

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Schmidt Reaction. II.¹ A New Rearrangement Observed during Degradation of Triethylacetic Acid

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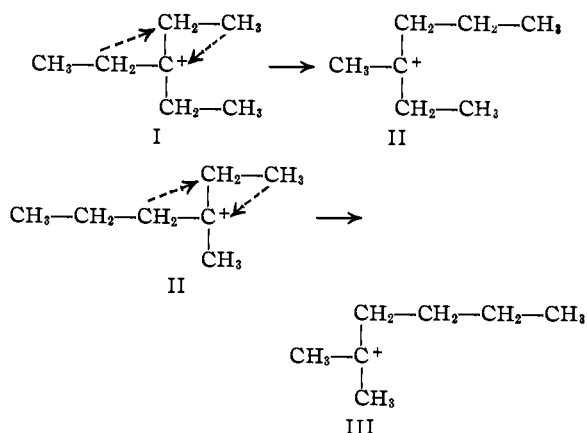
In investigating the reaction of trimethylacetic and dimethylethylacetic acids with sodium azide and sulfuric acid,¹ it was found that the yield of *t*-alkylamine was considerably less than theoretical, that the carboxylic group was degraded in part to carbon monoxide instead of carbon dioxide and that the alkyl group was cleaved to form ketones and primary amines. In order to determine whether this type of cleavage was general for tertiary aliphatic acids, the reaction of triethylacetic acid was chosen, since the expected cleavage products would be diethyl ketone and ethylamine, rather than a mixture of homologs.

When the reaction was carried out, it was found that both carbon monoxide and dioxide were evolved, but that a complex mixture of products was produced. Among the products definitely identified are acetone, methyl *n*-propyl ketone, a mixture of isomeric hexanones, carbon monoxide, carbon dioxide, nitrogen, ammonia, *n*-propylamine, *n*-butylamine and triethylacetamide. The presence of methyl *n*-butyl ketone is reasonably certain; and that of diethyl ketone, ethyl methyl ketone, ethyl *n*-propyl ketone, methylamine and ethylamine is probable. Considering the experimental difficulties involved, the yield of isolated products may be considered fairly high. The presence of still other substances (such as branched-chain isomers) is not completely excluded, but it seems probable that the most important reaction products have been found.

The rearrangement obviously occurring at some stage in the reaction appears not to have taken place upon the triethylacetic acid itself (or on ions formed from it in the presence of sulfuric acid) since triethylacetic acid in concentrated sulfuric acid at 50° can be recovered in good yield by dilution and since triethylacetamide is one of the products of the reaction. Triethylacetic acid, furthermore, can be prepared from the amide with nitrosyl sulfate in sulfuric acid.⁴

Rearrangement must have occurred, therefore, after elimination of carbon monoxide or dioxide from the molecule. In view of our results¹ with trimethylacetic and dimethylethylacetic acids, and also in view of the structures of the isolated

products, it appears probable that the rearrangement involves a triethylcarbonium ion, *e. g.*



Ion II on reaction with hydrazoic acid and subsequent hydrolysis should give ethyl methyl ketone, methyl *n*-propyl ketone, ethyl *n*-propyl ketone, methylamine, ethylamine and *n*-propylamine. Ion III should give rise to acetone, *n*-butyl methyl ketone, methylamine and *n*-butylamine. Evidence has been obtained that all these are formed perhaps with diethyl ketone from ion I and no evidence that other rearranged products are formed in significant amounts.

If the rearrangement is formulated as the usual Whitmore shift of one alkyl group at a time, it is necessary to assume four separate rearrangements and the formation of two neopentyl-type carbonium ions in order to explain the products formed. Since no products have been found which indicate the presence of carbonium ions of the neopentyl type, the rearrangement is shown instead as the simultaneous shift of two alkyl groups across a carbon-to-carbon single bond.

Although no exact parallel to this formulation has been found in the literature, there is some similarity to the concept used by Wallis and Bowman⁵ to explain the reaction of 2-methyl-2-phenylbutanol-1 with thionyl chloride. Since the chloride formed is both rearranged and optically active, they suggest that the anion must have entered the 2-position at the same time as the phenyl group was migrating to the 1-position with its electrons. In the proposed simultaneous shift of alkyl groups, both migrating groups act as anions entering a position as it is being vacated. Some analogy can also be drawn to the simultaneous shift of two groups across a double bond

(1) For Part I, Conditions and reaction mechanism with primary, secondary, and tertiary aliphatic acids, see *THIS JOURNAL*, **71**, 2233 (1949).

(2) This paper is constructed from part of a dissertation submitted by Conrad Schuerch, Jr., to the Faculty of the Massachusetts Institute of Technology in June, 1947, in partial fulfillment of the requirements for the degree of Doctor of Philosophy. It was presented before the Division of Organic Chemistry at the 112th meeting of the American Chemical Society in New York on September 18, 1947.

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(4) Haller and Bauer, *Compt. rend.*, **148**, 130 (1909).

(5) Wallis and Bowman, *J. Org. Chem.*, **1**, 383 (1936).

proposed as a mechanism for intramolecular Beckmann rearrangements.⁶

No rearrangements, similar to that observed in this work, have been previously reported^{6,7,8} to occur with related compounds. The mechanism does not appear improbable under the conditions of the Schmidt degradation, however, since the ion would be expected to be formed in high dilution and in a highly acid medium. These conditions would be expected to minimize both polymerization and proton emission, which are the usual methods by which the ion is stabilized.

Furthermore, if a triethylcarbonium ion is formed as postulated, there is present an electron pair-donor and -receptor system closely analogous to that of the methyl and ethylamines studied by Brown and co-workers⁹ and in which steric strain has been shown to become operative. In this case, the electron pair-receptor containing a small central atom surrounded by bulky groups is formed in the presence of an electron pair-donor, hydrazoic acid (or bisulfate ion). A consideration of molecular models shows that steric strain is greatly reduced after the triethylcarbonium ion has rearranged and that there is also more freedom of rotation of the alkyl groups after rearrangement.

The mechanism proposed, therefore, appears to be the simplest method of explaining the observed reaction, and accounts for the presence of all known products, except triethylacetamide.

Attempts were made to determine whether the rearrangement could be obtained with triethylcarbinol or 2-ethylpentene-2, and to determine whether the sulfuric acid or the hydrazoic acid was responsible. These experiments, however, were inconclusive.

Experimental

Reaction of Triethylacetic Acid.—Triethylacetic acid¹⁰ (30.6 g., 0.21 mole; b. p. 104–105° at 5 mm., f. p. 35.1°) dissolved in C. P. concentrated sulfuric acid (316 g., 3.2 moles) was allowed to react at 35–45° with sodium azide (28.7 g., 0.44 mole). Reaction was executed and acidic basic and neutral products isolated in the manner previously used for isobutyric acid. The evolved gases, after passing through a trap cooled with solid carbon dioxide, were collected over 5% sulfuric acid saturated with sodium sulfate. No material collected in the Dry Ice-trap. Each of the first three gas fractions comprised about 0.5 l.; the fourth and last was about 2.5 l. Analysis of the first fraction (collected when reaction was about one-third complete) gave carbon dioxide 8.8%, carbon monoxide 30.4%, other combustibles 0.0%, nitrogen 60.8%. The final fraction had the composition carbon dioxide 14.0%, carbon monoxide 22.2%, nitrogen 63.8%.

The mixture of volatile reaction products was appro-

(6) Wallis, in Gilman's "Organic Chemistry," 1st ed., John Wiley and Sons, New York, N. Y., 1938, p. 801.

(7) (a) Whitmore, *THIS JOURNAL*, **54**, 3274 (1932); (b) Whitmore and Woodburn, *ibid.*, **55**, 361 (1933); (c) Whitmore and Evers, *ibid.*, **55**, 813 (1933); (d) Whitmore and Williams, *ibid.*, **55**, 406 (1933).

(8) Marvel and Bateman, *ibid.*, **49**, 2914 (1927).

(9) Brown and co-workers, *ibid.*, **64**, 325, 2557 (1942); **66**, 435 (1944); **67**, 374, 378, 1765 (1945); *et al.*

(10) Schuerch and Huntress, *THIS JOURNAL*, **70**, 2824–2825 (1948).

riately separated into fractions containing acidic, basic and neutral components. The residual aqueous solution remaining after removal of the volatiles was not further investigated. Moreover, the distillate of acidic volatiles, even after saturation with salt gave only an insignificant quantity of oily material too small for identification. Our study of the neutral and basic volatiles, however, is recorded below.

Examination of Neutral Products.—The aqueous distillate containing only neutral reaction products was saturated with potassium carbonate causing separation of about 9 g. of a moist organic layer. Further working up of the carbonate layer increased this by about 0.3 g. These neutral fractions were combined, dried over solid potassium carbonate, and carefully fractionated through a Podbielniak column 60 cm. in length, 5 mm. in width and containing a hollow glass spiral. The results together with data for known ketones are assembled in Table I.

TABLE I
NEUTRAL PRODUCTS^{a,b,c,d}

Frac-tion	B. p., °C.	n _D ²⁰	Wt., g.	Ketone	B. p., °C.	n _D ²⁰
1 ^e	58.5–67	1.3642	0.3	Dimethyl	56	1.3590
2	62–77	1.3705	0.7			
3 ^f	77–81	1.3778	0.5	Ethyl methyl	80	1.3791
4	81–100	1.3823	1.3			
5	100–102.5	1.3892	0.5	Diethyl	102	1.3927
6	102.5–109	1.3914	0.5	Methyl <i>n</i> -propyl	102.3	1.3901
7	109–122	1.3958	1.2			
8 ^g	122–125	1.4002	0.7	Ethyl <i>n</i> -propyl	124	1.3990
9 ^h	125–127	1.4034	0.7	Methyl <i>n</i> -butyl	127.8	1.4007

^a A small amount of mesitylene added to diminish hold-up in the column comprised an eventual residue.

^b Fractions 4, 6, 7, 8 and 9 gave no fuchsin-aldehyde test with a reagent which responded positively upon subsequent addition of furfural. ^c All fractions gave negative alcohol tests with ceric ammonium nitrate reagent under conditions where addition of one drop of *n*-butyl alcohol gave immediate positive results. ^d All fractions gave positive tests for ketones either using phenylhydrazine or 2,4-dinitrophenylhydrazine reagent and fraction 9 gave a positive iodoform test even in the cold. ^e Fraction 1 gave a positive Legal test for acetone; comparative tests with authentic samples showed clear distinction between acetone and ethyl methyl ketone. ^f The semicarbazone prepared from fraction 3 melted at 128–133°, the recorded value for ethyl methyl ketone being 135–136°. ^g Fraction 8 after reaction with 2,4-dinitrophenylhydrazine gave a product containing 20.28% nitrogen (calculated for hexanone 2,4-dinitrophenylhydrazone 19.91%). After chromatographic separation on silicic acid¹¹ of a trace of 2,4-dinitrophenylhydrazine and further separation from the bulk of hexanone derivative, there resulted methyl *n*-propyl ketone 2,4-dinitrophenylhydrazone, m. p. 143.0–143.8° which did not depress the melting point of an authentic sample. ^h Treatment of fraction 9 as in ^g yielded a 2,4-dinitrophenylhydrazone, m. p. 105.5–109.5° regarded as *n*-butyl methyl ketone 2,4-dinitrophenylhydrazone, recorded m. p. 106–109° and other fractions of higher melting ranges with nitrogen analysis of 20.02% (calculated for hexanone 2,4-dinitrophenylhydrazone 19.91%).

Examination of Basic Products.—Fractionation of the aqueous solution of basic reaction products, collecting the gases evolved in a Dry Ice-trap, gave material summarized with comparative data in Table II.

Stability of Triethylacetic Acid.—Triethylacetic acid with concentrated sulfuric acid at 50° for one hour lost no carbon monoxide or carbon dioxide. It was subsequently recovered as an oil in almost quantitative yield, showed the correct neutralization equivalent and gave triethylacetamide of correct melting point.

(11) Roberts and Green, *Ind. Eng. Chem., Anal. Ed.*, **18**, 355 (1946).

TABLE II
 BASIC PRODUCTS^{a, b}

Fraction	B. p., °C.	<i>n</i> _D ²⁰	Wt., g.	Amine	B. p., °C.	<i>n</i> _D ²⁰
1 ^c	35-38	1.3831	2.9	Isopropyl	34	1.3770 at 15.4
2	38-45	1.3863	0.5	<i>n</i> -Propyl	48.7	1.3900 at 17
3 ^d	45-62	1.3870	0.5	<i>t</i> -Butyl	45	1.3794 at 18
4 ^d	62-65	1.3943	0.4	<i>s</i> -Butyl	63	1.3950 at 17
5 ^d	65-77	1.3985	0.3	Isobutyl	68	1.3988 at 17
6 ^e	77-82	1.4029	2.2	<i>n</i> -Butyl	78	1.4008 at 20
7	82-90	1.4043	0.4	Diethyl- carbonyl	91
8	90-92	1.4021	0.2	Methyl- <i>n</i> - propylcarbinol	92

^a The gases boiling below 35° were collected in a Dry Ice-trap and weighed 6-8 g. The material was further separated by distillation at 0 and 20°. The lower boiling portion was purified by recrystallization of its hydrochloride and shown by Nessler reagent to contain ammonia. The more soluble hydrochloride portion (presumably methylamine) and the higher boiling fraction (presumably ethylamine) could not, however, be made to give pure derivatives of these bases. ^b From the aqueous residue treatment with solid sodium hydroxide gave triethylacetamide (1 g.), m. p. 108.4-110°, which did not depress the melting point of an authentic sample. ^c Fraction 1 with diethyl oxalate gave N,N'-di-*n*-propyloxamide, m. p. 160°, which did not depress the melting point (160.5-161.5°) of an authentic sample. No evidence for the presence of isopropylamine (corresponding N,N'-diisopropylloxamide, m. p. 212°¹²) was observed. ^d These cuts were too impure to permit further identification. ^e Fraction 6 with diethyl oxalate gave N,N'-di-*n*-butyloxamide,

(12) Dermer and Hutcheson, *Proc. Oklahoma Acad. Sci.*, **23**, 60-63 (1943); *C. A.*, **38**, 2006 (1944).

m. p. 150-151°, which did not depress the melting point (150.5-151.0°) of an authentic sample. Analysis of this derivative showed N, 14.13% (calcd. 14.00%) and the free amine itself had a neutralization equivalent 75.2 (calcd.) 73.

Attempts to Rearrange Various Relatives. (a) Triethylcarbinol.—On warming with concentrated sulfuric acid at 50° for twenty minutes triethylcarbinol gave only polymeric products. In another experiment triethylcarbinol (58 g.) and sodium azide (50 g.) were gradually added to a mixture of concentrated sulfuric acid (310 g.) and chloroform (200 ml.) at the boiling point of the chloroform. Reaction occurred but isolation of the neutral products showed only diethyl ketone with no trace of higher homologs.

(b) 3-Ethylpentene-2.—This olefin (30 g.) in concentrated sulfuric acid (158 ml.) at 0° was treated with a small amount of sodium azide. Reaction began only after warming to 35°. Excess sodium azide was then added and the products isolated as usual. Both basic and neutral products were polymeric. Even in the absence of sodium azide and below 0°, 3-ethylpentene-2 with this quantity of concentrated sulfuric acid formed only polymeric products.

Summary

1. The products of the reaction of triethylacetic acid with sodium azide and concentrated sulfuric acid are a complex mixture of ketones, amines and other products.

2. The products found can be accounted for by formation and rearrangement of an intermediate carbonium ion.

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Studies in *p*-Cymene. III. Some N,N'-Diarythioureas*

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This study was made for the purpose of preparing several new N,N'-diarythioureas to be used in the anticipated preparation of substituted quinolines by the method of Dziewonski and Moszew.¹

N,N'-Di-2-*p*-cymylthiourea was made by standard procedure from 2-amino-*p*-cymene, then split with concentrated hydrochloric acid to form 2-*p*-cymyl isothiocyanate and 2-amino-*p*-cymene hydrochloride. There was no evidence of the formation of a substituted guanidine. The isothiocyanate was extracted directly with ether and, when isolated, was reacted with 2-amino-*p*-cymene to yield the original di-2-*p*-cymylthiourea. This was proved by the method of mixed melting points. Further, the *p*-cymyl isothiocyanate was allowed to react with phenylhydrazine to form phenyl-*p*-cymyl thiosemicarbazide. Analysis indicated that only one mole of the isothiocyanate reacted with one mole of the hydrazine, whereas

* An abstract of a thesis submitted by Leon H. Chance to the Graduate School, University of Georgia, in partial fulfillment of the requirements for the degree of Master of Science.

(1) Dziewonski and Moszew, *Roczniki Chem.*, **26**, 428, 925 (1932); **27**, 3937 (1933); **28**, 152 (1934).

the work of Otterbacher and Whitmore² showed that two moles of phenyl isothiocyanate react with one mole of phenyl hydrazine.

The preparation of N,N'-(*o*-, *m*-, *p*-)tolyl-2-*p*-cymylthioureas from the reaction of the toluidines with 2-*p*-cymyl isothiocyanate gave mixed products and the resulting separation gave poor yields. The mixed products were verified to be not only the desired products, but also di-*p*-cymylthiourea and the ditolythioureas. This type of interchange has not heretofore been reported. Since the yields were low, it was decided to treat the tolyl isothiocyanates with 2-amino-*p*-cymene. The results were excellent as evidenced in Table I.

Several methods of splitting these thioureas were tried. The most successful method experienced was by using acetic anhydride. Five to six minutes of refluxing yielded the isothiocyanates and free amine bases. Prolonged heating converted the amines first formed to their acet-compounds. As anticipated from the work³

(2) Otterbacher and Whitmore, *THIS JOURNAL*, **51**, 1909 (1929).

(3) Mainzer, *Ber.*, **16**, 2016-2018 (1883).