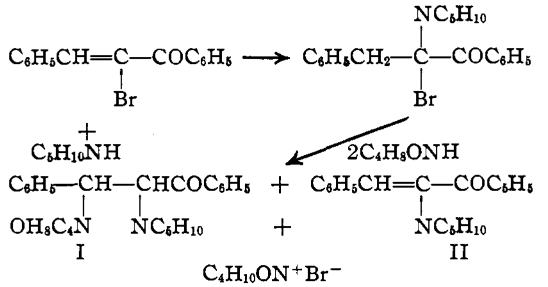
[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

α,β-Unsaturated Aminoketones. IV.[1] Mechanism Studies of the Reaction of α-Bromo-α,β-unsaturated Ketones with Secondary Amines

BY NORMAN H. CROMWELL

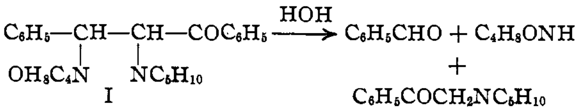
In paper II[2] of this series a mechanism was proposed for the reaction of morpholine with α-bromobenzalacetophenone, and with benzalacetophenone dibromide. The present investigation was undertaken in order to check this proposal and at the same time to eliminate certain other possible ways of explaining these reactions.

It was found that α-bromo-α-piperidinobenzylacetophenone[3] reacted with excess morpholine to give the two expected products, α-piperidino-β-morpholinobenzylacetophenone I and α-piperidinobenzalacetophenone II. Approximately two moles of product I to one mole of II resulted. The following scheme seems to explain these results.



$$C_6H_5CH{=}\underset{Br}{C}{-}COC_6H_5 + C_5H_{10}NH \longrightarrow C_6H_5CH_2{-}\overset{NC_5H_{10}}{\underset{Br}{C}}{-}COC_6H_5 \xrightarrow{2C_4H_8ONH} \underset{I}{C_6H_5{-}\underset{OH_8C_4N}{CH}{-}\underset{NC_5H_{10}}{CH}COC_6H_5} + \underset{II}{C_6H_5CH{=}\underset{NC_5H_{10}}{C}{-}COC_6H_5} + C_4H_{10}ON^+Br^-$$

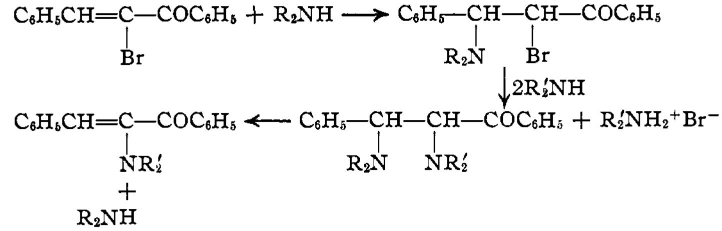
The structure of I was shown by hydrolyzing it with dilute acid. Only ω-piperidinoacetophenone and benzaldehyde were found in the reaction mixture. Compound II was identical with α-piperidinobenzalacetophenone prepared according to the method of Dufraisse.[4]



$$\underset{I}{C_6H_5{-}\underset{OH_8C_4N}{CH}{-}\underset{NC_5H_{10}}{CH}{-}COC_6H_5} \xrightarrow{HOH} C_6H_5CHO + C_4H_8ONH + C_6H_5COCH_2NC_5H_{10}$$

It was not possible to obtain the unsaturated amino ketone II from the diamino ketone I by long heating in alcoholic solutions. The diamino ketone does not seem to be the precursor of the unsaturated amino ketone.

These experiments may be taken as positive evidence for the mechanism previously proposed[2] for these reactions and as negative evidence against the following scheme.



$$C_6H_5CH{=}\underset{Br}{C}{-}COC_6H_5 + R_2NH \longrightarrow C_6H_5{-}\underset{R_2N}{CH}{-}\underset{Br}{CH}{-}COC_6H_5 \xrightarrow{2R_2'NH} C_6H_5{-}\underset{R_2N}{CH}{-}\underset{NR_2'}{CH}{-}COC_6H_5 + R_2'NH_2^+Br^- \longrightarrow C_6H_5CH{=}\underset{NR_2'}{C}{-}COC_6H_5 + R_2NH$$

A second study was conducted by using these same two secondary amines in the reverse order. The results of this second experiment were not of the same nature as those of the first investigation, but they contributed materially to these studies. When α-bromo-α-morpholinobenzylacetophenone[2] was treated with excess piperidine a much more rapid reaction took place than in the first experiment described above. Almost two moles of unsaturated amino ketone product to one mole of the diamino ketone product resulted. Neither of these two products was of a single chemical nature, but they were found to be mixtures that were almost impossible to separate because of the similar solubilities of constituents. Mixed melting point experiments with compounds differing only in the presence of a morpholino in place of a piperidino group gave only small depressions. Consequently, it was necessary to rely on carbon and hydrogen analyses and decomposition products for the chemical identification of the products.

The analyses of the unsaturated product indicated that it was probably a mixture of α-morpholinobenzalacetophenone IV and of α-piperidinobenzalacetophenone II. The analyses of the diamino ketone product also showed that it was not the normal product III, as expected, but that it more probably was a mixture of III with the dipiperidino ketone V of Dufraisse.[4] The hydrolysis of this diamino ketone product gave a mixture of ω-morpholino- and ω-piperidinoacetophenones.

From the experimental evidence it seems that the relative basic strengths of the amines used

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[1] For paper III of this series see Cromwell, THIS JOURNAL, **62**, 3470 (1940).

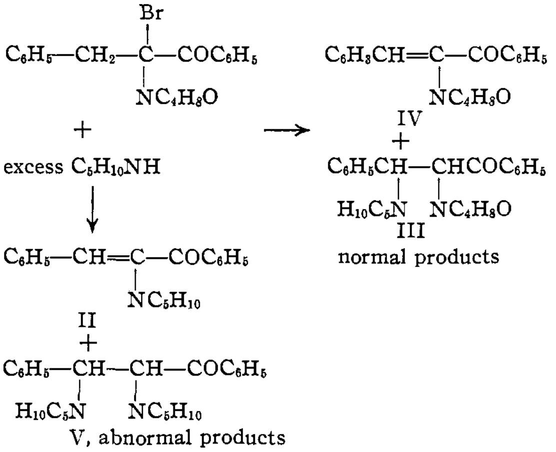
[2] Cromwell, *ibid.*, **62**, 2897 (1940).

[3] Dufraisse and Moureu, *Bull. soc. chim.*, (4^e^) **41**, 466 (1927).

[4] Dufraisse and Moureu, *ibid.*, (4^e^) **41**, 457 (1927).

affect not only the rate but also the course of these reactions. It appears unlikely that the results of this second experiment in any way invalidate the conclusions drawn from the clear course of all previously described experiments.[1,2]

It has been stated by others[5] that piperidine reacts more rapidly with halogen compounds and gives more by-products than does morpholine. These latter experiments not only bear out this contention, but, furthermore, indicate that possibly a morpholino radical already attached to carbon may be replaced by a piperidino radical under these conditions to give abnormal products.



IV

III

normal products

II

V, abnormal products

The reactions of α-bromo-α,β-unsaturated ketones with various pairs of secondary amines, as well as other studies of the mechanisms and products of these interesting reactions are in progress.

Experimental[6]

Reaction of α-Bromo-α-piperidinobenzylacetophenone with Morpholine.—A freshly prepared sample (15.7 g.) of α-bromo-α-piperidinobenzylacetophenone[3] (m. p. 160–162°), was mixed with absolute alcohol (30 ml.). To this suspension was added a two molar amount of morpholine (7.35 g.). The mixture was then heated to boiling to give a red-orange solution which set solid while still hot. After standing at room temperature for twenty hours a light yellow precipitate was filtered off and washed with 95% alcohol and then water to give light yellow needles (7.5 g.), m. p. 149–155°. Fractional recrystallization from benzene and petroleum ether gave two products: IA (2.2 g.), m. p. 174–175°; IB (3.5 g.), m. p. 155–157°. A mixture of IA and IB melted at 153–158°.

Anal. Calcd. for $C_{24}H_{30}N_2O_2$: C, 76.16; H, 7.98. Found: for IA, C, 76.41; H, 7.85; for IB, C, 76.22; H, 7.98.

The residual red reaction mixture was evaporated and cooled to give a red product. This was recrystallized from absolute alcohol to give orange-red plates (2.4 g.) compound II, m. p. 102–103°. Compound II was identical with α-piperidinobenzalacetophenone as prepared by Dufraisse.[4]

Anal. Calcd. for $C_{20}H_{21}NO$: C, 82.46; H, 7.24; N, 4.80. Found: C, 82.80; H, 7.24; N, 4.90.

Hydrolysis of IA and IB.—These products were hydrolyzed with dilute sulfuric acid (15%) in the usual way. Both gave ω-piperidinoacetophenone and benzaldehyde as the major products. The ω-piperidinoacetophenone was recovered as the hydrochloride and was found to be identical with a synthetic sample prepared from ω-bromoacetophenone.[7]

ω-Piperidinoacetophenone Hydrochloride.—IA (1.00 g.) gave 0.60 g. (m. p. 225–227°); IB (1.44 g.) gave 0.65 g. (m. p. 226–227°). A mixture of the hydrochlorides of ω-piperidinoacetophenone and ω-morpholinoacetophenone melted at 212–219°.

Anal. Calcd. for $C_{13}H_{18}NOCl$: C, 65.12; H, 7.55. Found: C, 65.15; H, 7.65.

Attempted Decomposition of IB.—A sample of the diamino ketone (0.551 g.) was refluxed with absolute alcohol (8 ml.) for five hours and then allowed to stand at room temperature for twenty hours. The light yellow solution did not darken after this treatment. All of the starting material was recovered unchanged (0.54 g., m. p. 156–158°).

Reaction of Piperidine with α-Bromo-α-morpholinobenzylacetophenone.—Freshly prepared α-bromo-α-morpholinobenzylacetophenone[2] (20.64 g.) was mixed with absolute alcohol (37 ml.). To this suspension piperidine (10.6 g., 2.2 molar amount) was added rapidly with stirring. A slow reaction set in, the solution slowly turning yellow and giving off a small amount of heat. After standing at room temperature for four days a mixture of orange and yellow crystals was filtered off and washed with water. Concentration of the filtrate gave more product, resulting in a total of 14.8 g. of mixed product.

The orange colored product was separated from the yellow one by washing with small amounts of 95% ethyl alcohol. Several recrystallizations of the orange product from absolute alcohol gave 5.0 g. of orange crystals, m. p. 96–97°; mixed with pure α-piperidinobenzalacetophenone, m. p. 96–99°, and with pure α-morpholinobenzalacetophenone, m. p. 93–96°.

Anal. Calcd. for $C_{19}H_{19}NO_2$: C, 77.80; H, 6.51; N, 4.77. Calcd. for $C_{20}H_{21}NO$: C, 82.46; H, 7.24; N, 4.80. Found: C, 78.90; H, 6.78; N, 5.08.

It was recrystallized several times more from alcohol and from benzene and petroleum ether (solutions seeded with α-morpholinobenzalacetophenone[2]).

Anal. Found: C, 80.30; H, 6.96; N, 4.95.

Acid hydrolysis of the mixed unsaturated product in the usual way gave 80–85% yields of benzyl phenyl diketone.[2]

The yellow product was recrystallized two times from absolute alcohol and then two times from benzene and petroleum ether to give 4.1 g. of pale yellow needles, m. p. 153–156°; mixed with IB, m. p. 148–151°; mixed with the

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(5) Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **70**, 406 (1937).

(6) Some of the microanalyses for carbon and hydrogen and Dumas nitrogen are by E. E. Renfrew of the School of Chemistry, University of Minnesota.

(7) Rabe and Schneider, *Ber.*, **41**, 874 (1908).

low melting form of α,β-dimorpholinobenzylacetophenone,[2] m. p. 145–152°.

Anal. Calcd. for $C_{24}H_{30}N_2O_2$: C, 76.16; H, 7.98; N, 7.40. Calcd. for $C_{25}H_{32}N_2O$: C, 79.77; H, 8.55; N, 7.44. Calcd. for $C_{23}H_{28}N_2O_3$: C, 72.61; H, 7.41; N, 7.36. Found: C, 77.64; H, 8.39; N, 7.41.

It was recrystallized again from the same solvents.

Anal. Found: C, 77.61; H, 8.20; N, 7.42.

These experiments were repeated three times and the above described products were obtained each time.

Hydrolysis of the diamino ketone product in the usual way gave a mixture of ω-morpholino- and ω-piperidinoacetophenones, which was isolated as the hydrochloride mixture. This mixture melted at 216–220°.

Anal. Calcd. for $C_{12}H_{16}NO_2Cl$: C, 59.64; H, 6.66; N, 5.79. Calcd. for $C_{13}H_{18}NOCl$: C, 65.2; H, 7.57; N, 5.84. Found: C, 63.18; H, 7.21; N, 5.54.

Several recrystallizations from absolute alcohol and dry ether did not change the melting point or composition of this mixture appreciably.

Summary

1. Further evidence is presented for a proposed mechanism[2] of the reaction of α-bromo-α,β-unsaturated ketones with secondary amines.
2. It has been shown that these reactions may take an abnormal course depending on the characteristics of the secondary amine used.
3. A new α,β-diaminobenzylacetophenone has been prepared.

LINCOLN, NEBRASKA RECEIVED DECEMBER 30, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Color Tests for Some Organobismuth and Other Organometallic Compounds[1]

BY HENRY GILMAN AND H. L. YABLUNKY

Different color tests have been proposed for organometallic compounds. The first of these, which is now being designated as Color Test I, is most comprehensive, and has been applied to a wide variety of organometallic compounds. This test uses Michler ketone and is applicable, in general, to all organometallic compounds which add to the carbonyl group in ketones.[2] The second color test[3] (Color Test II) has a two-fold utility. First, it can be used to differentiate organolithium compounds from the corresponding Grignard reagents. Second, it is useful, with some limitations, for differentiating alkyllithium compounds from aryllithium compounds.

The test about to be described, III, appears to be characteristic not only for triarylbismuth dihalides but also for the more reactive *aryl*metallic compounds. Test III is based on the observation of some years ago by Challenger[4a] that a transitory purple color developed when triphenylbismuth dibromide reacted with phenylmagnesium bromide incidental to an attempted preparation of tetraphenylbismuthonium bromide. The reaction apparently did not proceed as expected

$$(C_6H_5)_3BiBr_2 + C_6H_5MgBr \longrightarrow (C_6H_5)_4BiBr + MgBr_2$$

since the only products obtained were triphenylbismuth, diphenylbismuth bromide, phenylbismuth dibromide and bromobenzene. Later, Challenger and co-workers[4b] reported the same intense purple color in attempting to prepare other arylbismuthonium chlorides and fluorides by this reaction. It is unlikely that this reaction can be used to prepare bismuthonium compounds inasmuch as triphenylarsenic dichloride and methylmagnesium iodide gave triphenylarsenic[4c] and not the known stable methyltriphenylarsonium chloride.[4d]

Two suggestions were offered[4b] to account for the transient purple color. One of these was the possible formation of tetraarylbismuthonium halides (R_4BiX); and the other was the momentary formation of compounds of the type R_5Bi, analogous to the bright red triphenylmethyltetramethylammonium and benzyltetramethylammonium prepared by Schlenk and Holtz.[5] These are the only R_5 types reported in Group V. The purple color is probably not due to the formation of a bismuthonium halide because R_4AsX[6] and R_4SbX

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[1] This is paper XXXV in the series "Relative reactivities of organometallic compounds." Paper XXXIV is in THIS JOURNAL, **62**, 3206 (1940).

[2] Gilman and Schulze, *ibid.*, **47**, 2002 (1925). The most recent study concerned with this color test is by Gilman and Jones, *ibid.*, **62**, 1243 (1940). The latter article has references to several other reports on the range of applicability and degree of sensitivity of the color test.

[3] Gilman and Swiss, *ibid.*, **62**, 1847 (1940).

[4] (a) Challenger, *J. Chem. Soc.*, **105**, 2210 (1914). (b) Challenger and Goddard, *ibid.*, **117**, 762 (1920); Challenger and Wilkinson, *ibid.*, **121**, 91 (1922). (c) Challenger and Allpress, *ibid.*, **119**, 913 (1921). (d) Michaelis, *Ann.*, **321**, 166 (1902).

[5] Schlenk and Holtz, *Ber.*, **49**, 603 (1916); *ibid.*, **50**, 274 (1917).

[6] Blicke and co-workers, THIS JOURNAL, **55**, 3056 (1933); **57**, 720 (1935); **60**, 423 (1938); **61**, 88 (1939).