crystalline plates, m. p. 60.5–61.5°. A mixture of the solid with a sample of β-bromopropionic acid, m. p. 60–61.5°, melted at 60–61.5°.

Anal. Calcd. for $C_3H_5O_2Br$: neut. eq., 152.9. Found: neut. eq., 153.5.

When an ether solution of phenylmagnesium bromide (1 *M* in 400 ml.) was added to 1 mole (72 g.) of I in 400 ml. of ether at −28 to −35°, the isolated products were as follows: polymer of I, 31 g. (43.1%); β-bromopropionic acid, 44 g. (28.7%); distilled neutral fractions, 1, 75–120° (0.4 mm.), 20 g.; 2, 110–165° (0.4–0.3 mm.), 18 g.; 3, 155–230° (0.3–0.4 mm.), 23.5 g.; residue, 10.5 g. All fractions gave a positive Beilstein halogen test.

β-Anilinopropiophenone can be prepared by the reaction of aniline with either vinyl phenyl ketone or β-halopropiophenone.[6] This derivative was obtained from fractions 1 and 2 as faintly yellow plates, m. p. 115–116°.

Anal. Calcd. for $C_{15}H_{15}ON$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.85; H, 6.71; N, 6.26.

Reaction of I with Magnesium Bromide Dietherate.—Addition of 36 g. (0.5 mole) of I to magnesium bromide dietherate[7] (0.5 mole) in 400 ml. of anhydrous ether resulted in the precipitation of a yellow solid. The solid was filtered, washed with 100 ml. of ether and dissolved in 400 ml. of water. The water solution was acidified and the resulting orange oil extracted with 3–150 ml. portions of ether and dried over sodium sulfate. Following distillation of the ether, the undistilled product solidified. Recrystallization from hexane gave 63.5 g. (83%) of β-bromopropionic acid, m. p. 59–60°.

Reaction of I with Thiourea, Hydrochloric Acid and Magnesium Bromide.—Addition of I to a water solution of equal molar quantities of thiourea, magnesium bromide and hydrochloric acid resulted in an exothermic reaction. Neutralization of the cooled solution with sodium hydroxide gave a 70% yield of a white crystalline solid. A mixture of the solid, m. p. 176–178°, with a sample of β-isothioureidopropionic acid, m. p. 178–179°, produced no depression of the melting point. A similar experiment using magnesium β-bromopropionate, thiourea and hydrochloric acid gave no β-isothioureidopropionic acid.

Reaction of I with Diphenylmagnesium.—One mole (72 g.) of I was added over a period of one-half hour at −25 to −32° to an ether solution of diphenylmagnesium prepared from 1 mole of phenylmagnesium bromide by dioxane precipitation. The addition complex was decomposed as described above and the insoluble solid (84 g., consisting largely of polymers of I) filtered. Distillation of the products gave the following fractions: 1, 27–95° (40–24 mm.), 5.5 g.; 2, 100–150° (23 mm.), 12 g.; 3, 140–158° (23 mm.), 5.5 g.; and residue, 4.5 g. Fraction 2, consisting largely of vinyl phenyl ketone, gave 1,3-diphenyl-Δ^2-pyrazoline,[5] m. p. 151–153°, on treatment with phenylhydrazine.

Reaction of I with Methylmagnesium Iodide.—One mole of I was added to an ether solution of methylmagnesium iodide (1 mole) at −10 to −13°. The Grignard complex was decomposed giving polymer of I (3 g., 4.2%), a neutral oil (13 g., b. p. 29–78° (25–28 mm.)) and β-iodopropionic acid (87 g., 43.5%). The neutral oil contained methyl vinyl ketone as identified by treating with phenylhydrazine to give 1-phenyl-3-methylpyrazoline,[8] m. p. 75.5–76.5°.

Reaction of I with Benzylmagnesium Chloride.—One mole of I was added to an ether solution of benzylmagnesium chloride (1 mole) at −12 to 0°. The Grignard complex was decomposed giving polymer of I (16.1 g., 22.4%) and neutral and acidic portions. Distillation of the neutral portion gave two fractions from which no identifiable product could be isolated. Distillation of the acidic portion gave 17.5 g. (16.1%) of β-chloropropionic acid, m. p. 35–38° and 53.2 g. (32.4%) of γ-phenylbutyric acid, m. p. 47–48°. A mixture of the β-chloropropionic acid with an authentic sample produced no depression of the melting point. The analytical data for the γ-phenylbutyric acid are as follows:

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37; neut. eq., 164.2. Found: C, 73.37; H, 7.46; neut. eq., 165.2.

Addition of an ether solution of benzylmagnesium chloride to a suspension of magnesium β-bromopropionate in ether gave a neutral fraction containing toluene and dibenzyl and an acid fraction containing a relatively large amount of β-bromopropionic acid but only a trace of γ-phenylbutyric acid.

Summary

Reactions of β-propiolactone with Grignard reagents give mixtures of beta-halopropionic acids and vinyl ketones. The possible individual reactions with the components of the Grignard reagent are described. With benzylmagnesium chloride, phenylbutyric acid is a major reaction product.

(6) Collet, *Bull. soc. chim.*, [3] **17**, 80 (1897).

(7) Menschutkin, *Z. anorg. Chem.*, **49**, 34–35 (1906).

(8) Maire, *Bull. soc. chim.*, [4] **3**, 277–278 (1909).

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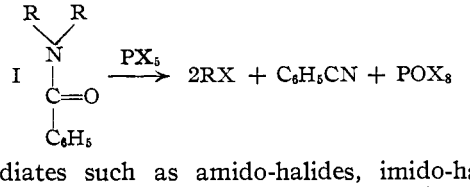
Studies on the Mechanism of the von Braun Reaction

BY NELSON J. LEONARD AND ERWIN W. NOMMENSEN

The reaction in which phosphorus pentahalide converts an N-substituted benzamide (I) to an alkyl halide or alkylene dihalide and benzonitrile has been termed the von Braun reaction.[1] Inter-



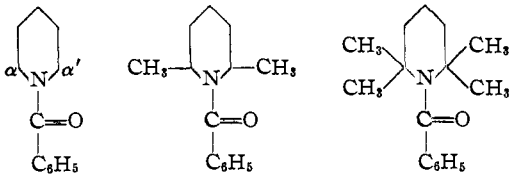
mediates such as amido-halides, imido-halides, and compounds containing a nitrogen–phosphorus link have been postulated, but in no case has the existence of such intermediates been definitely established. In the belief that the von Braun reaction might belong to the general class of displacement reactions at a saturated carbon, where bimolecular or unimolecular nucleophilic substitution is possible,[2] we have made a study of several series of N-substituted benzamides to determine the effect of hindrance and the fate of asymmetry at the α_N-carbon.

In the N,N-alkylene-substituted benzamide series, we have investigated the reaction of N-

(1) For leading reference, see von Braun, *Ber.*, **37**, 3210 (1904).

(2) Hughes, *J. Chem. Soc.*, 968 (1946).

benzoyl-2,6-dimethylpiperidine (III) and N-benzoyl-2,2,6,6-tetramethylpiperidine (IV) with phosphorus pentabromide. von Braun[1] obtained a 78% yield of 1,5-dibromopentane in the reaction



II III IV

of N-benzoylpiperidine (II) with phosphorus pentabromide. A decrease in yield of alkylene dihalide with increase in steric hindrance at the α_N-carbon was observed since compound III gave a 19% yield of 2,6-dibromoheptane and compound IV gave no dibromide.

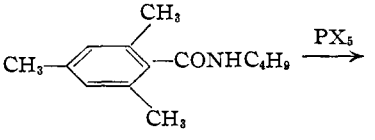
This potential generalization also held for the N-alkyl-substituted benzamide series (V).

$$C_6H_5CONHR \qquad V$$

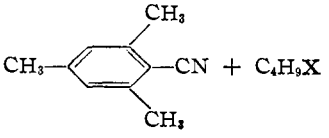
Where the alkyl group contained seven carbons, the von Braun reaction with phosphorus pentabromide gave alkyl bromides in yields which decrease roughly as the steric hindrance to rearward attack at the α_N-carbon increases (R = 4-isohexyl, 36%; 2-heptyl, 28%; 4-heptyl, 17%; 3-(2,4-dimethyl)-pentyl, 10%). Where R was *n*-butyl, *s*-butyl, *t*-butyl, and neopentyl, the first two benzamides gave good yields of *n*- and *s*-butyl bromide, respectively. N-benzoyl-*t*-butylamine gave only a trace of *t*-butyl bromide, and N-benzoylneopentylamine gave no neopentyl bromide. These results appear to indicate either that the reaction with N-benzoyl-*t*-butylamine and N-benzoylneopentylamine follows a different course from that of the first two in this series, or that the halides which may be produced are unstable in the reaction medium. Experiment has not permitted a definite decision between these alternatives, but the former is favored since *t*-butyl bromide and *t*-amyl bromide (probable rearrangement product of neopentyl bromide) are only 40–60% converted to olefin and hydrogen bromide when refluxed over phosphorus pentabromide for one hour.[3]

Since diminution of yield of alkyl halide with increasing steric hindrance to approach at the α_N-carbon would be the behavior expected of a bimolecular nucleophilic substitution reaction, it was desirable to learn whether inversion of configuration occurred at the α_N-carbon when that carbon was asymmetric. Optically pure N-benzoyl-(+)*s*-butylamine was converted to (−)*s*-butyl bromide in 60% yield by the action of phosphorus pentabromide. Since it has been shown that (+)*s*-butylamine (and its benzoyl derivative) and (+)*s*-butyl alcohol have the same steric configuration,[4,5] and that (+)*s*-butyl alcohol and (+)*s*-butyl bromide have the same configuration,[6−10] the inversion of optical rotation in going from N-benzoyl-(+)*s*-butylamine to (−)*s*-butyl bromide corresponds to an inversion of configuration.[11]

Since results with the N,N-alkylene- and N-alkyl-substituted benzamides indicated that hindrance at the α_N-carbon inhibited the formation of alkyl halide, it was of interest to learn if hindrance to approach at the carbon of the carbonyl group would inhibit reaction. The N-mesitoyl group was a logical choice to provide such hindrance.[12] N-Mesitoyl-*n*-butylamine and *s*-butylamine (VI) were made and were subjected to the von Braun reaction. The satisfactory yields of alkyl halide



VI



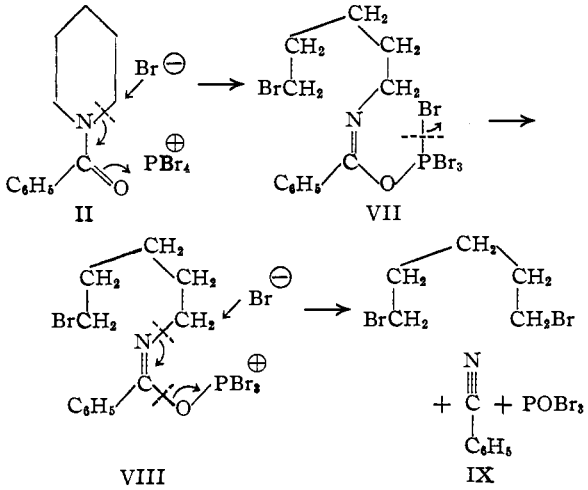
obtained (54% of n-C_4H_9Cl, 30% of s-C_4H_9Cl) indicated that hindrance at the carbonyl did not inhibit reaction.

Any mechanism suggested for the von Braun reaction should be consistent with the previous findings on this reaction and with the new observations here recorded: (a) decreasing yield of halide with increasing hindrance at the α_N-carbon, (b) predominant inversion of configuration at the asymmetric α_N-carbon of N-benzoyl-*s*-butylamine, and (c) negligible influence of hindrance at the carbonyl carbon, as indicated in the N-alkylmesitamide series. The mechanism should be consistent with the structure and behavior

(3) All of the von Braun reactions were completed in less than one hour.

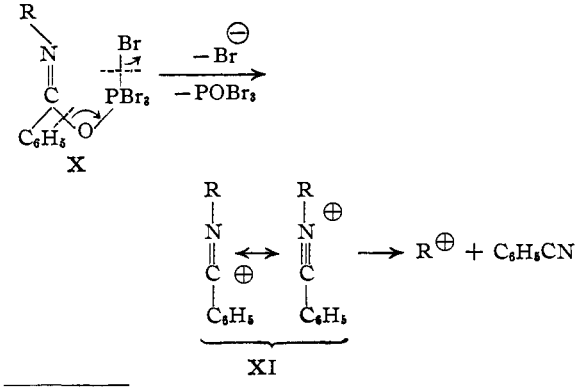
(4) Levene, Rothan and Kuna, *J. Biol. Chem.*, **120**, 777 (1937).
(5) Levene and Kuna, *ibid.*, **140**, 259 (1941).
(6) Levene and Marker, *ibid.*, **91**, 405 (1931).
(7) Letzinger, THIS JOURNAL, **70**, 406 (1948).
(8) Sprung and Wallis, *ibid.*, **56**, 1715 (1934).
(9) Kenyon, Phillips and Pittman, *J. Chem. Soc.*, 1072 (1935).
(10) Cowdrey, Hughes, Ingold, Masterman and Scott, *ibid.*, 1252 (1937).
(11) The extent of the inversion of configuration cannot be calculated accurately, since *s*-butyl bromide has never been obtained optically pure and a choice would have to be made among the several *calculated* maximum specific rotations: $[\alpha]^{25}D$ 28.6°,[6] 26.1°,[7] 22.8°,[8] and 15.4°.[9] Moreover, the active *s*-butyl bromide produced, $[\alpha]^{25}D$ −13.52°, underwent racemization in the presence of phosphorus pentabromide alone, as determined in a blank experiment, so that some activity must have been lost after initial formation of the (−)*s*-butyl bromide. The results, then, are in agreement with preponderant inversion of configuration with some racemization. The extent of inversion is in the range of that observed by Kenyon, Phillips and Pittman[9] for the reactions of active 2-butanol with hydrogen bromide at 60° and with phosphorus pentabromide in ether.
(12) Weinstock and Fuson, THIS JOURNAL, **58**, 1233 (1936).

of phosphorus pentahalides[13,14,15,16] and should account for the isolation of N-ω-bromoalkylbenzamides by hydrolysis at an intermediate stage[17,18,19] and the isolation of benzonitrile, phosphorus oxybromide and alkyl or alkylene halide at the final stage.[1] Our opinion is that the reaction may proceed by nucleophilic attack of bromide in some form with Walden inversion at the α_N-carbon, or by a "unimolecular" process leading to olefin or racemized halide. The "bimolecular" process is visualized as follows, as applied to N-benzoylpiperidine (II)



II VII VIII IX

When the substituted benzamide exhibits some hindrance to rearward attack at the α_N-carbon, the reaction may take a different course, as suggested by the isolation of benzonitrile and phosphorus oxybromide and the formation of isobutylene by the action of phosphorus pentabromide on N-benzoyl-*t*-butylamine. Using a mono-N-alkylbenzamide for illustration, the first attack



X XI

of bromide might lead to abstraction of hydrogen from the nitrogen. The intermediate (X) which would result could decompose through the carbonium-ammonium ion XI, to give benzonitrile and the carbonium ion, $R^{\oplus}$. The fate of the latter would depend upon its constitution and environment, permitting the production of olefin by proton elimination or the formation of alkyl bromide by combination of $R^{\oplus}$ with available bromide ion.

Experimental[20]

Amines

2,2,6,6-Tetramethylpiperidine.—Triacetonamine was prepared from phorone and ammonia by Guareschi's method.[21] By means of a modified Wolff–Kishner reduction[22] of the product, 2,2,6,6-tetramethylpiperidine was produced. Seventy-seven grams (0.044 mole) of triacetonamine, 75 ml. of 85% hydrazine hydrate solution, 70 g. (1.25 moles) of potassium hydroxide and 475 g. (3.28 moles) of triethylene glycol were mixed in a flask fitted with a take-off reflux condenser. The mixture was maintained at 135° for two hours, after which the temperature was raised to 195° while water and product (upper layer) were drawn off. The 2,2,6,6-tetramethylpiperidine was purified by distillation, b. p. 151–152° (750 mm.); $n^{20}D$ 1.4455; yield, 48.8 g. (70%).

Anal. Calcd. for $C_9H_{19}N$: C, 76.53; H, 13.55. Found: C, 76.68; H, 13.39.

Neopentylamine.—This compound was prepared by the action of hypobromite on *t*-butylacetamide according to the directions of Whitmore and Homeyer,[23] and was characterized by direct formation of the benzoyl derivative. The *t*-butylacetamide, m. p. 130–131°, was obtained in 41% yield by a Willgerodt reaction on pinacolone[24] and in 35% yield by treatment of *t*-butylacetic acid[25] with thionyl chloride followed by ammonia.

(+)*s*-Butylamine.—Racemic *s*-butylamine (Sharples Chemicals, Inc.) was resolved by means of *d*-tartaric acid according to the method of Thomé.[26] The optically active bitartrate was recrystallized until a product having $[\alpha]^{25}D$ 21.10° (c = 4.1, water; l = 1 dm.) was obtained. The benzoyl derivative was formed directly from this bitartrate salt.

Amides

Schotten–Baumann Reaction.—The N-benzoyl and N-mesitoyl derivatives of most of the amines were prepared by treating the amine with acid chloride in the presence of aqueous sodium hydroxide. The amides which were prepared are listed in Table I. Previously unreported amides were identified by elementary analysis and by their known precursors. The **N-benzoyl derivative of (+)*s*-butylamine** was formed directly from the bitartrate, using 84 g. (0.38 mole) of (+)*s*-butylamine bitartrate dissolved in 100 ml. of water, 45.2 g. (1.13 mole) of sodium hydroxide dissolved in 200 ml. of water, and 53 g. (0.38 mole) of benzoyl chloride. The product was recrystallized from aqueous ethanol as colorless needles, m. p. 92–92.5°; yield, 62 g. (93%); $[\alpha]^{25}D$ 30.74° (c = 4.0, ethanol; l = 1 dm.).[27]

Although N-mesitoylpiperidine and N-mesitoyl-*n*-butylamine were prepared satisfactorily by the usual Schotten–Baumann, *s*-butylamine persisted in giving a mixture of *s*-

(13) Powell and Clark, *Nature*, **145**, 971 (1940).
(14) van Driel and MacGillavry, *Rec. trav. chim.*, **62**, 167 (1943).
(15) Moureau, Magat and Westroff, *Compt. rend.*, **203**, 257 (1936); **205**, 276, 545 (1937); *Proc. Indian Acad. Sci.*, **8A**, 356 (1938).
(16) Powell, Clark and Wells, *Nature*, **145**, 149 (1940); *J. Chem. Soc.*, 642 (1942).
(17) von Braun, *Ber.*, **37**, 2812 (1904).
(18) von Braun, *ibid.*, **45**, 1263 (1912).
(19) von Braun and Pinkernelle, *ibid.*, **67**, 1218 (1934).
(20) Infrared absorption spectra determination by Mrs. James L. Johnson.
(21) Franchimont and Friedmann, *Rec. trav. chim.*, **24**, 404 (1905).
(22) Huang-Minlon, THIS JOURNAL, **68**, 2487 (1946).
(23) Whitmore and Homeyer, *ibid.*, **54**, 3435 (1932).
(24) Cavalieri, Pattison and Carmack, *ibid.*, **67**, 1783 (1945).
(25) Wideqvist, *Arkiv Kemi, Mineral. Geol.*, **B23**, No. 4 (1946) *Chem. Abstr.*, **41**, 1615 (1947).
(26) Thomé, *Ber.*, **36**, 582 (1903).
(27) Pope and Gibson, *J. Chem. Soc.*, **101**, 1702 (1912).

TABLE I

PREPARATION OF AMIDES

N-Benzoyl derivative	Yield, %	M. p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Piperidine	75	44[28]	$C_{12}H_{15}NO$				
2,6-Dimethylpiperidine	40	110[29]	$C_{14}H_{19}NO$				
2,2,6,6-Tetramethylpiperidine	55	85–88	$C_{16}H_{23}NO$	78.32	78.53	9.47	9.51[30]
n-Butylamine	94	28[31]	$C_{11}H_{15}NO$				
s-Butylamine	97	79–80[27]	$C_{11}H_{15}NO$				
t-Butylamine	87	131–132[32]	$C_{11}H_{15}NO$	74.54	73.99	8.53	8.60
Neopentylamine	92	112–113[22]	$C_{12}H_{17}NO$				
4-Aminoisohexane[33]	88	74–76	$C_{13}H_{19}NO$	76.05	76.34	9.33	9.32
2-Aminoheptane[33]	67	65–66	$C_{14}H_{21}NO$	76.66	76.56	9.65	9.95
4-Aminoheptane[33]	97	104–105	$C_{14}H_{21}NO$	76.66	76.17	9.65	9.78
2,4-Dimethyl-3-aminopentane[33]	69	129–130	$C_{14}H_{21}NO$	76.66	76.78	9.65	9.85
1-Phenyl-1-aminopropane[33]	88	105–106	$C_{16}H_{17}NO$	80.30	80.03	7.16	7.27
1-Phenyl-2-aminopropane[33]	72	127–128	$C_{16}H_{17}NO$	80.30	80.16	7.16	7.25
1,2,3,4-Tetrahydroisoquinoline	84	Oil[34]	$C_{16}H_{15}NO$				
N-Mesitoyl derivative							
Piperidine	72	70–72	$C_{15}H_{21}NO$	77.87	77.74	9.15	9.19
n-Butylamine	85	80–81	$C_{14}H_{21}NO$	76.66	76.69	9.65	9.64
s-Butylamine	90	119–120	$C_{14}H_{21}NO$	76.66	76.92	9.65	9.65

butylamine mesitoate and N-mesitoyl-*s*-butylamine. The latter was obtained pure by combining mesitoyl chloride and *s*-butylamine in ether solution (see below). Reaction between benzoyl chloride and 2,2,6,6-tetramethylpiperidine in the presence of aqueous sodium hydroxide under the usual Schotten-Baumann conditions gave only the salt, **2,2,6,6-tetramethylpiperidine benzoate**, m. p. 195–197°.

Anal. Calcd. for $C_{16}H_{25}NO_2$: C, 72.96; H, 9.57. Found: C, 73.12; H, 9.70.

N-Mesitoyl-*s*-butylamine.—The amide was best prepared by the action of 1 mole of mesitoyl chloride on 2 moles of amine in anhydrous ether solution. The *s*-butylamine hydrochloride was removed by filtration and the filtrate was evaporated to dryness. The residue was recrystallized from petroleum ether as colorless needles, m. p. 119–120°, which had the correct analysis (see Table I) for N-mesitoyl-*s*-butylamine; yield, 90%.

N-Benzoyl-2,2,6,6-tetramethylpiperidine.—Previous workers[21] claimed to have prepared the amide, m. p. 41–42°, by treatment of the amine with benzoyl chloride in anhydrous ether solution. However, under identical conditions the only products which we were able to isolate were 2,2,6,6-tetramethylpiperidine benzoate, m. p. 195–197°, 2,2,6,6-tetramethylpiperidine hydrate, m. p. 30–31° (previously reported at 28°),[21] and benzoic acid. Benzene proved to be more efficacious as a solvent. A solution of 15.2 g. (0.11 mole) of 2,2,6,6-tetramethylpiperidine and 7.6 g. (0.055 mole) of benzoyl chloride in 30 ml. of anhydrous benzene was held at reflux for seventy-five hours, when the formation of amine hydrochloride appeared to cease. Seven and one-half grams (0.042 mole) of hydrochloride was removed by filtration. After evaporation of the benzene solution the residue was dissolved in ether, and the ethereal solution was washed with 2 *N* hydrochloric acid. The ether layer was dried and evaporated, and the residue was recrystallized as colorless needles from petroleum ether; m. p. 85–88°; yield, 7.35 g. (55%). Because of the discrepancy between the melting point reported previously (41–42°)[21] and that observed, the analysis (see Table I) and infrared absorption spectrum of our product was determined and were found to be consistent with the structure assigned.

(28) Gilman and Blatt, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 99.

(29) Marcus and Wolffenstein, *Ber.*, **34**, 2426 (1901).

(30) Calcd. for $C_{16}H_{23}NO$: N, 5.70. Found: N, 5.71.

(31) Grimmel, Guenther and Morgan, THIS JOURNAL, **68**, 539 (1946).

(32) Schroeter [*Ber.*, **44**, 1201 (1911)] reported m. p. 135.5°.

(33) The authors are indebted to Alexander and Misegades [THIS JOURNAL, **70**, 1315 (1948)] for providing samples of these amines.

(34) Bamburger and Dieckmann [*Ber.*, **26**, 1205 (1893)] also found difficulty in obtaining this compound in the crystalline state.

von Braun Reaction

General Procedure.—An equimolar mixture of amide and phosphorus pentabromide was produced by adding first phosphorus tribromide and then bromine in the theoretical amounts to the amide with cooling and shaking. Phosphorus pentachloride was used with N-mesitoyl-*n*- and *s*-butylamines. The mixture was then heated in a distilling flask with an attached water condenser set for distillation. If the subsequent separation of the halogen derivative from the by-products was expected to be difficult by fractional distillation, the reaction mixture was distilled under reduced pressure until no further distillate could be collected and considerable charring and decomposition had taken place in the distilling flask. The distillate was allowed to stand in ice-water to decompose phosphorus oxybromide. The oil layer was then treated with 48% aqueous hydrobromic acid to hydrolyze the benzonitrile to benzoic acid. The oil layer was separated, steam-distilled, dried and purified by distillation. In some cases the crude hydrolyzed distillate was washed with concentrated sulfuric acid, as suggested by Johnson,[35] to remove benzonitrile.

If the halogen derivative was expected to be stable and of low boiling point, the von Braun reaction mixture was usually distilled at atmospheric pressure through a fractionating column. The distillate was then washed with water, dried and purified by distillation.

The results of the von Braun reaction with the various amides are assembled in Table II. Specific methods of isolation and identification of products, which were used with certain of the amides, are described below.

With N-Benzoyl-*n*-butylamine.—The von Braun reaction was carried out as described above and *n*-butyl bromide and benzonitrile were identified in the distillate (see Table II). The original distillation residue was shaken with ethanol. The ethanol-insoluble colorless solid (10 g., m. p. 230–231°) contained nitrogen, and its infrared absorption spectrum indicated the presence of

(35) Johnson, *J. Chem. Soc.*, 531 (1933).

TABLE II

VON BRAUN REACTION OF AMIDES

N-Benzoyl	Moles amide used[a]	Conditions of distillation[b] °C.	Mm.	Loss in total wt. (as moles HBr)	Benzonitrile and derivs.[c] (as moles C_6H_5CN)	Halide	Yield, %	Boiling point, °C.[b] Obs. °C.	Mm.	Lit. °C.	Mm.
Piperidine						1,5-Dibromopentane	78[1]				
2,6-Dimethylpiperidine	0.23	70–158	25	0.25		2,6-Dibromoheptane	19[d]	128–130	30	100	12[35]
2,2,6,6-Tetramethylpiperidine	.10	75–175	40–20	.13	0.07	2,6-Dibromo-2,6-dimethylheptane	None[e]			M. p. 35[37]	
n-Butylamine	.34	35–108	40	.47	.21	*n*-Butyl bromide	50	101–103		101[38]	
s-Butylamine	.30	82–85		.69	.16	*s*-Butyl bromide	61	90–92		91[38]	
t-Butylamine	.22	60–90		.41	.21	*t*-Butyl bromide	Trace[f]			72[39]	
Neopentylamine	.13	(Oil-bath to 190°)		.25	.04	Neopentyl bromide	None			105	732[40]
4-Aminoisohexane	.10	65–170				4-Bromoisohexane	36	142–143		61–63	71[41]
2-Aminoheptane	.04	90–110	50			2-Bromoheptane	28	164–167		165–167[42,43]	
4-Aminoheptane	.10	45–91	15			4-Bromoheptane	17	58–60	18	60	18[43]
2,4-Dimethyl-3-aminopentane	.07	40–106	55			3-Bromo-2,4-dimethylpentane	10	159–161		158–161[44]	
1-Phenyl-1-aminopropane	.10	70–120	30			α-Bromopropylbenzene	62[g]	127–128	40	129–130	43[45]
1-Phenyl-2-aminopropane	.04	55–108	25			β-Bromopropylbenzene	38	95	5	90–91	3[46]
1,2,3,4-Tetrahydroisoquinoline	.35	40–100	20			....[h]					
N-Mesitoyl											
s-Butylamine	.15	50–100		.25	.06[i]	*s*-Butyl bromide	25	89–92		91[38]	
n-Butylamine[i]	.10	70–105		.23[i]	.07[i]	*n*-Butyl chloride	54	75–77		76–78[47]	
s-Butylamine[i]	.16	50–100		.22[i]	.12[i]	*s*-Butyl chloride	30	67–69		66–68[47]	

[a] An equivalent amount of phosphorus pentahalide was used. [b] At atmospheric pressure unless otherwise indicated. [c] Mainly benzoic acid and cyaphenine. [d] *Anal.* Calcd. for $C_7H_{14}Br_2$: Br, 61.96. Found: Br, 62.05. [e] A small amount of liquid (b. p. 60–62° (4 mm.); $n^{20}D$ 1.4816; d^{20}_4 1.179; insoluble in sulfuric acid; gave an immediate precipitate with cold ethanolic silver nitrate) was obtained which had a composition corresponding to $C_{10}H_{19}Br$. *Anal.* Calcd. for $C_{10}H_{19}Br$: C, 54.80; H, 8.59; Br, 36.61. Found: C, 55.18; H, 8.56; Br, 37.28. The compound has not been identified as yet. [f] Schroeter[32] reported the formation, but not the isolation, of *t*-butyl chloride from the reaction of phosphorus pentachloride on the same amide. [g] Plus 1.5 g. α,β-dibromopropylbenzene, m. p. 65–66°. [h] Unsuccessful, although satisfactory with N-benzoyltetrahydroquinoline (von Braun, *Ber.*, 37, 2915 (1904)). [i] With PCl_5. Loss in weight calculated as moles HCl. [j] Mesitonitrile and mesitoic acid.

conjugated carbon-nitrogen double bonds. The compound was identified as cyaphenine, the trimer of benzonitrile, which has been previously reported in von Braun reaction distillation residues.[17] The ethanol-soluble portion of the distillation residue was evaporated to small volume and water was added. The oil which separated was drawn off and identified as benzonitrile by means of hydrolysis to benzoic acid. The water layer was decolorized and evaporated to small volume. The colorless crystalline solid (10 g.) which separated was high-melting and contained nitrogen and active bromine. Infrared absorption spectrum determination indicated the presence of the following groups: phenyl, —NH—, $\rangle C{=}N$. This information, coupled with the results of a Fajan's titration for active bromine, indicated that the compound was probably the amidine hydrobromide resulting from the combination of benzonitrile and *n*-butylamine, *i. e.*,

$$\left[C_6H_5C\begin{matrix}NH\\ \diagup\!\!+\\ NH_2C_4H_9\end{matrix}\right]Br^-$$

Anal. Calcd. for $C_{11}H_{17}BrN_2$: equiv. wt., 257.2. Found: equiv. wt., 257.8.

With N-Benzoyl-(+)*s*-butylamine.—The optically pure amide with an equivalent of phosphorus pentabromide was distilled over the temperature range 80–100°. The distillate was washed with water, dried and distilled with fractionation. The fraction boiling at 90–91.5° was collected; $n^{25}D$ 1.4350; $[\alpha]^{25}D$ −13.52° (homogeneous, l = 1 dm.).

Anal. Calcd. for C_4H_9Br: C, 35.06; H, 6.62. Found: C, 35.29; H, 6.81.

The optically active *s*-butyl bromide (11.65 g., 0.085 mole) was held at reflux temperature for thirty minutes with 0.085 mole of phosphorus pentabromide. After cooling, the bromide was decanted, washed with water and dried. The refractive index of the sample thus treated was unchanged, but the specific rotation indicated that some racemization had occurred: $[\alpha]^{25}D$ −12.60° (homogeneous, l = 1 dm.). This corresponds to a 7% loss in activity in the half-hour heating period.

Blank: Action of Phosphorus Pentabromide on *t*-Bromides.—When 0.1 mole of *t*-butyl bromide was held at reflux for one hour over 0.1 mole of phosphorus pentabromide, 0.041 mole of *t*-butyl bromide was recovered. Hydrogen bromide and isobutylene were evolved. When 0.1 mole of *t*-amyl bromide was held at reflux for one hour over 0.1 mole of phosphorus pentabromide, 0.056 mole of *t*-amyl bromide was recovered. Hydrogen bromide and olefin were evolved.

Summary

A comparative study of the von Braun reaction with a series of cyclic amides (N-benzoylpiperidine, -2,6-dimethylpiperidine and -2,2,6,6-tetramethylpiperidine) shows that the production of alkylene dihalide is inhibited by hindering groups on the α_N-carbons.

(36) Fargher and Perkin, *J. Chem. Soc.*, **105**, 1353 (1914).
(37) Harries and Weil, *Ber.*, **37**, 845 (1904).
(38) Skan and McCullough, THIS JOURNAL, **57**, 2439 (1935).
(39) Favorskii, *Ann.*, **354**, 245 (1907).
(40) Whitmore, THIS JOURNAL, **61**, 1585 (1939).
(41) Shonle, Waldo, Keltch and Coles, *ibid.*, **58**, 585 (1930).
(42) Wheeler, *ibid.*, **25**, 532 (1903).
(43) Sherrill, *ibid.*, **52**, 1982 (1930).
(44) Kizhner, *J. Russ. Phys.-Chem. Soc.*, **45**, 987 (1913).
(45) Kizhner, *ibid.*, **45**, 949 (1913).
(46) Carter, *J. Biol. Chem.*, **108**, 619 (1935).
(47) Norris and Taylor, THIS JOURNAL, **46**, 753 (1924).

A similar study with a series of open-chain amides indicates likewise that the production of alkyl halide decreases with increasing hindrance to rearward attack at the α_N-carbon.

The action of phosphorus pentabromide on N-benzoyl-(+)*s*-butylamine has been shown to give (−)*s*-butyl bromide. The extent of inversion of optical rotation corresponds to preponderant inversion of configuration with some racemization.

The mechanism of the von Braun reaction has been discussed in the light of the new observations.

URBANA, ILLINOIS RECEIVED JANUARY 24, 1949

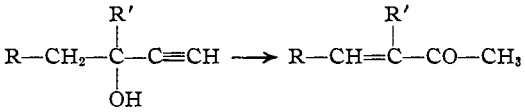
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

The Mechanism of the Rupe Reaction[1]

BY G. F. HENNION, R. B. DAVIS AND D. E. MALONEY

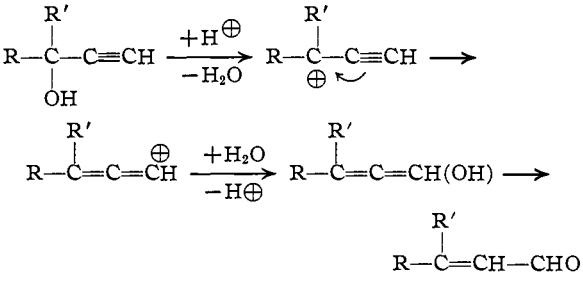
Introduction

The conversion of dialkylethynylcarbinols (I) to the corresponding α,β-unsaturated ketones (II) by heating with strong formic acid is known in this Laboratory as the Rupe reaction.[2] Rupe



(I) (II)

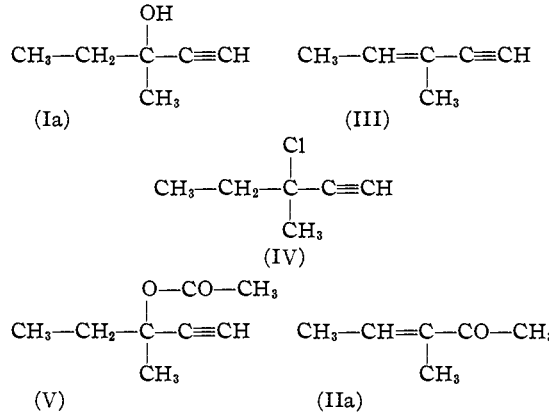
thought the products to be α,β-unsaturated aldehydes, R—CH_2—C(R′)=CH—CHO, but this notion has been corrected repeatedly.[3] Aldehydes of this type would be expected if the reaction followed the course of the Meyer–Schuster rearrangement,[4] which involves an anionotropic migration similar to the allylic rearrangement.[5]



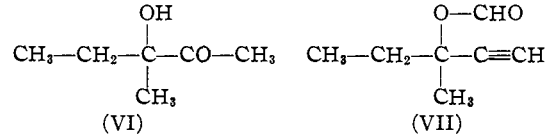
The Rupe reaction is thus an apparent 1,2-shift of the hydroxyl group while the Meyer–Schuster rearrangement is a 1,3- or allylic shift. There are a few cases in which these reactions occur in competition.[6] Actually formic acid is not the only reagent for such transformations since they are reported in a wide assortment of acetylenic alcohol reactions with numerous acidic reagents. While there seems to be little doubt about the mechanism of the Meyer–Schuster rearrangement, the mechanism of the Rupe reaction has not been established.

One of the simplest cases in which this reaction proceeds well is that of methylethylethynylcarbinol (Ia).[7] The product, however, is not "*s*-butylidine-acetaldehyde"[7] but rather 3-methyl-3-penten-2-one (IIa). We have proved that the latter is formed by dehydration of the carbinol (Ia) to 3-methyl-3-penten-1-yne (III) and subsequent hydration of the triple bond. This conclusion emerges from the following facts.

The carbinol (Ia) and the corresponding vinylacetylene (III), chloride (IV), and acetate ester (V) yielded the same product (IIa) by treatment with hot formic acid.



That hydration of the triple bond did not precede the dehydration was evident from the fact that the acyloin (VI) did not react with boiling formic acid. An alternative explanation involving thermal decomposition of the formate ester (VII) was considered untenable because



(VI) (VII)

(1) Paper LIII on the chemistry of substituted acetylenes; previous paper, THIS JOURNAL, **71**, 1964 (1949).

(2) Rupe, *et al.*, *Helv. Chim. Acta*, **9**, 672 (1926), and subsequent papers.

(3) (a) Fischer and Lowenburg, *Ann.*, **475**, 183 (1929); (b) Hurd, *et al.*, THIS JOURNAL, **56**, 1924 (1934); **59**, 118 (1937); **71**, 398 (1949); (c) Price and Meisel, *ibid.*, **69**, 1497 (1947).

(4) Meyer and Schuster, *Ber.*, **55B**, 819 (1922).

(5) MacGregor, THIS JOURNAL, **70**, 3953 (1948).

(6) Chanley, *ibid.*, **70**, 244 (1948).

(7) Rupe and Kambli, *Helv. Chim. Acta*, **9**, 672 (1926); Rupe U. S. Patent 1,670,825 (1928).