Reaction of N-Bromobenzamide with Allyl-1-d_2 Acetate[1]

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The reaction of N-bromobenzamide with allyl acetate in carbon tetrachloride has been shown to give 2,3-dibromopropyl acetate and benzamide as the major products. N-phenyl-N'-benzoylurea was also isolated but in low yield. The allylic hydrogen of the allyl acetate have been shown not to be the source of the hydrogen found to replace the bromide of the N-bromobenzamide by conducting the reaction with allyl-1-d_2 acetate and demonstrating that the benzamide obtained was free of deuterium. The synthesis and infrared spectra of allyl-1-d_2 alcohol, allyl-1-d_2 acetate, and benzamide-N,N-d_2 are presented.

During the course of a study concerning the reactivity of N-bromoamides toward unsaturated compounds, it was observed that the major products of the reaction of N-bromobenzamide with allyl acetate are 2,3-dibromopropyl acetate (57.4%) and benzamide (70%). The only other product identified was N-phenyl-N'-benzoylurea, which was isolated in low yield.

In general, the most common course of the reaction of N-bromoamides and -imides with unsaturated compounds is the formation of allylic or benzylic bromides and regeneration of the parent amide or imide. The allylic bromination reaction, frequently referred to as the Wohl-Ziegler reaction,[3] has found wide synthetic applicability; particularly in conjunction with use of N-bromosuccinimide and N-bromoacetamide. Occasionally these reactions take another course resulting in the addition of bromine to the double bond of the unsaturated reactant and regeneration of the parent amide or imide.[4] A simple representation of the addition reaction fails to reveal the source of the hydrogen observed to replace the bromine of the N-bromoamide.

$$2RCONHBr + {>}C{=}C{<} \longrightarrow$$
$$2RCONH_2 + {>}CBrC{<}Br$$
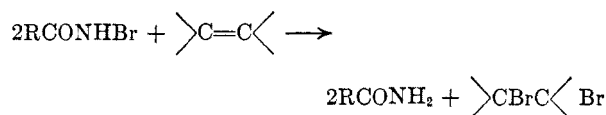
This obvious discrepancy has been noted by several investigators[5] but, no satisfactory explanation of the hydrogen source has been forthcoming.

The addition reaction has variously been suggested to occur via free radical,[4,5a] polar,[5d] and combined heterolytic and homolytic paths.[5c] Indeed the reactions of N-bromoamides and -imides are so sensitive to structural and environmental influences that the diverse mechanisms postulated may well be compatible with the individual systems in reference. One common aspect of the postulated mechanisms is their failure to account for the hydrogen found to replace the bromine of of the brominating agent other than to suggest that it must be the result of a step in which an amidyl or imidyl radical abstracts hydrogen from a donor present in the reaction mixture.[4,5b,c,d] The identity of the hydrogen donor, HZ, has not
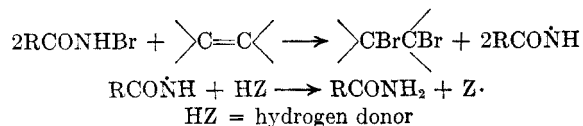
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(2) Texas U. S. Chemical Co., Research Center, Parsippany, N. J.

(3) C. Djerassi, Chem. Revs., 43, 271 (1948).

(4) For a competent review of the literature of the addition reaction see R. E. Buckles, R. C. Johnson, and W. J. Probst, J. Org. Chem., 22, 55 (1957).

(5) (a) E. R. Buchman and D. R. Howton, J. Am. Chem. Soc., 70, 2517, 3510 (1948); (b) R. E. Buckles, J. Am. Chem. Soc., 71, 1157 (1949); (c) E. A. Braude and E. S. Waight, J. Chem. Soc., 1116 (1952); (d) W. J. Bailey and J. Bello, J. Org. Chem., 20, 525 (1955).
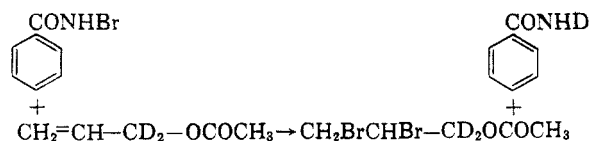
$$2\text{RCONHBr} + \text{>C=C<} \longrightarrow \text{>CBrĊBr} + 2\text{RCOṄH}$$

$$\text{RCOṄH} + \text{HZ} \longrightarrow \text{RCONH}_2 + \text{Z·}$$

$$\text{HZ} = \text{hydrogen donor}$$

been elucidated nor have products resulting from the subsequent reaction of Z· been isolated.

For the reaction of excess allyl acetate with N-bromobenzamide in carbon tetrachloride as the reaction medium, the most readily available hydrogen in the system from the standpoint of abstraction by a benzamidyl radical, should be the allylic hydrogen of the unsaturated ester. This follows from a consideration of the ability of the resulting allylic radical to be stabilized through resonance. The facile formation of allylic hydroperoxides and allylic, free radical halogenations,

$$\text{CH}_2=\text{CH—ĊH—OCOCH}_3 \longleftrightarrow$$
$$·\text{CH}_2\text{—CH=CH—O—COCH}_3$$
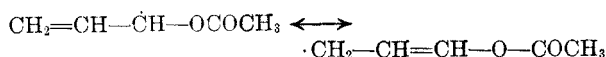
such as high temperature chlorination, testify to the relative ease of the abstraction of allylic hydrogens.
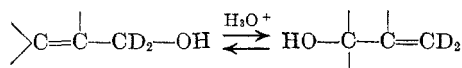
A direct experimental test of this possible explanation of the source for the unaccountable hydrogen is made possible by carrying out the addition reaction with allyl acetate in which the allylic hydrogen has been replaced with deuterium and determining if the resultant benzamide has deuterium on its nitrogen.

$$\text{CONHBr} \qquad\qquad\qquad \text{CONHD}$$

+   +

$$\text{CH}_2=\text{CH—CD}_2-\text{OCOCH}_3 \rightarrow \text{CH}_2\text{BrCHBr—CD}_2\text{OCOCH}_3$$

It has been reported[6] that attempts to reduce acrylic acid, its esters, or its salts directly in a manner suitable for the preparation of allyl-1-d_2 acetate failed due to accompanying polymerization. The deuterated ester was obtained by the addition of methyl acrylate to anthracene followed by reduction with lithium aluminum deuteride, acetylation, and pyrolysis.

In the present study the synthesis of allyl-1-d_2 acetate was achieved by reducing acrylyl chloride with lithium aluminum deuteride and acetylating the resulting deuterated allyl alcohol.

Since both allyl alcohol and allyl acetate can undergo an acid catalyzed oxotropic rearrangement,[7] resulting in an equal distribution of deuterium between the α and γ carbon atoms, it was necessary to maintain a neutral or basic medium throughout the reaction sequence. Accordingly, the lithium

$$\text{>C=C—CD}_2\text{—OH} \underset{\text{H}_3\text{O}^+}{\rightleftarrows} \text{HO—C—C=CD}_2$$

aluminum deuteride reduction complex was hydrolyzed with a calculated amount of water and 15% sodium hydroxide solution according to the procedure described by Amundsen and Nelson,[8] and the acetylation was carried out in the presence of pyridine after the method of Levine and Kuna who have used it to successfully acetylate allylic alcohols without isomerization.[9]

A sample of the allyl-1-d_2 acetate thus prepared was brominated with N-bromobenzamide; a 2:1 molar ratio of N-bromoamide was used. An infrared spectrum of the recovered benzamide did not indicate the presence of deuterium, demonstrating that the allylic hydrogens are not an important source of the hydrogen found to replace the bromine of the brominating agent. At the present time we are unable to offer a satisfactory explanation of the hydrogen source.

In order to check the ability of the infrared method to determine deuterium bound to benzamide nitrogen, a sample of benzamide-N,N-d_2 was prepared by hydrolyzing sodium benzamide with pure deuterium oxide. The infrared spectrum, Fig. 1, shows a broad N—D absorption band[10] at 3.9–4.3 μ which is absent in the infrared spectrum of ordinary benzamide.
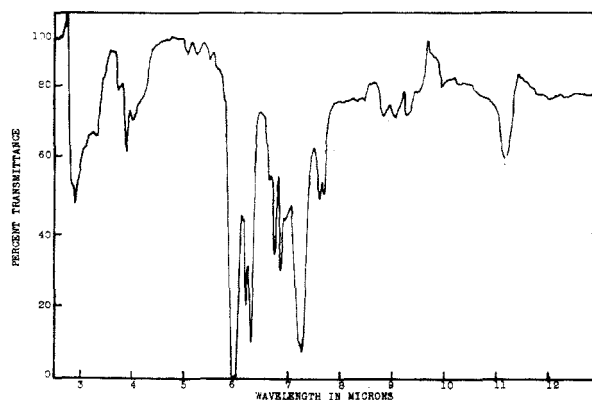

Fig. 1. Infrared spectrum of benzamide-N,N-d_2 chloroform solution

EXPERIMENTAL[11]

Materials. Lithium aluminum hydride was obtained from Metal Hydrides Inc., Beverly, Mass., and was 98% pure. Carbon tetrachloride was reagent grade material refluxed for 24 hr. with 15% sodium hydroxide, washed with water, dried in contact with calcium chloride, and distilled from

(6) P. D. Bartlett and F. A. Tate, *J. Am. Chem. Soc.*, **75**, 91 (1953).

(7) E. A. Braude, *Quart. Revs.*, **4**, 404 (1950).

(8) L. A. Amundsen and L. S. Nelson, *J. Am. Chem. Soc.*, **73**, 242 (1950).

(9) P. A. Levine and M. Kuna, *J. Biol. Chem.*, **118**, 315 (1937).

(10) H. M. Randall, N. Fuson, R. G. Fowler, and J. R. Daugle, *Infrared Determination of Organic Structures*, D. Van Nostrand Co., Inc., Toronto, Canada, 1949, p. 6.

(11) Melting points and boiling points are uncorrected. Infrared measurements were made on a Perkin-Elmer, Model 21, double beam infrared recording spectrophotometer fitted with a sodium chloride prism. The microanalyses were performed by Micro Tech Laboratories, Skokie, Ill.

phosphorous pentoxide. Allyl acetate was commercial material purified by fractional distillation in an efficient column.

Acrylyl chloride[12] and sodium benzamide[13] were prepared by methods described in the literature. N-Bromobenzamide was prepared according to the procedure of Hauser and Renfrow[14] and after two recrystallizations from a chloroform hexane mixture, melted at 129–130° (Literature value[14] m.p. 129–130°). Iodometric analysis indicated the N-bromobenzamide to be 99.8% pure.

Reaction of N-bromobenzamide with allyl acetate. A mixture of 250 ml. of carbon tetrachloride, 30 g. (0.30 mole) of allyl acetate, and 30.3 g. (0.15 mole) of N-bromobenzamide was refluxed gently under a nitrogen atmosphere until a negative starch-iodide test indicated the reaction to be complete (3.5 hr.). The crystalline deposit that formed on chilling was collected on a filter and washed with cold carbon tetrachloride. Extraction of this solid (m.p. 121–123°) with boiling water effected a separation into a water insoluble portion, 1.8 g., and 7.2 g. of pure benzamide which deposited from the extract on cooling. Recrystallization of the water insoluble fraction from benzene gave N-phenyl-N′-benzoylurea, m.p. 201–202°, identified via its infrared spectra (CHCl₃) and a mixed melting point with an authentic sample.[15]

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 70.0; H, 5.04; N, 11.7. Found: C, 70.18; H, 5.10; N, 11.49.

The combined carbon tetrachloride filtrate and washings were concentrated in vacuo to ca. 100 ml. and diluted with 100 ml. of cold petroleum ether, b.p. 30–60°. An orange, gummy solid precipitated which weighed 7.5 g. before recrystallization from hot water (Norite) gave 5.0 g. of pure benzamide, making the over-all yield of benzamide 12.7 g. (70%). The solvents were removed from the carbon tetrachloride-petroleum ether filtrate and the light orange residual oil was distilled through a small Vigreux column. Three fractions were collected: (a) b.p. 77–90° (6 mm.), 2.0 g., n_D^{20} 1.5112; (b) b.p. 90–94° (6 mm.), 5.7 g., n_D^{20} 1.5080; (c) b.p. 94–95° (6 mm.), 7.9 g., n_D^{20} 1.5107. Decomposition of the distilland with evolution of hydrogen bromide forced the discontinuation of the distillation. A black, resinous glassy material weighing 8.4 g. remained in the distillation flask. Fractions (b) and (c) were combined and redistilled to give 11.2 g. (57.4%) of 2,3-dibromopropyl acetate, b.p. 94–95° (6 mm.), n_D^{20} 1.5102 (Literature[16] values, b.p. 100–101° (5 mm.), n_D^{20} 1.5064).

Anal. Calcd. for $C_5H_8Br_2O_2$: Br, 61.47. Found: Br, 61.66.

The infrared spectrum was in agreement with that obtained for a sample of 2,3-dibromopropyl acetate prepared by the direct bromination of allyl acetate with bromine.

Allyl-1-d_2 alcohol. A slurry of 6 g. (0.14 mole) of lithium aluminum deuteride in 300 ml. of dry ether was prepared under a nitrogen atmosphere and then chilled in an ice bath. A solution of 20 g. (0.22 mole) of acrylyl chloride in 100 ml. of ether was added to the stirred hydride slurry at a rate permitting the reaction temperature to be maintained below 5°. After the acid chloride addition the mixture was stirred at room temperature for 2 hr. and again chilled in an ice bath. The reduction complex was then hydrolyzed by adding 7 ml. of water, 7 ml. of 15% sodium hydroxide, and 7 ml. of water, dropwise and in that order. The granular precipitate that formed was removed by filtration and thoroughly washed with dry ether. The combined filtrate and washings was dried with sodium sulfate, concentrated by distillation through a helice packed column to ca. 60 ml. and dried

again with sodium sulfate. Thirty ml. of n-butyl ether was added for a distillation chaser, and the solution was fractionally distilled using a semi-micro, glass helice packed column. After a solvent forerun, three fractions were collected: (a) b.p. 45–80°, 0.58 g.; (b) b.p. 80–95°, 1.17 g.; (c) b.p. 95–98°, 5.90 g. The infrared spectrum of fraction (c) (see Fig. 2) is similar to that of allyl acetate except for
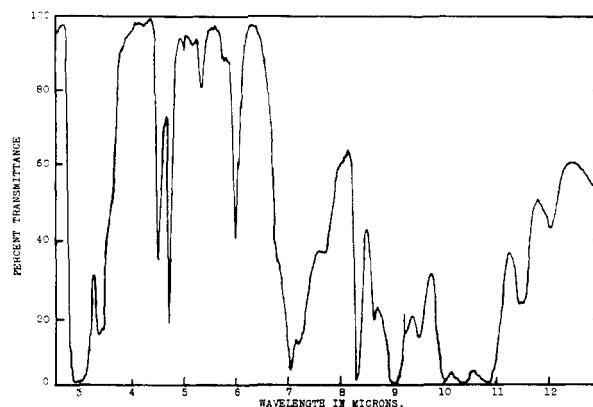

Fig. 2. Infrared spectrum of allyl-1-d_2 alcohol

the two absorption bands at 4.45–4.80μ (C—D)[17] which are absent in the spectrum of ordinary allyl acetate.

Allyl-1-d_2 acetate. Fractions (b) and (c) from the allyl-1-d_2 alcohol synthesis were combined and treated with an ice cold mixture of 15 ml. of pyridine and 12 g. of acetic anhydride. The mixture was allowed to stand at room temperature for 20 hr.; poured into a precooled solution of 10 ml. of conc. hydrochloric acid in 50 ml. of water contained in a separatory funnel, and extracted with four 20-ml. portions of pentane. The pentane extract was immediately washed with dilute sodium bicarbonate solution and dried over sodium sulfate. n-Butyl alcohol was added as a chaser and the solution was distilled using a semi-micro glass helice packed column. After a low-boiling forerun, a fraction boiling at 101–104° was accepted as allyl-1-d_2 acetate (literature value, b.p. allyl acetate, 102–104°). The yield was 7.8 g. (65%). The infrared spectrum (see Fig. 3) shows absorption at 4.4–4.8μ (C—D).[17]
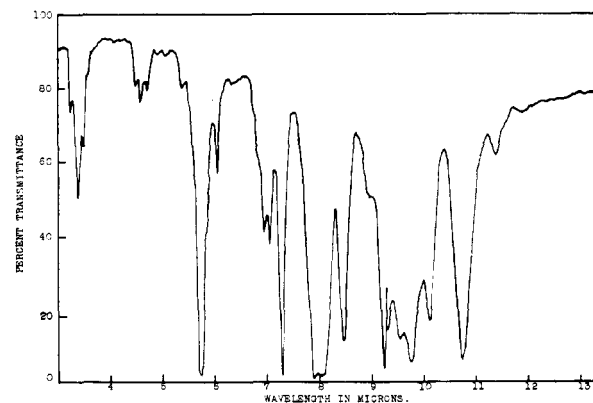

Fig. 3. Infrared spectrum of allyl-1-d_2 acetate. Carbon tetrachloride solution

Reaction of N-bromobenzamide with allyl-1-d_2. A small, all-glass apparatus was provided with a nitrogen atmosphere and charged with 25 ml. of carbon tetrachloride, 2.5 g. (0.0125 mole) of N-bromobenzamide and 2.5 g. (0.025 mole)

(12) G. G. Stemple, R. P. Cross, and R. P. Mariella, *J. Am Chem. Soc.*, **72**, 2299 (1950).

(13) A. W. Titherley, *J. Chem. Soc.*, **71**, 468 (1897).

(14) C. R. Hauser and W. B. Renfrow, *J. Am. Chem. Soc.*, **59**, 121 (1937).

(15) B. Kuhn, *Ber.*, **17**, 2881 (1884).

(16) V. P. Golender, *Sbornik State Obshchei Khim.*, **2**, 1261 (1953); *Chem. Abstr.*, **48**, 9914 (1954).

(17) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., N. Y., 1943, p. 171.

of allyl-1-d_2 acetate. The mixture was heated at gentle reflux for 90 min.; at which time a starch iodide test indicated complete reaction of the N-bromobenzamide. On being set aside overnight in a refrigerator, 0.89 g. of crude benzamide (m.p. 115–120°) deposited from solution. A single recrystallization from benzene (Norite) gave 0.6 g. (39.8%) of pure benzamide, m.p. 127°. The infrared spectrum (CHCl₃) was identical with that of nondeuterated benzamide and showed no absorption at 4.2μ.

Benzamide-N,N-d_2. A mixture of 0.9 g. of sodium benzamide and 3 ml. of deuterium oxide (99.8% isotropically pure) was warmed until a clear solution was obtained. The solution was protected from atmospheric moisture and allowed to crystallize. The benzamide-N,N-d_2 which deposited was isolated by filtration and dried *in vacuo*, m.p. 123–124°. One recrystallization from benzene gave 0.38 g.

(50%) benzamide-N,N-d_2, m.p. 127°. Infrared spectrum (see Fig. 1) shows absorption at 3.9–4.3 μ, N—D,[17] absent in the spectrum of ordinary benzamide. It is very likely that benzamide-N,N-d_2 rather than N-deuterobenzamide was formed in this preparation since the work of Brodskii[18] some years ago showed that amide hydrogen atoms exchange readily with the hydrogens of water, even in the absence of a catalyst. In the present case, by-product deuterated sodium hydroxide would be expected to catalyze the exchange of all amide hydrogen atoms in benzamide. However, the use of either the mono or di deutero benzamide would not alter the conclusions arrived at in the present investigation.

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(18) A. I. Brodskii, *Trans. Faraday Soc.*, **33**, 1180 (1937)

Solvent Effects in the Reaction of Free Radicals and Atoms. V. Effects of Solvents on the Reactivity of t-Butoxy Radicals
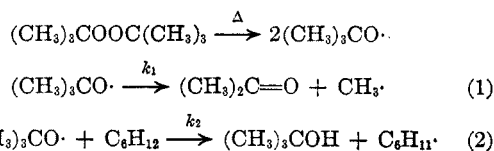
GLEN A. RUSSELL[1]

The effects of solvents upon the products of decomposition of di-*t*-butyl peroxide at 130° are considered. Quantitative data in regard to the peroxide-catalyzed reaction of chloromethanes with cyclohexane are presented. Evidence is presented supporting the displacement of a chlorine atom from 1-chloronaphthalene by a *t*-butoxy radical.

Previous papers in this series have demonstrated that aromatic solvents can drastically alter the reactivity of a chlorine atom.[2] These results have been interpreted in terms of a π-complex formed between the electrophilic chlorine atom and the electron-donating aromatic nucleus.
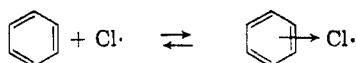
The complexed chlorine atom is apparently less reactive and more selective in its reactions than the free chlorine atom. Since *t*-butoxy radicals have a reactivity quite similar to chlorine atoms,[3] it was of interest to ascertain if similar solvent effects could be detected in the reactions of these radicals.

Solvent effects have been investigated in the decomposition of di-*t*-butyl peroxide in the presence of cyclohexane at 130° by measuring the fraction of *t*-butoxy radicals which enter into the decomposition reaction (1) and the hydrogen-abstraction reaction (2). From the ratio of acetone and *t*-

$$(CH_3)_3COOC(CH_3)_3 \xrightarrow{\Delta} 2(CH_3)_3CO\cdot$$

$$(CH_3)_3CO\cdot \xrightarrow{k_1} (CH_3)_2C{=}O + CH_3\cdot \quad (1)$$

$$(CH_3)_3CO\cdot + C_6H_{12} \xrightarrow{k_2} (CH_3)_3COH + C_6H_{11}\cdot \quad (2)$$

butyl alcohol formed it is possible to calculate the ratio of k_1/k_2 provided that the products do not result from radical-radical interaction and provided that acetone and *t*-butyl alcohol are formed only in reactions 1 and 2. The former requirement will always be satisfied when the ratio of acetone and *t*-butyl alcohol is independent of *t*-butoxy radical concentration, while the latter requirement will nearly always be satisfied when the combined yield of acetone and *t*-butyl alcohol is quantitative based on the starting di-*t*-butyl peroxide. Table I presents data wherein these requirements have been met.

The ratio of k_1/k_2 is 0.45–.47 when cyclohexane or methylene chloride are used as solvents. The same ratio is observed when the weakly basic benzotrifluoride is used as a solvent. For more basic aromatic solvents, such as benzene, chlorobenzene or diphenyl ether, higher values of k_1/k_2 are observed although the highest value observed is only 25% greater than the value observed in an aliphatic solvent. However, the increase in the ratio of k_1/k_2 is considerably above experimental uncertainty.

The possibility that hydrogen abstraction from the aromatic solvent could occur to a significant extent is easily eliminated. Aromatic solvents cause an increase in the ratio k_1/k_2 whereas production of *t*-butyl alcohol by abstraction of a hydrogen atom from the aromatic solvent would lead to a decrease in this ratio. Moreover, estimates of the relative reactivities of cyclohexane and benzene toward a *t*-butoxy radical have been reported by Williams,

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(2) G. A. Russell, *J. Am. Chem. Soc.*, **79**, 2977 (1957); **80**, 4987, 4997, 5002 (1958).

(3) G. A. Russell, *J. Am. Chem. Soc.*, **79**, 3871 (1957).