THE ACTION OF NITROUS ACID WITH TRIMETHYLACETAMIDE[1]

By Frank C. Whitmore and D. P. Langlois

The established fact[2] of the rearrangement of neopentyl alcohol and of neopentylamine when the hydroxyl and amino groups are removed in chemical reactions, caused us to study the corresponding reactions with trimethylacetic acid and its derivatives. The relation of the two sets of compounds is as follows:

$$(CH_3)_3CCH_2X \text{ and } (CH_3)_3C\overset{\overset{\displaystyle O}{\|}}{C}X$$
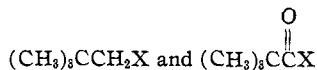
in which X may be OH, NH_2 or halogen. The entire trimethylacetyl series has been prepared.[3] The literature gives no indication of rearrangement during any of these preparations but also gives no yields.

Nitrous acid reacts with acid amides to give a quantitative yield of nitrogen.[4] No reference to the amount of organic acid formed has been found in the literature.

In the present work, acetamide is shown to give a quantitative yield of acetic acid.

If the action of trimethylacetamide with nitrous acid gave a similar rearrangement to that of neopentylamine, the products might be $(CH_3)_2$-$C(OH)COCH_3$,[5] $CH_2=C(CH_3)COCH_3$.[6] No such products were found. Trimethylacetamide (2 moles) was treated with nitrous acid at 30–35°. The products included 1.61 moles of nitrogen, 1.62 moles of trimethylacetic acid and 0.2 mole of unreacted amide. No other products were found.

The absence of rearrangement in reactions involving the trimethylacetyl group is further indicated by the fact that the changes, acid ⟶ acid chloride ⟶ acid amide ⟶ original acid, gave an over-all yield of 79% or an average of 93% for each step. Moreover, these reactions all take place with the greatest ease and at relatively low temperatures. The obvious explanation of these facts is that the initial step in each reaction is an addition to the carbonyl group of the trimethylacetyl, giving intermediate products such as

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[1] Presented by D. P. Langlois in partial fulfilment of the requirements for the Ph.D. degree at the Pennsylvania State College.
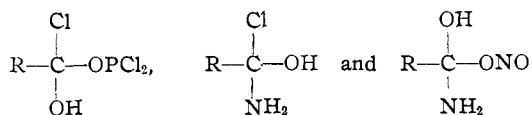
[2] See pp. 3431, 3441.

[3] Butlerow, *Ann.*, **173**, 373 (1874); Meyer, *Monatsh.*, **27**, 36 (1906); Franchimont and Klobbie, *Rec. trav. chim.*, **6**, 238 (1887); Scheuble and Loeble, *Monatsh.*, **25**, 1095 (1904); Aschan, *Ber.*, **31**, 2344 (1898).

[4] Plimmer, *J. Chem. Soc.*, **127**, 2651 (1925).

[5] Scheibler and Fisher, *Ber.*, **55**, 2915 (1922).

[6] Beilstein, "Handbuch," 4th ed., Vol. I, p. 733.

$$\begin{array}{ccc}
\text{Cl} & \text{Cl} & \text{OH} \\
| & | & | \\
\text{R--C--OPCl}_2, & \text{R--C--OH} \quad \text{and} \quad & \text{R--C--ONO} \\
| & | & | \\
\text{OH} & \text{NH}_2 & \text{NH}_2
\end{array}$$

which then become $RCOCl$, $RCONH_2$ and $RCOOH$, respectively. No one of these changes gives an intermediate ion which might cause a rearrangement.

On the other hand, reactions of neopentyl compounds must take place either through an initial ionization (Meerwein) or, more probably, through compound formation (oxonium or ammonium) with the hydroxyl or amino group attached to the neopentyl system. At the instant this oxonium or ammonium compound changes to give a stable inorganic molecule such as water or nitrogen, the neopentyl group is left with only 30 valence electrons and is consequently unstable.[7]

Experimental

Preparation of Trimethylacetamide.—Trimethylacetic acid was made according to "Organic Syntheses" (Vol. VIII, 1928, p. 104). Two moles (204 g.) of the acid was warmed on a steam-bath under a reflux condenser with 138 g. (50% excess) of phosphorus trichloride. Very little hydrogen chloride escaped. Two layers separated. After heating for one and a half hours, the mixture was cooled in ice. The acid chloride was decanted from the sirupy bottom layer and added to 1 liter of concentrated aqueous ammonia cooled to 0°. The white amide was filtered off and dried *in vacuo* over sulfuric acid. It was heated with 600 cc. of ethyl acetate and filtered hot to remove ammonium chloride. The solution was evaporated until crystals began to appear and 1200 cc. of petroleum ether was added. The mixture was heated to give a clear solution and then allowed to cool slowly. It was finally cooled in a refrigerator and filtered. The trimethylacetamide melted at 155–157°; yield 176.5 g. or 87% of the calculated amount based on the trimethylacetic acid used. Further crystallization did not change the melting point.

Action of Nitrous Acid on Acetamide.—One-half mole (29.5 g.) of acetamide (dried over phosphorus pentoxide) and 34.5 g. (0.5 mole) of sodium nitrite were dissolved in 350 cc. of water. The mixture was placed in an open flask fitted with a stirrer and a dropping funnel. To the mixture was added slowly with constant stirring 15 cc. of concentrated sulfuric acid in 100 cc. of water. After the addition of the acid another 34.5 g. of sodium nitrite was added and another 15 cc. of sulfuric acid in 100 cc. of water was added slowly. The mixture was stirred for six hours after all of the acid had been added. The temperature was kept at 50–60° during the addition of the acid and at 30–35° during the final stirring. The mixture was then heated for half an hour at 80° to drive off the excess nitrogen oxides and then distilled until no more acetic acid came over. The distillate was diluted to 1 liter in a volumetric flask and the acetic acid titrated, using 10-cc. portions; 10 cc. of the acid required 19 cc. of 0.2700 N base. Hence the acid was 0.513 N, and 0.51 mole of acid was obtained from 0.50 mole of acetamide.

Action of Nitrous Acid on Trimethylacetamide.—One mole of sulfuric acid was diluted to 2 liters and 2 moles of trimethylacetamide (202 g.) was dissolved in it. The mixture was warmed to 60° to effect solution. It was placed in a three-necked 5-liter flask and cooled. The flask was fitted with a mercury-sealed stirrer, a dropping funnel and an exit tube for gases. This tube was connected with an absorption train, consisting

of two ordinary wide-mouthed bottles fitted with bubblers and a Friedrich absorption tower, and a gas meter for measuring the gas evolved. The absorption train was filled with a saturated solution of potassium permanganate about 0.5 N in sulfuric acid. This was to remove any nitrogen oxides formed during the reaction, thus leaving pure nitrogen to be measured.

When the solution in the flask had cooled to 35°, stirring was started and a solution of 2 moles (138 g.) of sodium nitrite in 1 liter of water was run in at the rate of 1 cc. per minute. After this addition another half mole of sulfuric acid was run in and another mole of sodium nitrite (69 g.) in 500 cc. of water was added as before. The entire addition required about forty-eight hours. Stirring was continued another forty-eight hours as long as gas was evolved. An oily layer of trimethylacetic acid separated. The nitrogen evolved occupied 44 liters at an average temperature of 30° and an average pressure of 743 mm., thus amounting to 1.61 moles.

The contents of the reaction flask were poured out and the two layers separated. The water layer was extracted with four 250-cc. portions of ether, and the ether extracts combined with the acid layer. The water layer was reserved (1). The ether solution was extracted with three 150-cc. portions of 20% sodium hydroxide and the ether residue was reserved (2). The sodium hydroxide extract was heated to distil off the ether and any other volatile organic product. The distillate was reserved (3).

The sodium hydroxide solution was then cooled and acidified with sulfuric acid. A layer of trimethylacetic acid separated and was drawn off. The water layer was distilled until no more oily drops came over. The distillate was saturated with salt and the layer of acid drawn off. This water residue was then distilled until no more oily drops came over and the distillate was saturated with salt. The layer of acid was drawn off and all three lots of acid were combined. Twenty cc. of ether was added to the acid and the mixture was dried over sodium sulfate in the refrigerator. The solution was then distilled.

Fraction	B. p., °C.	Press., mm.	Weight
1	35– 55	743	15 cc.
2	55–162	743	1.5 g.
3	162–163	743	165 g.
4	Very little solid residue		

The 165 g. of the acid obtained is 1.62 moles.

The water layer (1) was made strongly alkaline with sodium hydroxide and cooled. It was extracted with six 200-cc. portions of ethyl acetate. The ethyl acetate was evaporated on a water-bath and 12 g. of a dry solid was obtained, m. p. 155–156° (unreacted trimethylacetamide). No other product could be detected.

The ether residue (2) was distilled on a water-bath. All of the volatile material came over at 35–55°, leaving 8 g. of a dry white solid, m. p. 155–157° (unreacted trimethylacetamide). No other product could be detected.

The distillate (3) was again distilled. Ether came over at 35°. There was then a gradual rise in temperature, more rapid toward the last, until it reached 98°, where it remained constant until all had distilled. Apparently it contained nothing but ether and water.

Summary

1.   Trimethylacetamide reacts with nitrous acid to give over 90% of the calculated amounts of nitrogen and trimethylacetic acid.

2.   The reactions of derivatives of trimethylacetyl give no rearrange-

ments.   This is in marked contrast to the rearrangements of the analogous neopentyl derivatives.

3.   The significance of this absence of rearrangement in relation to the mechanism of rearrangements is discussed.

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REARRANGEMENTS INVOLVED IN THE ACTION OF NITROUS ACID WITH NORMAL-BUTYLAMINE[1]

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The recorded data[2] on the reaction of nitrous acid and primary aliphatic amines make it of the utmost importance in the theory of rearrangements.[3] For instance, it can hardly be argued that a primary amine undergoes an "ionization" into R^+ and NH_2^- similar to that which is sometimes assumed as part of the mechanism of the rearrangement of carbinols (Meerwein). Moreover, this reaction results in the formation of olefins under conditions which would not cause the dehydration of even a tertiary alcohol.

n-Propylamine reacts with nitrous acid to give *n*-propyl alcohol, isopropyl alcohol and propylene.[4]   Isobutylamine gives tertiary butyl alcohol[5] and isobutylene.   No other organic products are mentioned.   *n*-Butylamine is reported to give *n*-butyl alcohol and isobutyl alcohol.[6] Other workers report *n*-butyl alcohol, secondary butyl alcohol, *n*-butenes and dibutyl nitrosamine but *no* isobutyl alcohol.[7]

Neopentylamine gives only the rearrangement product, tertiary amyl alcohol.[8]

n-Butylamine was chosen for the present study because of the simplicity of its molecule and the disagreement in the literature regarding its behavior with nitrous acid.   The amine was prepared from very pure *n*-butyl bromide obtained from highly purified *n*-butyl alcohol.   The yields of products of the action of nitrous acid were as follows

[1] Presented by D. P. Langlois in partial fulfilment of the requirements for the Ph.D. degree at the Pennsylvania State College.

[2] Porter, "Molecular Rearrangements," p. 140 (1928).

[3] See p. 3281.

[4] Siersch, *Ann.*, **144**, 140 (1867); Linnemann, *ibid.*, **161**, 44 (1872); *Ber.*, **10**, 1111 (1877); Meyer and Forster, *ibid.*, **9**, 535 (1876).

[5] Linnemann, *Ann.*, **162**, 24 (1872).

[6] Linnemann and Zotta, *ibid.*, **162**, 5 (1872); Ray and Rakshit, *J. Chem. Soc.*, **101**, 141 (1912).

[7] Meyer, Barbieri and Forster, *Ber.*, **10**, 132 (1877).

[8] Freund and Lenze, *Ber.*, **24**, 2150 (1891).