that the effect of the addition of neutral salts on ionic reaction rates is not dependent upon the ionic strength of the solutions. Their position is summarized as follows. "In reactions between ions of opposite charge sign, both salt ions may affect the rate, but the effect of one type may be dominant. The effects are quantitatively interpretable in terms of an ion association constant and specific rate constants for the associated and non-associated reactants."

This approach, taken by Olson and Simonson to treat the effects of ionic interactions on the rates of reaction of ionic species, is even more pertinent for reactions in alcohol than in water, for in ethanol, with its lower dielectric constant, ion association is far more important. In ethanol aggregates higher than ion-pairs probably should be considered, but for the sake of simplicity, we will limit this discussion to 1:1 associations. Our simplest experiments involve initially two salts (AB and CD) and four different ions in solution. This case will, therefore, involve the four equilibria

$$AB \rightleftharpoons A^+ + B^-$$
$$CD \rightleftharpoons C^+ + D^-$$
$$AD \rightleftharpoons A^+ + D^-$$
$$CB \rightleftharpoons C^+ + B^-$$
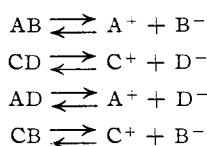
and as many as nine or more possible specific rate constants for the associated and non-associated species reacting to form products. In the most complicated case which we studied the solution contained three salts and six different ions. In this system there are nine equilibria, and the number of passes through the origin and has the correct theoretical slope, equal to

$$\frac{2N^2\epsilon^3(2\pi)^{1/2}}{2.303(DRT)^{3/2}(1000)^{1/2}}$$

This may, however, be largely fortuitous.

(13) A. R. Olson and T. R. Simonson, J. Chem. Phys., **17**, 1167 (1949).

possible specific rate constants is multiplied proportionately.

In the light of the foregoing it is not surprising to find that our measured rate constants cannot be accommodated in a satisfactory manner as a function of the ionic strength. Even more important, the apparent anomalies are understandable in terms of the above hypothesis. For example, the very substantial differences in rate observed for the reactions with sodium ethoxide and lithium ethoxide and the very different effects observed with the two neutral salts which we have studied are both qualitatively in accord with the intervention in these systems of the equilibria which we have described. Finally, the results of the first three experiments shown in Table III are readily encompassed by this picture. The three measurements are all at the same ionic strength and differ only in the nature of the anion associated with the quaternary ammonium ion, yet there are appreciable increases in rate as one goes from the bromide to the nitrate to the picrate. Moreover, these rates are in the order of degree of association of the quaternary ammonium salts, for the bromide is more associated than the nitrate, which is in turn more associated than the picrate.[14]

The present results are at least qualitatively in accord with the Olson hypothesis. A quantitative treatment has not been attempted and is unwarranted at this time. In the absence of measurements of the association constants of the pertinent salts in ethanol at 50.8°, there are so many adjustable parameters that even a success in fitting the data would be of questionable significance.

(14) Data on the degree of dissociation of the above quaternary ammonium salts in ethanol are not available. Data on the dissociation of tetrabutylammonium salts in acetone at 25° are available (H. S. Harned and B. B. Owen, "The Physical Chemistry of Electrolytic Solutions," Reinhold Publishing Corp., New York, N. Y., 3rd ed., 1958, p. 704). The ionization constants for tetrabutylammonium bromide, nitrate and picrate are 3.29×10^{-2}, 5.46×10^{-2} and 22.3×10^{-2} mole l. $^{-1}$, respectively.

[CONTRIBUTION FROM THE TOKYO INSTITUTE OF TECHNOLOGY, OOKAYAMA, MEGURO-KU, TOKYO, JAPAN]

The Reactions of Primary Nitroparaffins with Isocyanates[1]

By Teruaki Mukaiyama and Toshio Hoshino

The reactions of isocyanates with primary nitroparaffins, such as nitroethane, 1-nitropropane and phenylnitromethane, in the presence of a catalytic amount of tertiary alkyl amine have been found to give sym-disubstituted ureas, furoxane and carbon dioxide in excellent yields, instead of the expected addition compounds of N-substituted α-nitro-fatty acid amides. The reaction is thought to proceed through the intermediates amine and nitrile oxide, formed by the decomposition of the addition compound of isocyanate and aci-nitroparaffin with spontaneous evolution of carbon dioxide. The disubstituted urea is formed by the reaction of amine with isocyanate; the furoxane is formed by the dimerization of nitrile oxide. The intermediate nitrile oxide can be demonstrated by the formation of isoxazoline or oxadiazoline when isocyanate, nitroparaffin and tertiary amine are allowed to react in the presence of unsaturated compounds. The reaction is not observed in the absence of teritary alkyl amine or when tertiary nitroparaffins such as t-nitrobutane are allowed to react with isocyanate.

The reaction between the sodium salt of nitromethane and phenyl isocyanate has been found[2,3] to give α-nitroacetanilide and nitromalonanilide. Boyd and Leshin[4] recently extended the reactions of

(1) T. Hoshino and T. Mukaiyama, partly published in Japanese Patent Publication 34-9855 (1959).
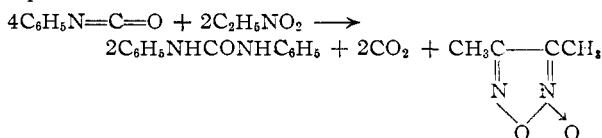(2) A. Michael, Ber., **38**, 22, 39, 46 (1905).
(3) W. Steinkopf and H. M. Daege, ibid., **44**, 497 (1911).
(4) R. N. Boyd and R. Leshin, THIS JOURNAL, **75**, 2762 (1953).

nitromethane and ethyl nitroacetate with isocyanates such as 1-naphthyl, o-chlorophenyl and o-tolyl isocyanates, and obtained a series of N-substituted α-nitroacetanilides and α-carbethoxy-α-nitroacetanilides. However, it has been reported that nitroethane, 1- and 2-nitropropane and phenylnitromethane do not condense with phenyl isocyanate, either in the presence of potassium

carbonate or when used in the form of their salts. Steinkopf and Daege[3] obtained sym-diphenylurea, triphenylbiuret, triphenyl isocyanurate, sodium carbonate and nitrogen when phenyl isocyanate was allowed to react with the sodium salt of nitroethane in benzene. Hantzsch and Schultze[5] obtained sym-diphenylurea from the reaction of phenyl isocyanate and aci-phenylnitromethane. The formation of sym-diphenylurea was attributed to the reaction of the isocyanate with water formed by the dehydration of the nitro compound. The dehydrated product, nitrile oxide or furoxane, was not obtained by these investigators.

In the present experiments, tertiary alkyl amines, such as triethylamine and tri-n-butylamine, were used as basic catalysts for the addition of phenyl isocyanate and nitroethane to yield N-phenyl-α-nitropropionanilide for use in the kinetic studies of the thermal dissociation of organic compounds[6] containing the acid amide linkage.

When a catalytic amount of amine is added to the mixture of phenyl isocyanate and nitroethane in dry ether, the reaction starts immediately, carbon dioxide is evolved, and sym-diphenylurea precipitates quantitatively at room temperature in about 1 hour. From the dark brown filtrate, dimethylfuroxane is obtained in high yield according to the equation

$$4C_6H_5N=C=O + 2C_2H_5NO_2 \longrightarrow$$
$$2C_6H_5NHCONHC_6H_5 + 2CO_2 + CH_3C\underset{\underset{O}{N}}{\overset{\overset{O}{N}}{\|}}\text{---}\overset{\overset{O}{N}}{\underset{\underset{O}{N}}{\|}}CCH_3$$

Similarly, 1-nitropropane and phenylnitromethane react with phenyl isocyanate in the presence of tertiary alkyl amine to form diethylfuroxane and diphenylfuroxane, respectively. In order to identify the yellow furoxanes thus obtained, dimethylfuroxane and diethylfuroxane were reduced under atmospheric pressure in the presence of Raney nickel. After the absorption of 1 mole of hydrogen colorless hydrogenated products $C_4H_8N_2O_2$ or $C_6H_{12}N_2O_2$ are obtained. These melt respectively at 109 ∼ 111° and 90 ∼ 92°, solidify at an elevated temperature and remelt finally at 231 ∼ 232° and 185∼186° with partial sublimation. These resolidified materials are identical with α-dimethylglyoxime and α-diethylglyoxime, respectively, and show no depression in mixed melting points with authentic samples. The products melting at 109° and 90° are therefore γ-isomers I of glyoximes readily isomerized to the α-isomers II on heating.

R—C——C—R → R—C——C—R → R—C——C—R
(structures I and II, glyoxime structures)
I   II
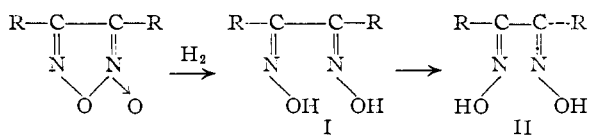
The diphenylfuroxane obtained showed no depression in mixed melting point with a colorless authentic sample.[7]

Ethyl isocyanate also reacts with nitroethane in the presence of tertiary alkyl amine to give di-

(5) A. Hantzsch and O. W. Shultze, *Ber.*, **29**, 2251 (1896).
(6) T. Mukaiyama and M. Iwanami, THIS JOURNAL, **79**, 73 (1957).
(7) J. H. Boyer and U. Toggweiler, *ibid.*, **79**, 895 (1957).

methylfuroxane, sym-diethylurea and carbon dioxide. However, the reaction is more sluggish than that of phenyl isocyanate.

These reactions of primary nitroparaffins (except nitromethane) with phenyl isocyanate proceed very rapidly at room temperature in the presence of a catalytic amount of tertiary alkyl amine, but the same reactions do not occur in the absence of catalyst even at the boiling point.

When weak bases such as pyridine or N-alkyl aniline are used, the reaction proceeds very slowly and gives only disubstituted urea in only 5% yield after three days at ordinary temperature.

The effect of catalysts indicates that the nitroparaffin at first forms nitronate ion and one of the oxygens of the nitronate ion in turn combines with the positively charged carbon of the isocyanate forming the addition compound III. Since the nitronate ion is an ambident anion, the carbon of the nitronate ion would on the other hand combine with isocyanate and form the N-substituted α-nitro-fatty acid amide IV. However, the latter reaction may be much slower in α-substituted nitroparaffins than O-addition or, if the amide IV is formed, it would readily dissociate to its components in the presence of tertiary amines. Thus α-substituted nitroparaffins give substituted urea in greater than 90% yield while nitromethane gives about 50% yield of sym-disubstituted urea under the same conditions.

$$RCH_2NO_2 + R_3N \rightleftarrows (RCHNO_2)^- + R_3N^+H$$

(reaction scheme showing structures III and IV)
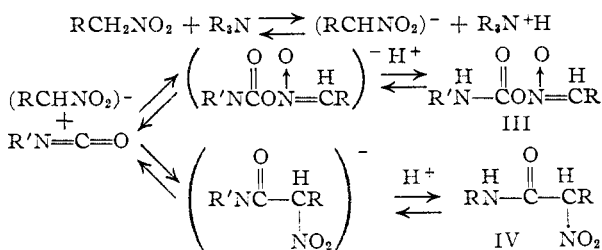
By a proton transfer the adduct III decomposes to nitrile oxide and carbamic acid. The latter decomposes easily to amine and carbon dioxide, and the amine then reacts with isocyanate to form the disubstituted urea. Nitrile oxide dimerizes[8] to form furoxane.

(reaction scheme)

III ⟶ R'NCOH + RC≡N→O
R'NH2 + CO2
R'N=C=O
(furoxane structure)
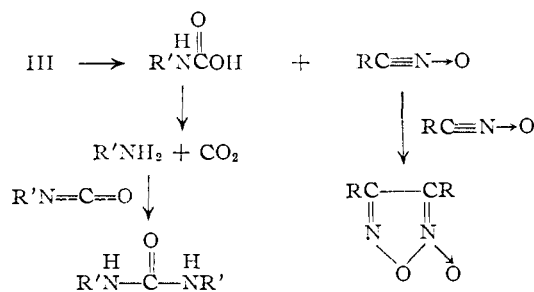
By this proposed mechanism primary nitroparaffins are able to react with isocyanate to form furoxane, urea and carbon dioxide. This is confirmed by the following experiments: Tertiary nitroparaffin, for example t-nitrobutane, does not react with phenyl isocyanate in the presence of triethylamine. On heating them for 60 hours, t-nitrobutane is recovered unchanged and phenyl isocyanate is con-

(8) H. Wieland, *Ber.*, **40**, 1671 (1907).

TABLE I

REACTIONS OF NITROPARAFFINS, PHENYL ISOCYANATE AND UNSATURATED COMPOUNDS IN THE PRESENCE OF TRIETHYLAMINE

| Unsaturated compounds	Di-phenyl-urea, %	Product (isoxazoline or oxadiazoline)	—B.p. (m.p.),— °C.	Mm.	Yield, %	—Carbon, %— Calcd.	Found	—Hydrogen, %— Calcd.	Found	—Nitrogen, %— Calcd.	Found
			(a)	Nitroethane							
1 Styrene	99	$C_{10}H_{11}NO$	133–134	6	79	74.51	74.00	6.88	6.94		
2 Acrylonitrile	85	$C_5H_6N_2O$	124–125	7	79	54.54	54.30	5.49	5.67		
3 Vinyl acetate	90.5	$C_6H_9NO_3$	(78)		53.5	50.34	50.41	6.34	6.25	9.79	10.04
4 n-Butyl vinyl ether	85	$C_8H_{15}NO_2$	96–97	8	82	61.12	61.00	9.62	9.42		
5 Allyl acetate	90	$C_7H_{11}NO_3$	124–125	6	88	53.49	53.11	7.05	7.12		
6 Ethyl cinnamate	91	$C_{13}H_{15}NO_3$	164–165	5	67.5	66.93	66.75	6.48	6.39	6.0	6.06
7 Diethyl maleate	95	$C_{10}H_{15}NO_5$	145	4	17.5	52.39	52.43	6.60	6.48		
8 Benzalaniline	90.5	$C_{15}H_{14}N_2O$	(76–77)		10.2	75.60	75.68	5.92	6.04	11.76	11.89
			(b)	1-Nitropropane							
1 Styrene	95	$C_{11}H_{13}NO$	146–147	8	57.5	75.40	74.90	7.48	7.20		
2 Acrylonitrile	92	$C_6H_8N_2O$	116	3	92	58.05	57.77	6.50	6.49	22.57	22.43
3 Vinyl acetate	85	$C_7H_{11}NO_3$	(37–38)		89					8.91	8.82
4 n-Butyl vinyl ether	85	$C_9H_{17}NO_2$	100–101	6	62	63.13	63.27	10.10	9.42		
5 Allyl acetate	86	$C_8H_{13}NO_3$	134–135	10	65	56.12	55.85	7.65	7.68		
6 Ethyl cinnamate	97	$C_{14}H_{17}NO_3$	166–168	5	76.5	67.97	6.771	6.93	6.82		
7 Benzalaniline	83.5	$C_{16}H_{16}N_2O$	(67–68)		17.8					11.10	11.28

TABLE II

REACTIONS OF NITROETHANE, 1-NITROPROPANE AND PHENYLNITROMETHANE WITH PHENYL ISOCYANATE

1. Nitro-ethane, g.	Phenyl isocyanate, g.	sym-Di-phenylurea, g.	Yield, %	Dimethyl-furoxane, $C_4H_6N_2O_2$, g.	Yield, %	B.p. °C.	Mm.	Nitro-ethane recovd., g.	B.p. °C.	Mm.
15.8	25	21.4	96	5.1	84.4	107–108	5	4.7	32–33	11

Anal. Calcd. for $C_4H_6N_2O_2$: C, 42.10; H, 5.30; N, 24.55. Found: C, 43.35; H, 5.59; N, 23.70.

2. 1-Nitro-propane, g.	Phenyl isocyanate, g.	sym-Di-phenylurea, g.	Yield, %	Diethyl-furoxane, $C_6H_{10}N_2O_2$, g.	Yield, %	B.p. °C.	Mm.	1-Nitro-propane recovd., g.	B.p. °C.	Mm.
18.7	25	22.0	98	6.9	93.2	120–122	20	7.8	36–38	18

Anal. Calcd. for $C_6H_{10}N_2O_2$: C, 50.70; H, 7.10; N, 19.71. Found: C, 50.93; H, 7.17; N, 19.28.

3. Phenyl-nitromethane, g.	Phenyl isocyanate, g.	sym-Di-phenylurea, g.	Yield, %	Diphenyl-furoxane, g.	Yield, %	M.p., °C.
15.0	25	21.6	97	10.7	82	114.5–115.5[a]
(0.11 mole)	(0.21 mole)					

[a] This furoxane was yellow after repeated recrystallization from ethanol but was identical with an authentic sample,[7] showing no depression in mixed melting point.

verted to triphenyl isocyanurate in about 90% yield. Secondary nitroparaffins, such as 2-nitropropane and α-methylphenylnitromethane, react with phenyl isocyanate in the presence of tertiary alkyl amine to give sym-diphenylurea in about 20% yield with evolution of carbon dioxide, but the corresponding dehydrated product is not obtained.

The intermediate, i.e., nitrile oxide, is demonstrated by the formation of isoxazoline or oxadiazoline when isocyanate, primary nitroparaffin and tertiary alkyl amine are allowed to react in the presence of unsaturated compounds. When vinyl acetate is used, for example, the reaction is expressed by the following equation, which involves the addition of nitrile oxide to vinyl acetate to form isoxazoline.[9]

$$RCH_2NO_2 + CH_2{=}CHOAc + 2C_6H_5N{=}C{=}O \longrightarrow$$
$$CO_2 + C_6H_5NHCONHC_6H_5 + AcOCH{-}{-}CH_2$$
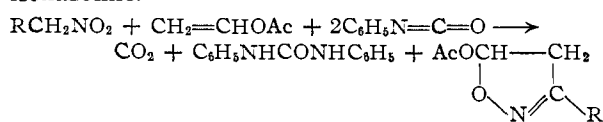
3-Phenylisoxazolines are prepared by using isolable benzonitrile oxide according to the procedure reported by Quilico; on the other hand, 3-alkyl isoxa-

(9) A. Quilico, G. Stagno D'Alcontres and P. Grünanger, *Nature*, 166, 227 (1950).

zolines in which unstable alkyl nitrile oxides participate can be synthesized by this method.

The yields of isoxazolines are fairly good in ordinary unsaturated compounds. However, benzalaniline having a carbon–nitrogen double bond gives the corresponding oxadiazoline in about 10 − 18% yield. This may be due to the difficulty with which nitrile oxide adds to this unsaturated compound, so that the dimerization of nitrile oxide to form furoxane is favored. The results of the experiment are summarized in Table I.

3-Methyl-5-acetoxy-isoxazoline and 3-ethyl-5-acetoxy-isoxazoline are converted to the corresponding 3-alkyl isoxazoles in high yield by eliminating acetic acid above 160°.
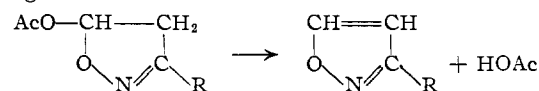
Experimental

Reactions of Nitroethane, 1-Nitropropane and Phenylnitromethane with Phenyl Isocyanate.—To an ice-cooled solution of phenyl isocyanate (0.21 mole) and nitroalkane (0.21 mole) in 50 ml. of dry ether was added 10 drops of triethylamine. The reaction started soon, evolving carbon dioxide, and sym-diphenylurea began to precipitate in 20 minutes. After shaking the reaction mixture for 1 hour,

it was refluxed for an additional hour, cooled and filtered. The precipitate of sym-diphenylurea was washed with ether and weighed. The dark brown ether solution was distilled in vacuo. The nitroalkane was recovered and the yellow furoxane was obtained. The details of each experiment are summarized in Table II.

The same results were obtained when tri-n-butylamine was used instead of triethylamine.

Reaction of p-Nitrophenylnitromethane and Phenyl Isocyanate.—A solution of p-nitrophenylnitromethane (3.3 g., 0.018 mole) and phenyl isocyanate (4.3 g., 0.036 mole) in 200 ml. of dry ether in the presence of 10 drops of triethylamine was heated to reflux for 6 hours to give sym-diphenylurea, 3.1 g. (80% of theoretical) and a dark brown resinous material instead of an expected di-p-nitrophenylfuroxane. This resinous material may be a polymer of p-nitrobenzonitrile oxide.

Reaction of 1-Nitropropane with Ethyl Isocyanate.—A solution of 1-nitropropane (6.3 g., 0.07 mole) and ethyl isocyanate (5.0 g., 0.07 mole) in 15 ml. of dry ether in the presence of 10 drops of triethylamine was heated under reflux for 55 hours to give sym-diethylurea, 3.1 g. (77.5% of theoretical), m.p. 108–110°, and diethylfuroxane, b.p. 109–110°(10 mm.), 1.6 g. (64% of theoretical). The 1-nitropropane, 1.3 g., was recovered.

Reduction of Dimethylfuroxane and Diethylfuroxane.—Dimethylfuroxane (2.7 g.), diluted with 40 ml. of 95% ethanol, was reduced by hydrogen under atmospheric pressure in the presence of Raney nickel at room temperature. It absorbs 1 mole of hydrogen in 5 hours. On evaporating the reaction mixture under reduced pressure, 0.15 g. of the red ether-insoluble product, $C_8H_{14}N_4O_4Ni$, and 1.4 g. of the ether-soluble product, $C_4H_8N_2O_2$, were obtained. The latter melted at 109–111°, solidified at an elevated temperature and remelted at 231–232°. The resolidified material was identical with α-dimethylglyoxime and showed no depression in mixed melting point with an authentic sample. The product melting at 109° may therefore be considered to be the γ-isomer of dimethylglyoxime.

Anal. Calcd. for $C_8H_{14}N_4O_4Ni$: N, 19.37. Found: N, 19.13. Calcd. for $C_4H_8N_2O_2$: C, 41.37; H, 6.94; N, 24.13. Found: C, 41.54; H, 6.97; N, 23.96.

Using the procedure described above, the reduction of 2.0 g. of diethylfuroxane gave 1.2 g. of hydrogenated product, $C_6H_{12}N_2O_2$, m.p. 90–92° recrystallized from benzene. It solidified also at an elevated temperature and remelted at 185–186° with partial sublimation. The resolidified material was identical with α-diethylglyoxime and showed no depression in mixed melting point with an authentic sample. The product melting at 90° may therefore be considered to be the γ-isomer of diethylglyoxime.

Anal. Calcd. for $C_6H_{12}N_2O_2$: C, 49.98; H, 8.39; N, 19.43. Found: C, 50.10; H, 8.35; N, 19.30.

Preparation of 3-Methyl(ethyl)isoxazolines and Oxadiazolines.—To 25 ml. of dry benzene containing 0.1 mole of phenyl isocyanate and 0.055 mole of unsaturated compound (Table I) was added to a solution of 0.055 mole of nitroethane (1-nitropropane) and 10 drops of triethylamine in 15 ml. of dry benzene. The reaction started, evolving carbon dioxide, and sym-diphenylurea precipitated. After shaking the reaction mixture for 1 hour, it was refluxed for an additional hour, cooled and filtered. The brownish-yellow benzene solution was then distilled and the liquid products were distilled under reduced pressure. The crystalline products obtained in the case of vinyl acetate were recrystallized from 95% ethanol. The yield of sym-diphenylurea and the yields, boiling points (melting points) and analyses for isoxazolines and oxadiazolines are listed in Table I.

Preparation of 3-Methyl(ethyl)isoxazoles.—By heating 14.3 g. of 3-methyl-5-acetoxyisoxazoline above 170° under atmospheric pressure, products boiling at 115–118° were obtained. They were taken up in ether and washed successively with a small amount of dilute sodium hydroxide solution and water, dried over calcium chloride, and distilled. 3-Methylisoxazole, C_4H_5NO, 5.2 g. (62.6% of theoretical), b.p. 114–114.5°, was obtained.

Anal. Calcd. for C_4H_5NO: C, 57.82; H, 6.07. Found: C, 57.40; H, 6.15.

Using the procedure described above, 3-ethyl-5-acetoxyisoxazoline decomposed at 160° and gave 3-ethylisoxazole. C_5H_7NO, b.p. 130–131°.

Anal. Calcd. for C_5H_7NO: C, 61.84; H, 7.27. Found: C, 61.2; H, 7.70.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF DELAWARE, NEWARK, DEL.]

The Oxidation of Aliphatic Esters with Lead Tetraacetate[1]

BY WILLIAM A. MOSHER AND CLIFTON L. KEHR

A novel reaction of lead tetraacetate resulting in acetoxylation of the alcoholic component of aliphatic esters has been investigated. A study of the products shows that an ionic mechanism involving methyl carbonium ions readily explains the course of the reaction. These results supplement previously reported evidence that lead tetraacetate is capable of functioning as an ionic reagent in oxidation reactions.

During an investigation[2] of the oxidation of organic acids with lead tetraacetate, it was noted that in the case of the lower aliphatic acids the material balances of the oxidation reactions were quite low. Because the lead tetraacetate was nevertheless invariably completely reduced, it became apparent that one or more of the initial reaction products was being attached by the oxidizing agent to give products too complex to isolate. The presence of small amounts of esters among the products of these reactions led to the present investigation. A summary of the products of the unique reaction of lead tetraacetate with esters is given along with pertinent reaction conditions in Table I (in each case glacial acetic acid was used as the solvent).

The course of the reaction of lead tetraacetate with the above esters apparently proceeds initially through the acetoxylation of the α-carbon atom of the alcoholic component of the ester. In each reaction studied the ester was used in excess of the required molar amount in order to ensure that a favorably high concentration be present even toward the end of the reaction. In spite of this precaution, however, the yields of any one product obtained were quite low. This is undoubtedly true because the product itself is a much better

(1) Presented in part before the Division of Organic Chemistry. American Chemical Society. Kansas City, Mo., April, 1954.

(2) W. A. Mosher and C. L. Kehr, THIS JOURNAL, 75, 3172 (1953).