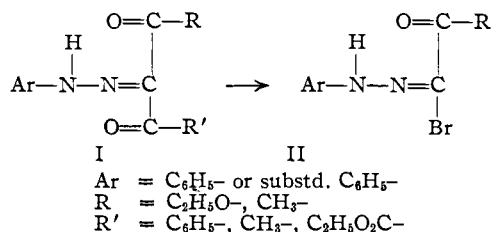


[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

A Mechanism for the Cleavage of Certain Phenylhydrazones by Bromine

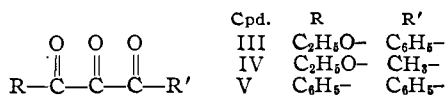
BY DEXTER B. SHARP¹

F. D. Chattaway and co-workers² published a number of papers describing the products obtained from the action of halogens on certain phenylhydrazones, represented by formula I. Bromine reacted almost quantitatively with



compounds of type I in cold acetic acid-sodium acetate solution to give halides of type II, a cleavage of a carbon-carbon bond having occurred during the reaction. The papers cited above reported no mechanism studies. This paper presents the results of experiments designed to elucidate the mechanism of this cleavage reaction.

Two of the three parent compounds of this series, *i.e.*, vicinal tricarbonyl compounds, were found to be unaffected by bromine under the conditions favoring cleavage of the hydrazones of type I. Ethyl 3-phenyl-2,3-dioxopropanoate

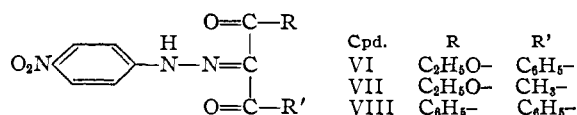


(III) and 1,3-diphenylpropane-1,2,3-trione (V) were prepared and added to a solution of bromine and sodium acetate in glacial acetic acid. After one to three days at room temperature, the reaction mixtures were diluted with water and the starting compounds were recovered as hydrates in good yields. Ethyl 2,3-dioxobutanoate (IV) decolorized bromine over a four-hour period and no hydrate was isolated. This result may be attributed to a bromine attack upon the terminal methyl group rather than a C₂-C₃ cleavage.

The stability of III and V toward bromine indicates that the hydrazone group at carbon number two is necessary for the cleavage reaction and it was found that the 2-*p*-nitrophenylhydrazone derivatives of compounds III, IV and V (VI, VII, VIII) were cleaved in excellent yields by bromine in acetic acid-sodium acetate solutions maintained at or below room temperature.

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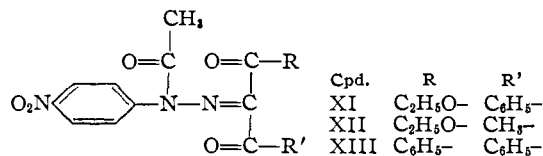
(2) (a) Chattaway and Lye, *Proc. Roy. Soc. (London)*, **A135**, 282 (1932); (b) **A137**, 489 (1932); (c) Chattaway and Ashworth, *J. Chem. Soc.*, 475 (1933); (d) Chattaway and Lye, *ibid.*, 480 (1933); (e) Chattaway and Ashworth, *ibid.*, 1143 (1933); (f) 1624 (1933); (g) 930 (1934); (h) 1985 (1934).



In all cases the bromine was decolorized as rapidly as it was added. Compounds VI and VII both gave the same bromo compound, ethyl α -bromoglyoxylate α -*p*-nitrophenylhydrazone (IX), the bromine having replaced a benzoyl and an acetyl group, respectively. Compound VIII gave ω -bromophenylglyoxal *p*-nitrophenylhydrazone (X), a benzoyl group having been replaced by a bromine atom. The cleavage of VII was reported by Chattaway,^{2c} and earlier by Bowack and Lapworth.³ The cleavage of VI and VIII is in line with the observations of Chattaway.

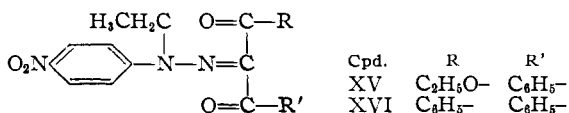
Bromine in glacial acetic acid containing no sodium acetate was found to have no action on compounds VI, VII or VIII. These compounds were recovered in very good yield. The influence of substances of higher basic strength than sodium acetate was not investigated due to the sensitivity of the halogen compounds (II) toward more basic agents.

The hydrazone groups in VI, VII and VIII were modified by direct N-acetylation with acetic anhydride. The N-acetyl compounds,



ethyl 3-phenyl-2,3-dioxopropanoate-2-(acetyl-*p*-nitrophenylhydrazone) (XI), ethyl 2,3-dioxobutanoate-2-(acetyl-*p*-nitrophenylhydrazone) (XII), and 1,3-diphenylpropane-1,2,3-trione-2-(acetyl-*p*-nitrophenylhydrazone) (XIII) were unaffected by bromine under conditions favoring cleavage of type I compounds.

N-Ethyl-*p*-nitrophenylhydrazones analogous to VI and VIII were prepared by the reaction of α -ethyl- α -*p*-nitrophenylhydrazine (XIV) with III



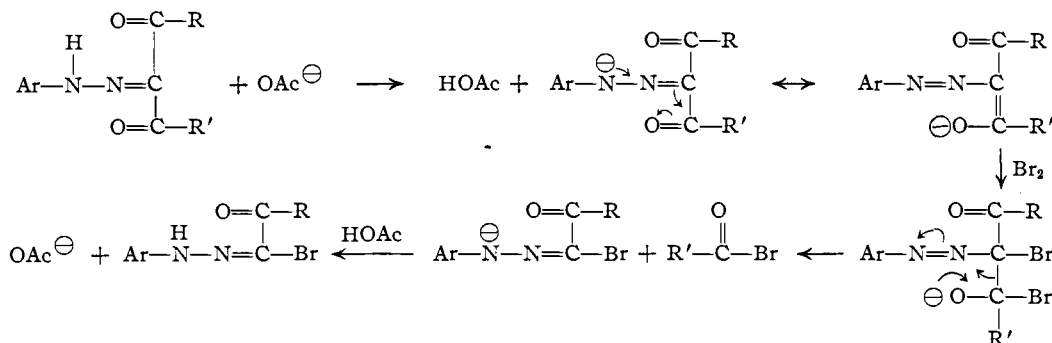
and V. Ethyl 3-phenyl-2,3-dioxopropanoate-2-(ethyl-*p*-nitrophenylhydrazone) (XV) and 1,3-diphenylpropane-1,2,3-trione-2-(ethyl-*p*-nitrophenylhydrazone) (XVI) were unaffected by bromine under conditions favoring cleavage of

(3) Bowack and Lapworth, *J. Chem. Soc.*, **87**, 1854 (1905).

type I compounds. Compounds III and V with *p*-nitrophenylhydrazine gave substances identical with VI and VIII, respectively, whose structures as 2-*p*-nitrophenylhydrazones are fixed through their synthesis by the Japp-Klingemann reaction. By analogy, it is inferred that the central carbonyl groups in III and V were attacked by the disubstituted hydrazine molecule. Since IV with *p*-nitrophenylhydrazine gave a derivative which was not identical with VII from the coupling reaction, the corresponding ethyl-*p*-nitrophenylhydrazone was not prepared. Attempts to ethylate VI, VII and VIII directly were unsuccessful.

Summarizing the results above, the following facts are clear. (1) Rapid cleavage of compounds of type I by bromine occurred almost quantitatively under mild conditions in glacial acetic acid containing sodium acetate. (2) No cleavage occurred in the absence of sodium acetate. (3) Replacement of the hydrogen on the nitrogen of the hydrazone link by an acetyl or ethyl group prevented cleavage, thus demonstrating the requirement that this hydrogen is necessary for cleavage to occur.

From a consideration of these facts, the following base-catalyzed mechanism is proposed for the reaction.



Experimental⁴

Vicinal Tricarbonyl Compounds. Ethyl 3-Phenyl-2,3-dioxopropanoate (III).—Ethyl benzoacetate (96 g.) was converted to III by adapting the method described by Bigelow and Hanslick⁵ for the preparation of 1,3-diphenylpropane-1,2,3-trione. The product (47 g., 45%) was a yellow oil; b. p. (2 mm.) 117–123° (reported,⁶ 150–153° at 13 mm.), d_{20}^{25} 1.179 (reported,⁶ d_{20}^{25} 1.188), n_{20}^{20} 1.5191.

Ethyl 2,3-Dioxobutanoate (IV).—Ethyl acetoacetate (130 g.) was converted to IV by the method of Denis.⁷ The nitrogen oxides were generated by the action of sirupy phosphoric acid on excess sodium nitrite. The product (7.3 g., 5%) was a yellow oil; b. p. (14 mm.) 68.5–72° (reported,⁷ 76–82° at 18–22 mm.), d_{20}^{20} 1.151 (reported,⁸ d_{20}^{20} 1.125), n_{20}^{20} 1.4240 (reported,⁸ n_{20}^{20} 1.42210).

1,3-Diphenylpropane-1,2,3-trione (V).—A sample of V hydrate, m. p. 89–91° (reported,⁹ 90–92°), was dehydrated by distillation at reduced pressure to give V, a yellow-orange solid; m. p. 69–71° (reported,⁵ 68–70°).

(4) Each m. p. and b. p. was corrected for stem exposure.
 (5) Bigelow and Hanslick, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 244.

(6) Wahl, *Compt. rend.*, **144**, 212 (1907).

(7) Denis, *Am. Chem. J.*, **38**, 587 (1907).

(8) von Auwers, *Ber.*, **51**, 1120 (1918).

Bromine Action on III, IV and V.—Mole portions of III, IV and V, respectively, were added to appropriate volumes of glacial acetic acid containing an excess of anhydrous sodium acetate and a mole portion of bromine. The mixtures were maintained at room temperature for varying periods. Excess bromine was removed at reduced pressure, water was added, and the respective hydrates precipitated.

A sample of III (4.0 g.) gave III hydrate (3.6 g., 80%); m. p. and mixed m. p. 55–59° with authentic III hydrate.

Compound IV decolorized bromine over a four hour period, possibly due to an attack on the highly activated methyl group rather than C₂-C₃ cleavage. No IV hydrate was obtained from this reaction.

A portion of V (15.8 g.) gave V hydrate (15.2 g., 90%); m. p. and mixed m. p. 82–90° with authentic V hydrate.

2-*p*-Nitrophenylhydrazone Derivatives of III, IV and V. A. Coupling Reaction.—*p*-Nitrobenzenediazonium chloride coupled with the appropriate β -dicarbonyl compounds in sodium acetate buffered solutions to give the desired derivatives, following the method of Chattaway and Ashworth.²⁰ Ethyl benzoacetate (19 g.) gave ethyl 3-phenyl-2,3-dioxopropanoate 2-*p*-nitrophenylhydrazone (VI). The product (21 g., 61%) crystallized as yellow platelets from dilute ethanol; m. p. 112.5–114° (reported,⁹ 114°).

Ethyl acetoacetate (65 g.) gave ethyl 2,3-dioxobutanoate 2-*p*-nitrophenylhydrazone (VIII). The product (120 g., 86%) crystallized as yellow needles from dilute ethanol; m. p. 126–127° (reported,²⁰ 126–127°).

Dibenzoylmethane (22.5 g.) gave 1,3-diphenylpropane-1,2,3-trione 2-*p*-nitrophenylhydrazone (VIII). The product (24.5 g., 66%) separated as yellow needles from dilute acetone; m. p. 172–173° (reported,¹⁰ 173°).

B. Direct Action.—Compounds VI and VIII were obtained by the direct action of *p*-nitrophenylhydrazine on III and V, respectively. Mole portions of the hydrazine and tricarbonyl compound were added to ethanol containing several drops of acetic acid. Filtration and dilution of the filtrate with water caused the product to crystallize.

By this method, III (1.0 g.) gave compound VI (1.6 g., 94%); m. p. and mixed m. p. 112–114° with VI prepared by the coupling reaction.

Similarly, V hydrate (3.33 g.) gave VIII (4.40 g., 86%); m. p. and mixed m. p. 170–171° with authentic VIII prepared by the coupling reaction.

Compound IV gave a red substance, m. p. 175–176°, quite different from the desired compound (VII); m. p. 126–127°.²⁰

Bromine Action on VI, VII and VIII. A. With Sodium Acetate.—A mole portion of VI, VII and VIII, respectively, was added to glacial acetic acid containing an excess of sodium acetate. The reaction mixture was stirred at room temperature or less while a mole portion of bromine in acetic acid was added. In each case a rapid decoloration of bromine was noted. The solid products were obtained by filtration after the reaction mixtures were diluted with water.

(9) Bülow and Hailer, *ibid.*, **35**, 926 (1902).

(10) Dimroth, *ibid.*, **40**, 2409 (1907).

Compound VI (5.0 g.) gave ethyl α -bromoglyoxylate- α -*p*-nitrophenylhydrazone (IX). The product (4.3 g., 93%) crystallized as granular yellow crystals from benzene; m. p. 199–201° (reported,²⁰ 202–203°).

Anal. Calcd. for $C_{10}H_{10}BrN_2O_4$: C, 37.99; H, 3.19. Found: C, 38.19; H, 3.60.

Compound VII (25.0 g.) gave IX (26.5 g., 94%); m. p. and mixed m. p. 199–201° with IX from the preceding reaction.

Compound VIII (5.0 g.) gave ω -bromophenylglyoxal-*p*-nitrophenylhydrazone (X). The product (4.5 g., 96%) separated as yellow needles from ethyl acetate; m. p. 245–247° (reported,²¹ 247°).

B. Without Sodium Acetate.—The reactions in (A) were repeated without the sodium acetate: From VI (5.0 g.) there was recovered VI (4.7 g., 94%); m. p. 112–114°. From VII (5.0 g.) there was recovered VII (4.6 g., 92%); m. p. 125–127°. From VIII (5.0 g.) there was recovered VIII (4.7 g., 94%); m. p. 171–172°.

N-Acetyl Derivatives of VI, VII and VIII.—Following a method described by Bülow and Hailer,⁹ compounds VI, VII and VIII were acetylated by treatment with acetic anhydride containing several drops of concentrated sulfuric acid. The excess acetic anhydride was hydrolyzed by pouring the reaction mixture onto ice and the solid product was collected and recrystallized repeatedly from dilute acetone and dilute acetic acid.

Compound VI (5.0 g.) gave ethyl 3-phenyl-2,3-dioxopropanoate 2-(acetyl-*p*-nitrophenylhydrazone) (XI). The product (1.0 g., 18%) crystallized as white needles from dilute acetone; m. p. 141–142°.

Anal. Calcd. for $C_{19}H_{17}N_3O_6$: C, 59.53; H, 4.47. Found: C, 59.90; H, 4.40.

Compound VII (28 g.) gave ethyl 2,3-dioxobutanoate-2-(acetyl-*p*-nitrophenylhydrazone) (XII). The product (2.5 g., 8%) crystallized as white needles from dilute acetone; m. p. 135–136°.

Anal. Calcd. for $C_{14}H_{15}N_3O_6$: C, 52.34; H, 4.71. Found: C, 52.37; H, 4.92.

Compound VIII (3.0 g.) gave 1,3-diphenylpropane-1,2,3-trione-2-(acetyl-*p*-nitrophenylhydrazone) (XIII). The product (1.1 g., 33%) separated as yellow needles from dilute acetic acid; m. p. 202–202.5°.

Anal. Calcd. for $C_{23}H_{17}N_3O_6$: C, 66.50; H, 4.13. Found: C, 66.39; H, 4.03.

Bromine Action on Compounds XI, XII and XIII.—Mole portions of XI, XII and XIII, respectively, were added to appropriate volumes of acetic acid containing mole portions of bromine and excess sodium acetate. After one day at room temperature the reaction mixtures were diluted with water and the solids were removed by filtration. From XI (0.452 g.) there was recovered XI (0.343 g., 76%); m. p. and mixed m. p. 138–140° with authentic XI. From XII (1.0 g.) there was recovered XII (1.0 g., 100%); m. p. and mixed m. p. 133–135° with authentic XII. From XIII (0.859 g.) there was recovered XIII (0.837 g., 97%); m. p. and mixed m. p. 201–202° with authentic XIII.

N-Ethyl Derivatives of VI and VIII.—Compound XIV, α -ethyl- α -*p*-nitrophenylhydrazine, was prepared in poor

yield by the method of Ciusa and Rastelli.¹¹ Benzaldehyde *p*-nitrophenylhydrazone (50 g.) gave XIV (6.2 g., 16%), a yellow crystalline solid from ligroin; m. p. 68.5–69.5° (reported,¹¹ 74°).

Anal. Calcd. for $C_8H_{11}N_3O_2$: C, 53.02; H, 6.12. Found: C, 52.73; H, 6.07.

Mole portions of III and V, respectively, were added to ethanol-acetic acid (3:1 by volume) containing mole portions of XIV. The reaction mixtures, after one hour on the steam-bath and one day at room temperature, were diluted with water and the solid products were removed by filtration.

Compound III (1.60 g.) with XIV (1.36 g.) gave ethyl 3-phenyl-2,3-dioxopropanoate-2-(ethyl-*p*-nitrophenylhydrazone) (XV), (2.05 g., 74%). The product crystallized as yellow needles from dilute acetone; m. p. 128–129°.

Anal. Calcd. for $C_{19}H_{19}N_3O_5$: C, 61.78; H, 5.19. Found: C, 61.96; H, 5.40.

V hydrate (0.66 g.) with XIV (0.45 g.) gave 1,3-diphenylpropane-1,2,3-trione 2-(ethyl-*p*-nitrophenylhydrazone) (XVI). The product (0.35 g., 33%) crystallized as yellow needles from dilute acetone; m. p. 166–167°.

Anal. Calcd. for $C_{23}H_{19}N_3O_4$: C, 68.81; H, 4.77. Found: C, 69.08; H, 5.05.

In view of the anomalous behavior of IV with *p*-nitrophenylhydrazine the corresponding N-ethyl derivative was not prepared.

Bromine Action on XV and XVI.—Mole portions of XV and XVI, respectively, were added to appropriate volumes of glacial acetic acid containing mole portions of bromine and excess sodium acetate. The reaction mixtures, after one day at room temperature, were diluted with water and the solids were removed by filtration. From XV (1.60 g.) there was recovered XV (1.0 g., 62%); m. p. and mixed m. p. 126–128° with authentic XV. From XVI (0.50 g.) there was recovered XVI (0.46 g., 92%); m. p. and mixed m. p. 164–166° with authentic XVI.

Acknowledgments.—The author wishes to express his appreciation to Dr. C. F. Koelsch for his extremely helpful guidance and deep interest throughout this problem. The carbon-hydrogen microanalyses were carried out by Messrs. R. Amidon and J. Buckley, and Dr. S. Sundet.

Summary

A study of the carbon-carbon cleavage by bromine of 2-*p*-nitrophenylhydrazones of 1,2,3-trioxo compounds revealed that the reaction is base-catalyzed and applies only to mono-substituted phenylhydrazones of the type mentioned.

A mechanism is proposed to account for these facts.

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(11) Ciusa and Rastelli, *Gazz. chim. ital.*, **54**, 72 (1924).