, **29**, 102 (1957); W. Reeve, *ibid.*, **31**, 1066 (1959).

[4] W. H. Preston, J. W. Mitchell and W. Reeve, *Science*, **119**, 437 (1954); P. J. Linder, J. C. Craig and T. R. Walton, *Plant Physiol.*, **32**, 572 (1957); J. W. Mitchell, B. C. Smale and W. H. Preston, *J. Agr. Food Chem.*, **7**, 841 (1959).

[5] J. W. Howard, *J. Am. Chem. Soc.*, **52**, 5059 (1930).

dehyde provides another example of the superiority of the one-step reaction which avoids the isolation of the trihalocarbinol; the trichloromethyl-*m*-chlorophenylcarbinol can be obtained in only 12% yield,[6] presumably because of a competing Cannizzaro reaction, but the α-methoxy acid obtained directly from the aldehyde and bromoform is obtained in 75% of the theoretical yield.

The first step of the reaction involving the base-catalyzed condensation of bromoform and the aldehyde would appear to be quite similar in mechanism to the many well known base-catalyzed condensations in which a carbanion adds to a carbonyl group. Accordingly, assuming the first step to be the rate-controlling step in the series of reactions, the relative reactivities of aldehydes in this over-all sequence of reactions should be comparable with such standard reactions as the Darzens glycidic ester condensation[7] or the Perkin reaction.[8] Insufficient data are available for many comparisons with the Darzens condensation, but most of the aldehydes examined in this work have been studied in the Perkin reaction, and the relative reactivities of substituted benzaldehydes in the two reactions have been found to be quite similar. Table I lists the results with aldehydes examined, and for comparative purposes, there are included data on the Perkin reaction and also the Hammett σ-values for the substituent groups. The single ketone examined, acetophenone, is also included. The precentage yields given in Table I are based on results obtained in at least two runs with each aldehyde, and are believed to be accurate to within a few per cent.

From the data in Table I it is apparent that in the aldehyde bromoform condensation, as in the Perkin reaction, a monochloro substituted benzaldehyde gives an increased yield relative to benzaldehyde itself; increased yields are also observed with the *m*- and *p*-fluorobenzaldehydes.

The effect of a *p*- or a *m*-methyl substituent is to lower the yield, as would be expected on the basis of either the electron-releasing properties of this group or the Hammett σ-values, although it is unexpected in both this reaction and the Perkin reaction for the *para* isomer to give a higher yield than the *meta*. Of considerable interest is the fact that a single *o*-methyl group actually favors the reaction. This "accelerative *ortho* effect" has been previously observed in the Perkin reaction with the *o*- as compared to the *p*-methoxybenzaldehydes.[8] It can be rationalized as being due to a steric effect which forces the carbon oxygen bond of the carbonyl carbon out of the plane of the ring and thereby lessens resonance between the ring and the carbonyl group. This neutralizes the electron-releasing abilities of the *ortho* methyl or methoxyl groups. This same explanation has been given to account for *o*-methylbenzoic acid being stronger than the unsubstituted benzoic acid.[9] The same explanation may account for the 1-naphthaldehyde being twice as reactive as the 2-naphthaldehyde.

TABLE I

YIELDS OF α-METHOXYARYLACETATES AND OF CINNAMIC ACIDS FROM ARYLALDEHYDES

Carbonyl component	Methoxy acid, % yield	Arylacrylic acid, % yield[a]	Sigma value[b]
Benzaldehyde	40[c]	50	0.00
o-Chloro-	79	71	
m-Chloro-	75	63	+0.37
p-Chloro-	70	52	+ .23
2,6-Dichloro-	2[h]	82	
o-Fluoro-	40		
m-Fluoro-	59		+ .34
p-Fluoro-	69		+ .06
2,4,6-Trimethyl-	1	0	
p-Hydroxy-	0[h]	62	−1.0
p-Dimethylamino-	0[h]	0	−0.6
3,4-Dimethoxy-	19[c]	20	
3,4-Methylenedioxy-	16	Near 0	−0.16
m-Nitro-	4	75	+ .71
p-Nitro-	0	82	+ .79
p-Cyano-	48[d]	Good[e]	+ .63
o-Tolualdehyde	49	15	
m-Tolualdehyde	24	23	− .07
p-Tolualdehyde	33	33	− .17
1-Naphthaldehyde	49	Good[f]	
2-Naphthaldehyde	24	Poor[f]	
2-, 3- or 4-Pyridinecarboxaldehydes	0		
2-Thiophenecarboxaldehyde	20	Good[g]	
Acetophenone	16	Near 0	

[a] From ref. 8, particularly Table I, p. 218. [b] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953). [c] From ref. 2; sodium methoxide was the base used with the 3,4-dimethoxybenzaldehyde. [d] Yield of crude acid. [e] N. Moses, *Ber.*, **33**, 2625 (1900). [f] L. Rousett, *Bull. soc. chim. France*, [3] **17**, 813 (1897). [g] A. Biedermann, *Ber.*, **19**, 1855 (1886). [h] Aldehyde recovered unchanged in 75 to 90% yield.

Benzaldehydes with two *o*-substitutents were inert, regardless of whether the substituent groups were methyl or chlorine. This is undoubtedly due to steric hindrance of the classical type. In the Perkin reaction, the 2,6-dichlorobenzaldehyde is quite reactive, but this reaction involves a much higher temperature, no solvent and a smaller attacking anion.

The Perkin reaction will occur with hydroxybenzaldehydes, but the arylaldehyde–bromoform reaction will not. In the former case, the reacting species is actually an acetoxybenzaldehyde; in the second case, the hydroxy substituent would be present as a phenoxide ion, the electron-releasing properties of which would certainly hinder the development of a positive charge on the carbonyl carbon.

The *p*-dimethylamino group deactivates the aldehyde function in both the Perkin reaction and the reaction studied. This would be expected in view of the electron-releasing properties of this group; the Hammett σ-value is one of the more negative of the common substituents.

As would be expected for a negatively substituted benzaldehyde, the *p*-cyanobenzaldehyde gave a good yield, especially if allowance is made for some of the cyano group being attack by the alcoholic

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(6) E. D. Bergmann, D. Ginsburg and D. Lavie, *J. Am. Chem. Soc.*, **72**, 5012 (1950).

(7) M. S. Newman and B. J. Magerlein in "Organic Reactions," Vol. 5, John Wiley and Sons, Inc., New York, N. Y., 1949, p. 413 ff.

(8) J. R. Johnson in "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, N. Y., 1942, p. 210 ff.

(9) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 744.

alkali. The reaction was unsatisfactory with the *m*- and *p*-nitrobenzaldehydes, probably because the methanolic potassium hydroxide solution reacted with the nitro group. In addition, a side reaction occurred giving the substituted glycidic acid. This reaction has been observed before with benzaldehyde.[2]

It is not clear why 2-thiophenecarboxaldehyde was less reactive than benzaldehyde. With the pyridinecarboxaldehydes, only tars were obtained.

Sodium Acid Salts.—The interesting and unusual ability which many of the α-methoxyarylacetic acids have of forming sodium acid salts which are difficultly soluble in water and acetone often makes it possible to isolate easily the desired α-methoxy acid from the reaction mixture in this acid salt form, and to free it from all acetone-soluble and water-soluble impurities by washing successively with these solvents.[2] The acid salts can often be recrystallized from water or ethanol. Of the eighteen α-methoxyarylacetic acids prepared in this study, eight were found to form sodium acid salts. The information now available about the relationship of structure to the ability of these α-methoxyarylacetic acids to form sodium acid salts, and their properties, can be summarized: 1. Any structural change in the methoxy acetate side chain prevents the formation of an acid salt (mandelic acid is an exception). 2. *o*-Substituents, except methoxy or ethoxy groups, likewise prevent acid salt formation The failure of α-methoxy-(1-naphthalene)-acetic acid to form a sodium acid salt can be explained on this basis. 3. 3,4-Methylenedioxy, *m*-nitro, *p*-isopropyl and *p*-cyano substituents on the ring prevent the formation of sodium acid salts. This may be a steric effect in some cases; in other cases it may be due to the repulsive effects of the strongly polar groups. 4. The sodium acid salts derived from the *m*- and *p*-chloro and the *p*-bromo substituted acids are relatively insoluble in water; those from *m*- and *p*-fluoro substituted acids have about the same water solubility as the sodium acid salt from the unsubstituted acid; and a methoxy group or a methyl group increases the solubility of the sodium acid salt in water. 5. Replacing the phenyl group by other aryl groups such a 2-furyl or 1-naphthyl yields α-methoxy acids which do not form sodium acid salts. On the other hand, the sodium acid salt from α-methoxy-(2-thiophene)-acetic acid does form but is quite soluble in water, and the one from α-methoxy-(2-naphthalene)-acetic acid is more insoluble than any other found so far.

Pertinent solubility data are summarized in Table II.

TABLE II

Anion forming sodium acid acetate	Solubility at 28 ± 1°, g./100 ml.		
	Water	Ethanol	Acetone
α-Methoxyphenyl-	2.6[a]	0.18[a]	0.02
m-Fluoro-α-methoxyphenyl-	2.1		
p-Fluoro-α-methoxyphenyl-	2.1		
m-Chloro-α-methoxyphenyl-	0.70		
p-Chloro-α-methoxyphenyl-	.31	0.14	0.011
3,4-Dichloro-α-methoxyphenyl-	.43[b]	.49	.024
p-Bromo-α-methoxyphenyl-	.79[b]	.26	.028
α,3,4-Trimethoxyphenyl-	17[b]		
α-Methoxy-*p*-tolu-	4.6		
α-Methoxy-(2-naphthalene)-	0.19	.076	.006

[a] From ref. 3. [b] From ref. 2

Other Salts.—Certain members of the α-methoxyarylacetic acid series of compounds appear to have the surprising property of forming difficultly soluble salts *selectively* with one of the following elements and not with the others: magnesium, lithium, sodium, potassium, rubidium and cesium. Thus, α-methoxy-(1-naphthalene)-acetic acid forms a relatively insoluble normal lithium salt (0.94 g./100 ml. water; 3.4 g./100 ml. ethanol; 0.053 g./100 ml. acetone; all at approximately 28°), and α-methoxy-α-phenyl-propionic acid forms a difficultly soluble normal rubidium salts.

It has been reported previously that *p*-isopropyl-α-methoxy-phenylacetic acid forms a difficultly soluble normal sodium salt,[10] and that cesium forms a sparingly soluble acid salt with α-methoxyphenylacetic acid behaving like sodium rather than like potassium.[3]

More work will be needed to tell whether or not any of these salts, or the new sodium acid salts discussed above, will be useful in analytical chemistry.

Physiological Activity in Plants.—All of the acids prepared were examined for physiological activity in plants by J. W. Mitchell, B. C. Smale and W. H. Preston of the U. S. Department of Agriculture, and their results have been presented in detail elsewhere.[4] In general, these α-methoxyarylacetic acids affect dicotyledonous plants in a way similar to that induced by some chlorinated phenoxyacetic acids. The following conclusions have been drawn about the effect of structural modifications on activity in the α-methoxy acid series when tested on bean plants. The substitution of a fluorine or a chlorine atom in the *m*- or *p*-position gave exceedingly potent plant growth regulating materials. In addition, the *m*-fluoro, the *p*-fluoro and the *m*-chloro substituted α-methoxyphenylacetic acids had the unusual property of exuding from the roots into the soil and thereby affecting adjacent untreated plants. In contrast, the α-methoxyphenylacetic acids substituted in the ring with methyl, nitro, cyano or methylenedioxy groups were much less active. The acids with substituents in the 2- and 6-positions were inactive regardless of whether the substituents were chlorine or methyl.

Experimental

All melting points are corrected. Analyses are by Mrs. Kathryn Baylouny and Miss Jane Swan.

General Procedure for Preparing Substituted α-Methoxyphenylacetates.—In a 500-ml. 3-necked flask were placed 0.1 mole of the arylaldehyde, 31 g. (0.12 mole) of bromoform and 50 ml. of methanol. A solution containing 28 g. (0.5 mole) of potassium hydroxide dissolved in 110 ml. of commercial methanol was added over a period of 3 hours. The reaction temperature was held between 0 and 5° by means of an ice and salt bath. The reaction is exothermic and will get out of control if the temperature gets in the twenties. For this reason, one neck of the flask should be unstoppered. After completion of the addition, the reaction mixture was allowed to stand overnight and slowly

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(10) M. Fileti and V. Amoretti, *Gazz. chim. ital.*, **21** [I], 44 (1891), from *Chem. Zentr.*, **62** [I], 539 (1891).

warm up to room temperature. The reaction mixture was then transferred to a beaker using 100 ml. of water for washing purposes, and 300 ml. of a half-saturated, aqueous sodium chloride solution was added. The beaker was warmed to complete the dissolution of the precipitate. Insoluble material was removed by filtration or extraction with ether, the aqueous solution was warmed to remove the dissolved ether, and the *p*H of the cooled aqueous solution was then adjusted to 3.3 with hydrochloric acid. If a precipitate of the sodium hydrogen di-(α-methoxyarylacetate) formed within a few hours, the reaction mixture was stirred in an ice-bath for 3 hours to complete the precipitation, and then filtered. The sodium acid salt was purified by extracting organic impurities with acetone and inorganic salts with water. The sodium acid salts could sometimes be recrystallized from methanol or aqueous ethanol. Treatment with potassium hydroxide solution formed the normal, soluble mixture of sodium and potassium salts, and pouring this solution into excess hydrochloric acid caused the α-methoxy acid to be set free.

Acids which would not form sodium acid salts were isolated as the crude free acid by extracting the alkaline reaction mixture with ether to remove neutral material, then acidifying and again extracting with ether to remove the acid.

o-**Chloro-α-methoxyphenylacetic acid** was isolated as the **normal sodium salt** by treating the crude acid with a five-fold excess of 40% sodium hydroxide, and filtering the precipitate. It was washed first with small amounts of water, then with acetone, and finally recrystallized from 95% acetone–5% water. The yield was 38 g. (79% of theor.) from 35 g. of *o*-chlorobenzaldehyde. Acidification of the sodium salt gave the **free acid**, m.p. 78–79° after recrystallization from water.

Anal. Calcd. for $C_9H_9O_3Cl$: C, 53.88; H, 4.52; $-OCH_3$, 15.47. Found: C, 54.01; H, 4.61; $-OCH_3$, 15.17.

m-**Chloro-α-methoxyphenylacetic acid** was isolated as the **sodium acid salt**, m.p. 220–221° after recrystallization from 50% ethanol, neut. equiv. 422 compared to theory of 423. The yield was 18 g. (75% of theor.) from 15 g. of *m*-chlorobenzaldehyde. **The free acid** was an oil. The **ammonium salt**, formed by evaporating a solution of the acid in excess aqueous ammonia, had a m.p. of 160–163° after recrystallization from 75% ethyl acetate–25% ethanol containing a few drops concd. ammonium hydroxide.

Anal. Calcd. for $C_9H_{12}O_3NCl$: C, 49.66; H, 5.56; N, 6.44; $-OCH_3$, 14.26. Found: C, 50.11; H, 5.58; N, 6.14; $-OCH_3$, 14.44.

p-**Chloro-α-methoxyphenylacetic acid** was isolated as the **sodium acid salt**, m.p. 240–241° dec. after recrystallization from 50% aqueous ethanol, neut. equiv. 426 compared to theory of 423. From 35 g. of *p*-chlorobenzaldehyde there was obtained 37 g. (70% of theor.) of the sodium acid salt; this became 25 g. after two recrystallizations. Acidifying an alkaline solution of the sodium acid salt gave the **free acid**, m.p. 85–86° (lit.[11] 85–86°), neut. equiv. 201 compared to theoretical of 201.

2,6-Dichloro-α-methoxyphenylacetic acid was isolated as the **ammonium salt** by treating the crude acid with excess ammonium hydroxide and evaporating to dryness. After two recrystallizations from a 6:1 ethyl acetate–ethanol solution containing some ammonia, an analytical sample was obtained, m.p. 204–206°. The yield was about 200 mg. (2% of theor.) from 5 g. of 2,6-dichlorobenzaldehyde.

Anal. Calcd. for $C_9H_{11}O_3NCl_2$: C, 42.88; H, 4.40; $-OCH_3$, 12.31. Found: C, 43.11; H, 4.49; $-OCH_3$, 12.46.

The use of chloroform and a reaction temperature of 45° gave similar results.

o-**Fluoro-α-methoxyphenylacetic acid** was isolated as the **ammonium salt** by treating the crude acid with excess ammonium hydroxide and evaporating to dryness. After two recrystallizations from a 2:1 ethyl acetate–ethanol solution containing some ammonia, the material melted at 155–157.5°. From 9.5 g. of *o*-fluorobenzaldehyde, there was obtained 7.2 g. (51% of theor.) of the unrecrystallized ammonium salt and 4.2 g. (30% of theor.) of the twice recrystallized material.

Anal. Calcd. for $C_9H_{12}O_3NF$: C, 53.72; H, 6.01; N, 6.96; $-OCH_3$, 15.43. Found: C, 53.66; H, 5.92; N, 7.10; $-OCH_3$, 15.61.

The **free acid** was an oil.

m-**Fluoro-α-methoxyphenylacetic acid** was isolated as the **sodium acid salt**, m.p. 209–211° after two recrystallizations from 50% aqueous ethanol. Its neutral equivalent was 392 compared to the theoretical value of 390. From 10 g. of *m*-fluorobenzaldehyde, 8.7 g. (59% of theor.) was obtained of the washed but unrecrystallized sodium acid salt. **The free acid** obtained from the sodium acid salt was an oil. **The ammonium salt**, obtained as above, was recrystallized three times from 2:1 ethyl acetate–ethanol solution and then melted at 153–155°.

Anal. Calcd. for $C_9H_{12}O_3NF$: C, 53.72; H, 6.01; N, 6.96; $-OCH_3$, 15.43. Found: C, 54.04; H, 5.82; N, 6.97; $-OCH_3$, 15.64.

p-**Fluoro-α-methoxyphenylacetic acid** was isolated as the **sodium acid salt**, m.p. 235–237° after two recrystallizations from 50% aqueous ethanol. Its neutral equivalent was 388 compared to the theoretical value of 390. From 10 g. of the *p*-fluorobenzaldehyde, 10.2 g. (69% of theor.) of the washed but unrecrystallized acid salt was obtained. **The free acid** was crystallized at −20° from a 3:1 ligroin–chloroform mixture, and melted at 54–56°.

Anal. Calcd. for $C_9H_9O_3F$: C, 58.70; H, 4.93; $-OCH_3$, 16.85; neut. equiv., 184. Found: C, 58.89; H, 4.70; $-OCH_3$, 16.70; neut. equiv., 184.

α-Methoxy-*o*-toluacetic acid was isolated as the **ammonium salt** by treating the crude acid with ammonium hydroxide. It melted at 153–155° after recrystallization from 2:1 ethyl acetate–ethanol solution. From 30 g. of *o*-tolualdehyde, 24 g. (49% of theor.) of recrystallized salt was obtained.

Anal. Calcd. for $C_{10}H_{15}O_3N$: C, 60.89; H, 7.67; N, 7.10; $-OCH_3$, 15.74. Found: C, 60.67; H, 7.86; N, 7.22; $-OCH_3$, 15.95.

The free acid was an oil.

α-Methoxy-*m*-toluacetic acid was isolated as the **sodium acid salt**, m.p. 209–210°, neutral equivalent 382 compared with the theoretical value of 382, after two recrystallizations from 50% aqueous ethanol. From 5 g. of the *m*-tolualdehyde, 1.8 g. (24% of theor.) of the washed but unrecrystallized sodium acid salt was obtained. The recrystallized sodium acid salt was analyzed in preference to the ammonium salt since the latter consistently gave an analysis high in carbon by about 1%, presumably because of loss of ammonia.

Anal. Calcd. for $C_{20}H_{23}O_6Na$: C, 62.82; H, 6.06; $-OCH_3$, 16.23. Found: C, 62.87; H, 6.36; $-OCH_3$, 16.43.

α-Methoxy-*p*-toluacetic acid was isolated as the **sodium acid salt**, m.p. 202–204°, neutral equivalent 382 compared with the theoretical value of 382, after two recrystallizations from absolute ethanol. Eight grams (33% of theor.) of the washed but unrecrystallized acid salt was obtained from 15 g. of *p*-tolualdehyde. **The free acid** was an oil. **The ammonium salt**, m.p. 148–151° after recrystallization from a 6:1 ethyl acetate–ethanol solution containing ammonia, gave an analysis indicating some loss of ammonia.

Anal. Calcd. for $C_{10}H_{15}O_3N$: C, 60.89; H, 7.67; N, 7.10; $-OCH_3$, 15.74. Found: C, 61.21; H, 7.40; N, 6.82; $-OCH_3$, 15.75.

α-Methoxymesitylacetic acid was isolated as the **ammonium salt by treating the crude acid** (0.3 g. from 20 g. of 2,4,6-trimethylbenzaldehyde) with ammonium hydroxide. It could not be obtained in an analytically pure form. The acid was converted to the **normal sodium salt** by titrating with sodium hydroxide to the phenolphthalein end-point, evaporating the solution to obtain the crude salt, and recrystallizing from a 1:1 ethyl acetate–ethanol solution.

Anal. Calcd. for $C_{12}H_{15}O_3Na$: C, 62.60; H, 6.57; $-OCH_3$, 13.47. Found: C, 62.49; H, 6.49; $-OCH_3$, 13.18.

α-Methoxy-3,4-methylenedioxyphenylacetic acid was isolated as a mixture of the normal sodium salt and the free acid by following the general procedure for precipitating sodium acid salts, but omitting the water and acetone washes. From 19 g. of piperonal, there was obtained 8.2 g. (25% of theor.). **The free acid** was recrystallized alternately from 50% aqueous ethanol and a ligroin–benzene mixture. It melted at 90–91°.

Anal. Calcd. for $C_{10}H_{10}O_5$: C, 57.14; H, 4.80; $-OCH_3$, 14.76. Found: C, 57.01; H, 4.84; $-OCH_3$, 14.92.

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[11] F. Straus, *Ann.*, **393**, 319 (1912).

From the reaction of piperonal, chloroform and sodium methoxide in excess methanol at temperatures below 30°, a small amount (4 g. from 37 g. of piperonal) of **3,4,3',4'-di-(methylenedioxy)-deoxybenzoin**, m.p. 114° after recrystallization from ethanol was obtained. The literature melting point is 114.5°.[12]

α-Methoxy-*m*-nitrophenylacetic acid was obtained first as the crude acid, and this was distilled at 163–166° at 1.5 mm. Recrystallization of the distillate from benzene gave yellow crystals, m.p. 109–110°. From 10 g. of *m*-nitrobenzaldehyde, 0.6 g. (4% of theor.) was obtained.

Anal. Calcd. for $C_9H_9O_5N$: C, 51.19; H, 4.29; $-OCH_3$, 14.69; neut. equiv., 211. Found: C, 51.35; H, 4.07; $-OCH_3$, 14.62; neut. equiv., 210.

α,β-Di-(*p*-nitrophenyl)-glycidic acid was obtained as the **sodium salt** by treating *p*-nitrobenzaldehyde in the usual way and attempting to precipitate the sodium acid salt. From 19 g. of *p*-nitrobenzaldehyde, 4 g. was obtained. Acidification yielded the **free acid**, m.p. 188–190° after recrystallization from 50% aqueous ethanol.

Anal. Calcd. for $C_{15}H_{10}O_7N_2$: C, 54.55; H, 3.05; neut. equiv., 330. Found: C, 54.66; H, 3.16; neut. equiv., 328.

***p*-Cyano-α-methoxyphenylacetic acid** was isolated as the **ammonium salt** by treating the crude acid (6 g. from 10 g. of *p*-cyanobenzaldehyde, 48% of theor.) with ammonium hydroxide. The ammonium salt was recrystallized from a 95:5 ethyl acetate–ethanol mixture. It melted at 154–155°.

Anal. Calcd. for $C_{10}H_{12}O_3N_2$: C, 57.68; H, 5.81; N, 13.4; $-OCH_3$, 14.91. Found: C, 57.47; H, 5.91; N, 13.2; $-OCH_3$, 15.06.

α-Methoxy-(1-naphthalene)-acetic acid was isolated as a mixture of the normal sodium salt and the free acid by following the general procedure for precipitating sodium acid salts, but omitting the acetone and water washes. Acidification of an alkaline solution of the mixture yielded the **free acid**, m.p. 149–150° after recrystallization from 50% aqueous ethanol. From 40 g. of 1-naphthylaldehyde, 31 g. (49% of theor.) was obtained.

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.60; $-OCH_3$, 14.33; neut. equiv., 216. Found: C, 72.37; H, 5.51; $-OCH_3$, 14.01; neut. equiv., 216.

α-Methoxy-(2-naphthalene)-acetic acid was isolated as the **sodium acid salt,** m.p. 243–244°, neutral equivalent 457 compared with the theoretical value of 454, after recrystallization from 50% aqueous ethanol. From 5 g. of the 2-naphthylaldehyde, 2 g. (24% of theor.) was obtained. **The free acid** was obtained by dissolving the sodium acid salt in dilute sodium hydroxide solution and acidifying with an excess of 2 *N* hydrochloric acid. The acid melted at 98.5–99.5° after recrystallization first from hot water and then from ligroin (b.p. 60–80°).

Anal. Calcd. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.60; $-OCH_3$, 14.33; neut. equiv., 216. Found: C, 72.18; H, 5.56; $-OCH_3$, 14.43; neut. equiv., 219.

The 2-naphthaldehyde was prepared by a Sommelet reaction on 2-(bromomethyl)-naphthalene. It was purified by means of its sodium bisulfite addition product.

α-Methoxy-(2-thiophene)-acetic acid was obtained first as the crude acid (11 g. from 10 g. of thiophene-2-carboxyaldehyde). This was converted to the **sodium acid salt** by treatment with the theoretical amount of 20% sodium hydroxide solution, and the sodium acid salt was recrystallized from absolute ethanol. The sodium hydrogen di-(α-methoxy-2-thiopheneacetate) melted at 207–210° dec., and had a neutralization equivalent of 364 compared with a theoretical value of 366. Three grams of the acid salt, washed with acetone but not recrystallized, was obtained (20% of theor.). The **ammonium salt** was made from the free acid obtained by acidifying the sodium acid salt. The ammonium salt melted at 145–146° dec. after recrystallization from acetone. This melting point value was obtained by placing the capillary in melting point bath at 140° with the temperature rising 2° per min.

Anal. Calcd. for $C_7H_{11}O_3SN$: C, 44.43; H, 5.86; N, 7.51; $-OCH_3$, 16.40. Found: C, 44.73; H, 6.04; N, 7.60; $-OCH_3$, 16.13.

α-Methoxy-α-phenylpropionic acid was isolated as a mixture of the normal sodium salt and the free acid. There was obtained 8.2 g. (16% of theor.) from 30 g. of acetophenone. **The free acid** was an oil. **The ammonium salt** melted at 175–176° after recrystallization from a 3:1 ethyl acetate–ethanol solution containing ammonia.

Anal. Calcd. for $C_{10}H_{15}O_3N$: C, 60.89; H, 7.67; N, 7.10; $-OCH_3$, 15.74. Found: C, 61.09; H, 7.46; N, 6.98; $-OCH_3$, 15.42.

Preparation of Salts.—Using 50% aqueous methanol as the solvent, one molar solutions were made up using the acids prepared or their ammonium salts, with the exception of 2,6-dichloro-α-methoxyphenylacetic acid which was obtained in insufficient amounts. The acid solutions were half neutralized with ammonium hydroxide. To four drops of each solution was added an equivalent amount of a one molar solution in 50% aqueous methanol of one of the chlorides of magnesium, lithium, potassium, rubidium or cesium. The two precipitates observed were voluminous and formed within 30 min.

The solubility data were determined by evaporating known values of saturated solutions to dryness or, in the case of the acid salts, by titrating a sample of the saturated solution.

Acknowledgment.—It is a pleasure to acknowledge the financial aid received from the Union Carbide Company.

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The Importance of Steric Effects in the Baeyer–Villiger Oxidation

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RECEIVED FEBRUARY 20, 1961

From a study of the peroxidation of 1-methylnorcamphor, fenchone, camphor and epicamphor, it has been possible to demonstrate the importance of two types of steric effects on the course of the Baeyer–Villiger reaction.

The mechanism of the Baeyer–Villiger reaction has been a subject of considerable current interest.[1-5] From the established migrational aptitude sequence for alkyl groups, 3°>2°>1°, it appears that electronic effects are the dominant factors in controlling the course of the reaction. Although several authors[3,6-8] have discussed the importance of steric effects, there are no examples

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