103. Reaction of Guanidine on Tropolone Methyl Ether¹⁾

By Tetsuo NOZOE, Toshio MUKAI, Kahei TAKASE,
Ichirô MURATA, and Katsuhiko MATSUMOTO

Chemical Institute, Faculty of Science, Tôhoku University,
Sendai, Japan

(Comm. by R. MAJIMA, M.J.A., Oct. 12, 1953)

The carbonyl group of tropone has been found in this laboratory to react with practically all the carbonyl reagents²⁾. Such a fact suggests the possibility of synthesizing a new type of compounds in which the unsaturated, seven-membered carbon ring is fused to a heterocyclic ring containing nitrogen or other hetero atoms.

Following this line of thought, condensation reactions of 2-halotropones, tropolone methyl ether, and tropolone acetyl compounds with guanidine, thiourea³⁾, and urea were examined. Of these reactions, tropolone methyl ether was found to react easily with guanidine when sodium ethoxide is used as a catalyst. The present paper describes the structure and properties of the condensation products thereby obtained.

Refluxing of tropolone methyl ether with an equivalent of sodium ethoxide and guanidine hydrochloride, in absolute alcohol, results in coloration of the solution to deep red, and reddish orange to yellow prisms (I), m.p. 295° (decomp.) (Anal. Calcd. for $C_8H_7N_3$: C, 66.18; H, 4.87; N, 28.95. Found: C, 65.65; H, 4.79; N, 29.21)⁴⁾ are obtained in 70% yield. (I) can be sublimed at a reduced pressure, dissolves in water, alcohol, and glacial acetic acid, but is insoluble in other organic solvents. It is easily soluble in acids but insoluble in aqueous alkali solutions. Ultraviolet absorption spectrum of (I) is shown in Fig. 1, and its infrared absorp-

Fig. 1. Ultraviolet absorption spectra of (I) in methanol (—), in 0.1 N HCl (---) and in 0.1 N NaOH aqueous solution (-.-.-)

tion spectrum in Fig. 2.

(I) possesses basic properties and gives the following salt. Hydrochloride: White crystals, m.p. 283° (decomp.) (Anal. Calcd. for $C_8H_7N_3 + HCl$: N, 19.29. Found: N, 19.74). Nitrate: Pale yellow needles, m.p. 197° (decomp.) (Titration. Sample 4.400 mg. Calcd. for $C_8H_7N_3 + HNO_3$: 1.89 ml. of 0.01 N NaOH ($f=1.119$) Found: 1.87 ml.). Chloroplatinate: Orange needles, m.p. over 300° (Anal. Calcd. for $C_8H_7N_3 + H_2PtCl_6$: Pt, 35.92. Found: Pt, 35.17). Oxalate: Pale yellow prisms, m.p. 147° (decomp.) (Titration: Sample 6.658 mg. Calcd. for $C_8H_7N_3 + C_2H_2O_4$: 3.87 ml. of 0.01 N NaOH ($f=1.465$). Found: 3.83 ml.). Picrate: Deep yellow plates, m.p. 281° (decomp.) (Anal. Calcd. for $C_8H_7N_3 + C_6H_3O_7N_3$: N, 22.46. Found: N, 22.79).

Fig. 2. Infrared absorption spectrum of (I) in nujol

(I) also gives the corresponding acyl derivative when heated with acetic or phthalic anhydride, or when benzoyl chloride is applied in the presence of alkali. Acetyl compound: Colorless needles, m.p. 260° (decomp.) (Anal. Calcd. for $C_{10}H_9ON_3$: N, 22.45. Found: N, 21.37). Phthalyl compound: Brownish prisms, m.p. 190° (decomp.) (Anal. Calcd. for $C_{16}H_{11}O_3N_3$: N, 14.33. Found: N, 13.66). Benzoyl compound: Pale yellow needles, m.p. 176.5° (decomp.) (Anal. Calcd. for $C_{22}H_{15}O_2N_3$: N, 11.89. Found: N, 11.32).

The formation of these acyl compounds indicates the presence of an amino or allied group in the condensation product. Diazotization of (I) followed by the addition of an alkaline solution of naphthol results in beautiful red coloration.

No absorption of hydrogen occurs on catalytic reduction of (I) in alcohol with palladium-charcoal but the use of platinum oxide as the catalyst results in the absorption of three molar equivalents of hydrogen against $C_8H_7N_3$, and yields a vitreous substance (II).⁵⁾

(I) is an extremely stable substance and does not undergo any change when heated with concentrated sulfuric acid or refluxed with alcoholic alkali for a long period. No absorption band of

carbonyl group at 1580 cm^{-1} ($6.33\text{ }\mu$) that is unique to tropones can be detected in Fig. 2.

In order to explain the foregoing properties and from the fact that the analytical values do not contain oxygen, the following structure is proposed for (I) which makes it possible to assume the existence of a numerous resonance hybrids as in the case of benzimidazole.

The more important point is the fact that when the two methyl ethers⁶⁾, m.p. 97° and m.p. 46° , of 4-methyltropolone are separately reacted with guanidine under the same conditions, only one kind of a condensation product is formed as yellow needles (III), m.p. 285° (decomp.)⁷⁾ (Anal. Calcd. for $\text{C}_9\text{H}_9\text{N}_3$: N, 26.41. Found: N, 26.51). This fact endorses the probability of the foregoing structure.

A mixture of the two methyl ethers of hinokitiol (4-isopropyltropolone) also gives only one kind of a condensation product under the same conditions as yellow needles (IV), m.p. 222° , in a 70% yield (Anal. Calcd. for $\text{C}_{11}\text{H}_{13}\text{N}_3$: N, 22.46. Found: N, 22.29). A small amount of colorless needles (V), m.p. 211° (Anal. Calcd. for $\text{C}_{11}\text{H}_{14}\text{ON}_3$: N, 20.58. Found: N, 19.75) are formed as a by-product. Analytical values of (V) suggest that it should be a condensation product of a different series.

It is still not clear which of the two structures, (A) and (B), should be given to (I), (III), and (IV), and whether two tautomers (A) and (B) could actually exist. The formation of the foregoing acyl compounds could be explained by (B) but it is possible to assume that the acyl group has attached to the nuclear nitrogen in (A).⁸⁾ (I) does not undergo condensation with benzaldehyde or m-nitrobenzaldehyde when warmed with these in alcohol in the presence of piperidine. Diazotization of (I) described above only indicates qualitatively the formation of a dye and attempts to isolate the compound failed. Moreover, addition of sodium nitrite to the acid solution of (I) results in the formation of a stable salt when the acid concentration is higher, and when the acidity is weak, the nitrite of (I) is formed as dark yellow scales, m.p. 198° (decomp.) (Titration Sample 5.328 mg. Calcd. for $\text{C}_9\text{H}_7\text{N}_3 + \text{HNO}_2$: 1.87 ml. of 0.01 N. NaOH ($f=1.465$). Found: 1.83 ml.).

(I) discolors potassium permanganate solution at a room temperature but when warmed with diluted nitric acid, it only forms

a nitrate and does not submit to oxidation. Heating of the acetyl compound of (I) with chromium in glacial acetic acid seems to result in oxidation but the majority forms orange needles (VI) which turns brownish at 200° (Anal. Calcd. for $C_{10}H_9ON_3 + CrO_3$: Cr, 18.49. Found: Cr, 19.37). Since (VI) yields (I) when heated with alkali, it is assumed to be the chromate of the acetyl compound of (I).

Addition of aqueous silver nitrate solution to the alcoholic solution of (I) precipitates the silver compound as white solid, m.p. over 300° (Anal. Calcd. for $C_8H_7N_3 + AgNO_3$: Ag, 34.59. Found: Ag, 34.43). (I) also yields a mercury compound by the addition of an aqueous solution of mercuric chloride as a white solid, m.p. 282° (decomp.).

(I) is not sulfonated by conc. sulfuric acid, nor nitrated by

conc. or fuming nitric acid, or by mixed acids, only forming the nitrate of (I). This is assumed to be due to the fact that (I) is present in a conjugate acid form and does not submit to electrophilic substitution.

However, addition of bromine to the acetic acid solution of (I) immediately yields brick red crystals which change to orange plates (VII) m.p. 190° (decomp.) (Anal. Calcd. for $C_8H_5N_3Br_3$: C, 24.95; H, 2.09. N, 10.89. Found: C, 25.78; H, 2.71; N, 11.08). Addition of hot alcoholic solution of iodine to the alcoholic solution of (I) yields dark grey crystals (VIII), m.p. 190° (decomp.) (Anal. Calcd. for $C_8H_7N_3I_2$: C, 24.06; H, 1.77. Found: C, 21.62; H, 1.72). Reductive decomposition of both (VII) and (VIII) by their addition to aqueous solution of sulfurous acid results in the recovery of (I) in a fairly good yield. The constitution of (VII) and (VIII) are not determined definitely from their analytical values, but the above fact indicates that both (VII) and (VIII) are the addition products or molecular compounds of halogen and (I).

Tropolone methyl ether undergoes condensation with urea in the presence of sodium ethoxide to yield yellow needles, m.p. 175.5° (decomp.), and with urea to yield orange prisms, m.p. $68-80^{\circ}$.⁹ Examinations of these compounds are now being carried out.

Grateful acknowledgement is hereby expressed for the donation Grant in Aid for Scientific Research from the Ministry of Education and monetary assistance from Sankyô Company.

References

- 1) Paper read before the Tôhoku Local Meeting of the Chemical Society of Japan in Akita, Oct. 2, 1953.
- 2) T. Nozoe, T. Mukai, K. Takase, and T. Nagase: *Proc. Japan Acad.*, **28**, 477 (1952).
- 3) Cf. report on the reaction product of 2-halotropones and thiourea. T. Nozoe, M. Sato, and K. Matsui: *Sci. Repts. Tôhoku Univ., First Series*, **37**, 211 (1953).
- 4) Microanalyses were carried out by Mr. Kawamoto of Sankyô Co., Ltd., and Miss K. Katô of this Laboratory. The Compounds of this series generally have high melting points and their combustion is attended with difficulty.
- 5) Imidazole nucleus is known to be fairly stable against hydrogenation. Cf. *Chem. Rev.*, **48**, 319 (1951).
- 6) P. Akroyd, R. D. Haworth, and J. D. Hobson: *J. Chem. Soc.*, **1952**, 3427.
- 7) The products obtained from two methyl ethers failed to show any depression of the melting point on admixture because of their high decomposition points but this cannot be taken as proof of identity. Comparison of their infrared absorption spectra have shown that the absorption bands of the two substances agree well.
- 8) The hydrogen attached to the nuclear nitrogen in benzimidazole is substituted with an acyl group.
- 9) In spite of the fact that the crystals seem to be pure, the melting point is not sharp, and the crystals change to that of m.p. over 300° during standing or by the action of hydrochloric acid.