The von Braun Reaction. I. Scope and Limitations

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The von Braun reaction in which an N-alkylamide is converted into an alkyl halide has been studied with particular attention to structural and electronic characteristics which influence the course of the reaction and yield of alkyl halide. For benzamides of non-benzylamines the yields will parallel the accessibility of the α_N-carbon to nucleophilic attack. For amides of benzylamines the yields will parallel the relative stabilities of the corresponding benzyl carbonium ions for a given acyl group, and for a given benzyl group they will parallel the ability of the radical in any acyl group to stabilize a positive charge on the acyl carbon. Thionyl chloride offers certain advantages over phosphorus pentachloride. The unlikelihood of there being a single mechanism is discussed, and the relationship of the reaction to the so-called "second-order" Beckmann rearrangement is considered.

The reaction between an N-alkylbenzamide and a phosphorus pentahalide to produce benzonitrile, an alkyl halide, phosphorus oxyhalide and hydrogen halide, which bears von Braun's name, was discovered at the turn of the century by von Pechmann[2] and subsequently confirmed, in 1903, by Ley and Holzweissig.[3] The extensive researches of von Braun into the scope and nature of the reaction began in 1904[4] and cover more than a quarter of a century. But surprisingly, in spite of the lack of any other satisfactory method for removal of a primary aliphatic amino group, the reaction has never found general application. Its only competitor is so-called deamination, which affords facile rearrangements and a multiplicity of products derived from the parent amine, which limit its general applicability. The only apparent disadvantages of the von Braun reaction from the synthetic standpoint are found in the nature of the by-products which limit it to preparation of alkyl halides which boil outside the ranges of the phosphorus oxyhalide or benzonitrile, or which are insensitive to procedures for chemically disposing of them.[5]

The replacement of phosphorus pentachloride by thionyl chloride, first suggested by von Braun himself[6] for the preparation of imidoyl chlorides but not actually adopted for preparation of alkyl chlorides for unexplained reasons, offered an attractive possibility for extending the synthetic scope of the reaction; and the possibility of using non-aromatic acyl groups appeared to offer a means of obviating the undesirable benzonitrile. These modifications constitute one objective of the present investigation.

Since the synthetic scope of the reaction is necessarily limited by its chemical nature, two features of the latter invited investigation. The excellent work of Leonard and Nommensen[7a] has suggested a dual mechanism, and thus the importance of the nature of the process by which halogen replaces nitrogen in the alkyl moiety of various types of N-alkylamides constituted one area for further study. The second area involves the question of the existence of intermediates, also considered by Leonard and Nommensen,[7a] who state, "Intermediates such as amido-halides, iminohalides, and compounds containing a nitrogen–phosphorus link have been proposed, but in no case has the existence of such intermediates been definitely established."[7a,b]

Our objectives with respect to mechanism, then, were to study the effect of structure of the alkyl group on the substitution process and to look for imidoyl halides as possible, if not necessary, intermediates.

Thionyl chloride has been used throughout the present study with entirely satisfactory results provided 2.5–3.0 equivalents are used. The use of an indifferent solvent (nitromethane) is useful where it does not interfere with product isolation, but it is not essential. A systematic comparison of yields with thionyl chloride and phosphorus pentachloride was not undertaken, inasmuch as we encountered only one type of amide (from pivalic acid) which failed to give satisfactory results with the former reagent. In general, nitromethane was used where its boiling point did not interfere with facile isolation of products by simple distillation of the reaction mixture. Table I illustrates yields obtained with this reagent and includes three examples of N-alkylbenzamide reactions (n-butyl, t-butyl and N-benzyl-N-phenyl) with phosphorus pentahalides from earlier work for comparison where the present study omitted reaction with benzamides corresponding to the alkanamides. The applicability of thionyl chloride to amides of secondary amines remains to be studied, but the simplicity of product isolation recommends the use of thionyl chloride even when the expected chloride (or nitrile) boils near the same temperature (cf. reaction of N-butylbenzamide in Experimental).

The use of non-aromatic amides proved to be limited; e.g., formamides which would be ideal from the standpoint of by-products proved unsatisfactory for all amines investigated and afforded a reasonable yield in only one instance (Table I). However, other alkanamides were only slightly less satisfactory than benzamides provided that the α_N-carbon affords a carbonium ion center better than simple benzyl, e.g., α-methylbenzylalkanamides afford α-methylbenzyl chloride in yields which increase in the order, acetamide < propionamide < butyramide (Table I).

(1) Abstracted in the main from the Ph.D. dissertation of Richard David Carlson, University of Michigan, 1959.

(2) H. von Pechmann, Ber., 33, 611 (1900); cf. 28, 2362 (1895), where related data first appear.

(3) H. Ley and E. Holzweissig. ibid., 36, 18 (1903).

(4) J. von Braun, ibid., 37, 2812 (1904).

(5) J. v. Braun and W. Sobecke, ibid., 44, 1464 (1911); J. v. Braun and A. Steindorff, ibid., 38, 2336 (1905); J. D. A. Johnson, J. Chem. Soc., 1531 (1932).

(6) J. v. Braun and W. Pinkernell, Ber., 67, 1218 (1934).

(7) (a) N. J. Leonard and E. W. Nommensen, J. Am. Chem. Soc., 71, 2808 (1949); (b) O. Wallach, Ann., 184, 1 (1877); H. Klinger, ibid., 184, 261 (1877); F. Hallman, Ber., 9, 846 (1876).

The question of imidoyl halides as intermediates was attacked by first demonstrating that benzanilide with thionyl chloride readily afforded N-phenylbenzimidoyl chloride, which was identified by its boiling point, melting point and reaction with aniline to give N,N'-diphenylbenzamidine. Next, N-methylbenzylamide was similarly treated, and the resultant N-methylbenzimidoyl chloride was isolated, identified and decomposed by heating for 8 hr. at 150° to leave only benzonitrile and its trimer, cyaphenine. Thus von Braun's observation that N-alkyl-benzimidoyl halides can afford benzonitrile and alkyl halide[8] is confirmed. Similarly, N-benzylbenzamide was converted to N-benzylbenzimidoyl chloride *under conditions of the von Braun reaction* with thionyl chloride replacing distillation at atmospheric pressure with distillation at reduced pressure, and the product was identified by preparation of derivatives and hydrolysis to the original amide and was also decomposed by distillation at atmospheric pressure to benzyl chloride and benzonitrile. With N-butylbenzamide it was observed that the initial reaction with thionyl chloride afforded sulfur dioxide and hydrogen chloride and that the excess thionyl chloride could be removed at steam-bath temperature leaving a liquid product which afforded *n*-butyl chloride and benzonitrile only on heating above 100°. When these data are added to the observation of Lander[9] that benzimidoyl halides can be prepared from N-alkylbenzamides and phosphorus pentahalides, it becomes clear that imidoyl halides may indeed be intermediates in the von Braun reaction (unless an N,N-dialkylamide is used) and that they may be isolated unless the reaction is carried out above their decomposition temperatures. The formation of the imidoyl halide may be pictured as proceeding from a structure such as

$$\begin{array}{c} OZCl \\ | \\ Ar\!-\!C\!=\!N\!-\!R \end{array}$$
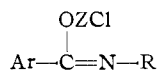
where Z = SO or PX₃(*cf.* ref. 7a). The transformation would involve separation into an ion-pair, the anion of which can then lose ZO with collapse of the remaining halide–cation pair to imidoyl halide. It is obvious that in the course of this transformation the fate of the cation may well be influenced by temperature and medium and lead to products without intervention of the imidoyl halide, and thus one cannot postulate the latter as a necessary intermediate in all cases, but a probable one under certain conditions. Specifically, under the conditions used in this study, the reaction appears to proceed stepwise to the imidoyl halide which affords products when the temperature is raised for final distillation.

Since the work of Leonard and Nommensen[7a] leaves no room to doubt the possibility of an SN2 displacement in appropriately constituted, purely aliphatic benzamides, we investigated the possibility of an alternative reaction path with N-benzylacetamides and thionyl chloride. To this end the series benzyl, *p*-methoxybenzyl (A); α-methylbenzyl (B); and α-cyclopentylbenzyl, benzhydryl

(8) J. v. Braun, *Angew. Chem.*, **47**, 611 (1934).

(9) G. D. Lander, *J. Chem. Soc.*, **83**, 320 (1903).

TABLE I

REACTIONS OF N-ALKYLAMIDES WITH THIONYL CHLORIDE

RNHCOR' + SOCl₂ ⟶ SO₂ + HCl + RCl + R'CN

R	R'	Alkyl Yield, %	Ref.[a]	Aryl (C₆H₅) Yield, %	Ref.[a]
n-Butyl	H	Trace[b]	c	69–75	
				50 with PBr₅	7
t-Butyl	CH₃	20–50[d]	e	Trace with PBr₅	7
Phenethyl	H	Trace[f]	c	87.4 (v.p.c.)	
	CH₃	Trace[f]	g		
Cyclohexyl	CH₃	None	h		
Benzyl	H	Trace[f]	c	90 with PCl₅[i]	
	CH₃	8	j		
	t-C₄H₉	56[k]	l	20–50[m]	n
p-Methoxybenzyl	CH₃	40–50	u		
	C₂H₅	65	l	40–45	
				92 C₆H₅CN	
α-Methylbenzyl	H	50	o		
	CH₃	55–75	p,q		
	C₂H₅	72	l		
	n-C₃H₇	75	l		
	t-C₄H₉	30[k]	l	80–85	r
α,*p*-Dimethylbenzyl	CH₃	20–30[s]	l		
	C₂H₅	34[s]	l	20–35	l
α-Methyl-*p*-methoxybenzyl	CH₃	Polymer	l	Polymer	
				79 C₆H₅CN	l
α-Methyl-*p*-nitrobenzyl	CH₃	None[t]	l		
α-Cyclopentylbenzyl	CH₃	75–85	28	80–85	28
				80.5 C₆H₅CN	
α-Phenylbenzyl (benzhydryl)	CH₃	75–85	u	80–85	v
α,α-Dimethylbenzyl	CH₃	Polymer[w]	q		

[a] References pertain to preparation of amide; see Table III for benzyl chlorides. [b] See text for natures of this reaction. [c] F. F. Blicke and Chi-Sung Lu, *J. Am. Chem. Soc.*, 74, 3933 (1953). [d] Yield probably higher owing to difficulty in separation from solvent (nitromethane). [e] R. Scholl, A. C. Weil and K. Holdermann, *Ann.*, 338, 1 (1905). [f] Identified by infrared spectrum. [g] W. H. Carothers and G. A. Jones, *J. Am. Chem. Soc.*, 47, 3051 (1925). [h] A. Baeyer, *Ann.*, 278, 88 (1894). [i] From C₆H₅CON(C₆H₅)-CH₂C₆H₅ (ref. 4). [j] H. O. Nicholas and J. L. E. Erickson, *J. Am. Chem. Soc.*, 48, 2174 (1926). [k] Obtained with phosphorus pentachloride; no product with thionyl chloride. [l] Table II. [m] Yield estimated; probably higher owing to difficulty in separation from benzonitrile. [n] E. Beckmann, *Ber.*, 37, 4136 (1904). [o] M. C. de Leeuw, *Rec. trav. chim.*, 30, 241 (1911). [p] A 59.5% yield obtained from (−)-N-α-methylbenzylacetamide [A. Campbell and J. Kenyon, *J. Chem. Soc.*, 25 (1946)]: $[\alpha]^{25}$D +3.7°; pure (+)-chloride, $[\alpha]$D 109–129° [R. L. Burwell, Jr., A. D. Shields and H. Hart, *J. Am. Chem. Soc.*, 76, 908 (1954)]. A sample of this chloride (2.45 g., α +3.97° (*l* 1.0) was dissolved in 25 ml. of nitromethane (as supplied) and refluxed with 3.2 ml. of thionyl chloride (as supplied) for 1 hr. After fractionation of the chloride, α = 3.87°; excess inversion over retention = 3.5%. [q] J. J. Ritter and P. P. Minieri, *J. Am. Chem. Soc.*, 70, 4045 (1948). [r] M. Metayer, *Ann. chim.*, [12] 4, 196 (1949). (−)-N-α-methylbenzylbenzamide afforded 78% benzonitrile. The chloride (9.3% by weight by vapor phase chromatography) was slightly dextrorotatory, $[\alpha]$D +1.3°. [s] Considerable dehydrohalogenation; see text for propionamide. [t] The chloride is unknown and is probably a solid; no liquid distillate was obtained, and the residue charred. [u] O. Exner, *Chem. Listy*, 48, 1634 (1954); *C. A.*, 49, 14674 (1955). [v] G. E. P. Smith, Jr., and F. W. Bergstrom, *J. Am. Chem. Soc.*, 56, 2095 (1934). [w] Appreciable dehydrohalogenation.

(C) was studied. The yields of chlorides increased in the order A,B,C (Table I), with no difference in the members of the C pair and *p*-methoxybenzyl being better than benzyl. The general order is the reverse of that expected if hindrance at the αN-carbon is an important factor, and the difference in the *p*-methoxybenzyl–benzyl pair suggests the significance of potential carbonium ion

character at the α_N-carbon in the series. This is supported by the stereochemical results with (−)-N-α-methylbenzylacetamide which was shown to produce but slightly optically active chloride, whose optical activity was essentially unaltered by being returned to the environment of the original reaction, suggesting that racemization occurred during and not subsequent to the reaction.

It now becomes possible to picture two limiting mechanistic paths for the von Braun reaction when it proceeds from an intermediate imidoyl halide; one requires dissociation of the imidoyl halide followed by displacement of nitrile from the imidonium cation by halide (I); and the other may proceed by a "fragmentation"[10] of the imidoyl halide followed by union of the resultant similar halide and carbonium ions (II).
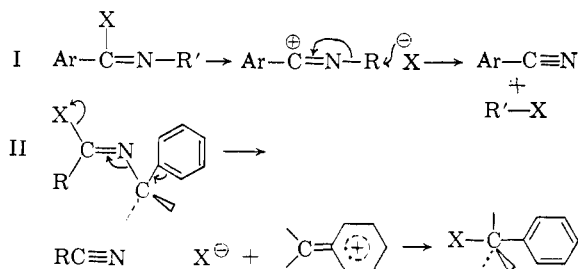
Path I is necessarily limited to imidoyl halides in which a positive charge can be stabilized on the original carbonyl-carbon and in which R′ is accessible to displacement. But forcing condition may be presumed to allow dissociation of a carbonium ion from the imidonium cation. The fate of the carbonium ion will depend upon its immediate environment and may include halide formation rearrangement, deprotonation to olefin and/or polymer formation. Where dissociation of the imidoyl halide (e.g., from alkanamides) is inhibited, alternative modes of decomposition are open (e.g., dehydrohalogenation followed by complex reactions). The resemblance of this path (I) to the decomposition of imidoyl ester hydrochlorides[11] is striking.

Path II is essentially independent of the nature of R but requires the participation of an electron pair from the aromatic system. The more readily this can be supplied, owing either to electronic or steric factors (e.g., p-methoxy group, α-substituents), the more readily fragmentation can occur. However, the more readily the carbon–halogen bond can suffer fission, the more readily the reaction may be expected to occur. Thus the order of yields in a series of alkanamides of a given amine follows the inductive effects of progressively larger alkyl groups and reaches a maximum with the resonance effect of phenyl. The character of the carbonium ion determines its fate: alkyl halide or olefin and/or polymer may be expected as with path I (Table I).

Both paths may be modified to include alternative product formation from the suggested imidoyl halide precursor by replacing X in the initial structure by OZX (Z = XO or PX$_3$) and including OZ

(10) C. A. Grob, *Experientia*, **13**, 126 (1956).

(11) C. L. Stevens, D. Morrow and J. Lawson, *J. Am. Chem. Soc.*, **77**, 2341 (1955).

in the products. In this case the first path is essentially like one proposed by Leonard and Nommensen,[7a] with the provision that the intervening imidonium-halide ion pair may "collapse" to the imidoyl halide if the temperature is not high enough to promote direct decomposition.

The resemblance of the imidoyl halide (or ester) or imidonium cation to possible final states in the Beckmann rearrangement[12a] is sufficiently striking to permit the inference that the so-called "second-order" Beckmann[12b−e] reaction which does *not* involve an adjacent carbon–oxygen[12b] (or carbon–nitrogen) function may occur as a result of a von Braun reaction following initial rearrangement. Thus the rearrangements of the oximes of 2-phenylpropyl phenyl ketone and 1-phenyl-cyclohexyl phenyl ketone by thionyl chloride lead to the same products anticipated for treatment of N-α,α-dimethylbenzylbenzamide (*cf.* the corresponding acetamide, Table I) and N-1-phenyl-cyclohexylbenzamide: the alkenes 1-phenylpropene and 1-phenylcyclohexene,[12c] respectively. Presumably the carbonium ions are more readily stabilized by deprotonation than by union with halide, and similar results obtained in other cases.[12d] We suggest that the reasons the number of such "second-order" reactions is comparatively small are (1) that relatively few rearrangements are carried out on mixed alkyl aryl ketoximes whose stereochemistry permits the necessary alkyl migration; and (2) the temperature usually employed for the rearrangement is too low to induce decomposition of the imidoyl halide (or corresponding ester), which thus is usually hydrolyzed during the work-up. With purely dialkyl ketoximes the intermediate imidoyl halide on heating may be expected to undergo the more complex reactions of such compounds rather than the von Braun reaction, as suggested above. When a "second-order" reaction affords a product *not* derivable from the rearranged imidoyl derivative it may be more properly ascribed to direct fragmentation of the ketoximino derivative as pictured by Grob.[13]

Experimental[14,15]

N-Alkyl amides.—The appropriate amine (0.50 mole), 25% sodium hydroxide (110 g.) and 150 g. of crushed ice

(12) References to specific examples of the Beckmann rearrangement will be found in the recent excellent review by L. G. Donaruma and W. Z. Heldt, in "Organic Reactions," Vol. XI, A. C. Cope, Editor, John Wiley and Sons, Inc., New York, N. Y., 1960. The following references are to page numbers in this review: (a) pp. 5–6 (structures III, IV, XI); (b) p. 35; (c) p. 19; (d) p. 28–29; (e) p. 33.

(13) C. A. Grob, ref. 10 and; "Kekulé Symposium, Theoretical Organic Chemistry," Butterworth's Scientific Publications, London, 1959, pp. 114–125.

(14) Boiling points and melting points (open capillaries) uncorrected.

(15) Microanalyses by Spang Microanalytical Laboratory, Ann Arbor, Mich.

TABLE II

NEW AMIDES[a]

	Yield, %	M.p., °C.	Formula	Calcd. C	H	N
N-α-α-Dimethylbenzylacetamide[b,c]	75	103–104	$C_{11}H_{15}NO$	74.54	8.53	7.91
			Found	74.73	8.59	7.92
N-α,p-Dimethylbenzylpropionamide[d]	67	83–84	$C_{11}H_{17}NO$	75.35	8.96	7.32
			Found	75.28	8.86	7.22
N-p-Methoxybenzylpropionamide[c,e]	70	88.0–89.5	$C_{11}H_{15}NO_2$	63.37	7.82	7.25
			Found	68.21	7.72	7.09
N-α-Methylbenzylpropionamide	77	59.5–61.0	$C_{11}H_{15}NO$	74.51	8.53	7.90
			Found	74.55	8.53	8.02
N-α-Methylbenzylbutyramide		107–108 (0.1 mm.)[f]	$C_{12}H_{17}NO$	75.33	8.96	7.32
			Found	75.33	8.87	7.27
N-α,p-Dimethylbenzylbenzamide[2g]	70	118–119	$C_{16}H_{17}NO$	80.30	7.16	5.85
			Found	80.03	7.02	5.75
N-p-Methoxybenzylbenzamide[c]	85	97.5–99.0	$C_{15}H_{15}NO_2$	74.70	6.27	5.81
			Found	74.77	6.39	5.66

[a] If no reference is given, amine was commercially available. [b] Recrystallized from ethanol–ether. [c] A. C. Cope, T. T. Foster and P. H. Towle, J. Am. Chem. Soc., 71, 3929 (1949). [d] R. E. Lyle and H. J. Troscianiec, J. Org. Chem., 20, 1757 (1955). [e] Recrystallized twice from ethanol–water only. [f] Product separated as an oil which was taken up in benzene and distilled. The distillate solidified to a waxy substance without a well-defined m.p.

were rapidly stirred with cooling (methanol–ice-bath for propionamides, ice–salt-bath for benzamides) while the anhydride or benzoyl chloride (0.55 mole) was added in one portion. Stirring with cooling was continued for 1 hr. and then the mixture was suction filtered. After washing with water, the residue was taken up in absolute ethanol, boiled with Norit (when necessary) for 15 min., filtered and diluted with water to the cloud point at about 45°. Slow cooling to room temperature followed by chilling to 0° and suction filtration afforded the product, which was then recrystallized from benzene–petroleum ether (30–60°). Data for new compounds are collected in Table II. Known compounds were prepared as previously reported or by suitable modification of the foregoing procedure.

N-α-Methyl-p-nitrobenzylacetamide.—Nitric acid[16] (242 ml., sp.gr. 1.5) was cooled to −10° in an ice–salt-bath and N-α-methylbenzylacetamide[17] added, with rapid stirring, at such a rate that the temperature of the reaction mixture stayed below 5°. After all the amide had been added the solution was stirred for an additional 25 min. and then diluted with a mixture of ice and water (300 g.) until the solution appeared milky. The solution was then neutralized with ammonium hydroxide (sp. gr. 0.9). The product which precipitated from the solution was filtered off and recrystallized twice from aqueous ethanol to give 43 g. (50%) of product, m.p. 122–124°.

Anal. Calcd. for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.46. Found: C, 57.69; H, 5.83; N, 13.56.

A portion of the amide (0.7 g.) was heated on a steam-bath with 2.5 g. of potassium dichromate, 5 ml. of concd. sulfuric acid and 15 ml. of water for 15 hr. The crystals which separated from the hot solution were filtered off and recrystallized from water to give 4-nitrobenzoic acid, m.p. 239.5–242.5°; Johnson and Guest[18] report 237–238°.

Reactions of N-Alkylamides with Thionyl Chloride. (Data are summarized in Table I; Table III gives data for chlorides produced.)

(A) General Procedure.—A solution of 0.25 mole of the amide in 150–175 ml. of nitromethane was distilled (to azeotrope traces of water) until the temperature held constant at 98° for 5 min. It was then cooled to below room temperature and 3–4 molar equivalents of thionyl chloride (as furnished by manufacturer) was added dropwise with stirring. The mixture was then allowed to stand at room temperature for 5 hr., after which it was slowly heated to the reflux temperature, which was maintained for 3 hr. It was then distilled until most of the solvent had been removed at atmospheric pressure. The pressure was then reduced (water-pump) and the products were fractionated and subsequently redistilled at suitably reduced pressures.

(16) *Cf.* H. Reihen and E. Herzel, *Ann.*, 487, 213 (1931), for a similar procedure.

(17) J. J. Ritter and P. P. Minieri, *J. Am. Chem. Soc.*, 70, 4045 (1948).

(18) T. B. Johnson and H. H. Guest, *Am. Chem. J.*, 43, 310 (1910).

TABLE III

BENZYL CHLORIDES FROM THE VON BRAUN REACTION

Benzyl chloride	B.p., °C. (mm.), and n_D^t (t, °C.) Observed	Reported	Ref.
Unsubstituted	62–64 (8)	66 (13.5)	25
p-Methoxy[a]	81–82 (2.5)	113 (10.5)	b
	1.5479 (25)	1.5481 (20)	b
α-Methyl	82–83 (20)	80–81 (19)	25
	1.5250 (26)	1.5252 (25)	25
α,p-Dimethyl[c]	88–90 (13.5)		c
	1.5252 (22)		
α-Cyclopentyl[c]	103–104 (2.5)		c
	1.5380 (25)		
α-Phenyl (benzhydryl)[d]	98–100 (0.1)	96 (0.2)	e
	1.5935 (25.5)	1.5962 (20)	e

[a] Identified further by reaction with anisole and anhydrous zinc chloride to give p,p'-dimethoxydiphenylmethane, m.p. 50–51° (methanol), reported 51–52° [G. Sunagawa, *Pharm. Bull. (Japan)*, 3, 116 (1955)]. [b] A. Sosa, *Ann. chim.*, 14, 5 (1940). [c] New compound, see text. [d] Identity confirmed by conversion to benzhydrol, m.p. 65–68° (aqueous ethanol), reported 68° [A. Sosa, *Ann. chim.*, 14, 5 (1940)]. [e] W. Gerrard and B. D. Sheperd, *J Chem. Soc.*, 2069 (1953).

(B).—When the boiling point of the expected chloride would render fractionation from nitromethane difficult, the solvent was omitted. The amide (e.g., n-butylbenzamide) was added to thionyl chloride with cooling and then allowed to stand at room temperature overnight. Next, the mixture was refluxed on the steam-bath for 4 hr., during which time sulfur dioxide and hydrogen chloride were evolved copiously. When the temperature was gradually increased the excess thionyl chloride distilled over, but then the temperature at the still-head dropped until a substantial increase in temperature in the pot was achieved, whereupon additional hydrogen chloride was evolved and the low molecular weight alkyl chloride distilled over.

(C) N-Butylformamide.—The amide (50.5 g., 0.500 mole) was cooled in an ice-bath and thionyl chloride (75 ml., 1.0 mole) was added dropwise with stirring over a 45-min. period. After the addition of thionyl chloride was complete, the dark red solution was stirred in the ice-bath for 2 hr., the ice-bath removed and the solution stirred overnight. The solution was next slowly distilled from an oil-bath. An acidic gas was evolved when the bath temperature reached 60°. Only a very small amount of distillate was collected, even though the bath temperature reached 170°. Distillation of the residue was then attempted at water-pump pressure. A small fraction of distillate was collected at approximately 70° (40 mm.), and on standing a white solid separated and was filtered off and identified as the hydrochloride of n-butylamine, some of which was also obtained from the walls of the still-head. The filtrate was redistilled, b.p. 170–171°.

Anal. Calcd. for C₅H₉NS: C, 52.12; H, 7.87; N, 12.16; S, 27.83. Found: C, 52.25; H, 7.81; N, 12.14; S, 27.62.

This sample was shown by identity of infrared spectra to be *n*-butyl isothiocyanate.[19]

This experiment was repeated using the same conditions, but varying the amount of thionyl chloride. Mole ratios of thionyl chloride to *n*-butylformamide of 1:1, 1:0,9, 1:0.8, 1:0.5 and 1:0.25 were used with approximately the same results. Small amounts of *n*-butyl chloride, *n*-butyl isothiocyanate, *n*-butylamine hydrochloride, starting amide and unidentified products were isolated.

The reaction was repeated using chloroform and then nitromethane as a solvent with 1:1 ratio of thionyl chloride to amide. The reaction was also repeated using nitromethane as solvent and the reaction temperature maintained between 75 and 90°. The thionyl chloride was added below the surface of the nitromethane solution of the amide, which was kept in this temperature range. The solution was maintained at this temperature with slow distillation for 1.5 hr. and then distillation at a higher temperature was attempted. Once again, the results were the same as above.

N-Phenylbenzimidoyl Chloride.—Benzanilide (49 g., 0.25 mole) was mixed with thionyl chloride (56 ml., 0.75 mole), and the mixture was allowed to stand at room temperature for 2 hr., heated to 50° for 3 hr. and the excess thionyl chloride removed at water-pump pressure. The residue was quickly filtered by suction and distilled at reduced pressure. The material boiling 175–176°/11–12 mm., solidified in the receiver, m.p. 40–41°, to give 48 g. (89%) of N-phenylbenzimidoyl chloride; Coleman and Pyle[20] report b.p. 175–178° (14–15 mm.) and m.p. 40–41°.

N,N'-Diphenylbenzamidine was prepared by adding an ether solution of aniline to an ether solution of the imidoyl chloride, evaporating off the solvent and recrystallizing the product from aqueous ethanol; m.p. 145.5–146.5°; Chapman[21] reports 146–147°.

N-Methylbenzamide and Thionyl Chloride. (A).—The amide (34 g., 0.25 mole) was mixed with thionyl chloride (40 ml., 0.53 mole) with no apparent reaction. The reaction flask was immersed in a water-bath, heated to 45° for 3 hr., then at 80° for 2 hr., and allowed to stand at room temperature overnight. The excess thionyl chloride was removed by distillation from an oil-bath (temperature always <105°) at atmospheric pressure and the residue distilled at reduced pressure. The fraction boiling at 78–83° (7–10 mm.) was collected and redistilled to give N-methylbenzimidoyl chloride, b.p. 88–90° (12 mm.); v. Braun and Pinkernelle[6] report 90–93° (13 mm.). The infrared spectrum of this product had no trace of absorption in the nitrile region. This compound was placed in a 50-ml. flask, equipped with a reflux condenser, the exit protected with a calcium chloride drying tube, and heated to 150° in an oil-bath for 8 hr. The material was then distilled at atmospheric pressure to give only one fraction, b.p. 184–186° (750 mm.), which was identified as benzonitrile. The residue from this distillation contained a solid which was recrystallized from absolute ethanol; m.p. 230–231°; Cook and Jones[22] report 232° for the trimer of benzonitrile (cyaphenine).

(B).—A solution of the amide (27 g., 0.20 mole) in 175 ml. of nitromethane was distilled until the distillation temperature remained at 99° for 10 min. and then cooled to below room temperature. Thionyl chloride (72 g., 0.61 mole) was added and the solution heated to a pot temperature of 100° over a 45-min. period. This temperature was maintained for 1 hr. The excess thionyl chloride was removed by distillation at atmospheric pressure and the nitromethane removed at water-pump pressure. An elemental analysis of the residue showed only the presence of chlorine and nitrogen, with only a minute trace of sulfur. This residue was divided into two parts.

Part A was dissolved in anhydrous ether and slowly added to an ether solution of aniline. An exothermic reaction took place and a solid precipitated from the reaction mixture. The solid was filtered off, 10% sodium hydroxide added to the solid until the mixture remained definitely basic, and steam distilled to remove aniline. The residue was made

homogeneous with absolute ethanol and cooled in an ice-bath. The solid which separated was recrystallized twice from an ethanol-water mixture to give N-methyl-N'-phenylbenzamidine, m.p. 135–136°; picrate, m.p. 169–170°; Pyman[23] reports 135–136° and 169–170°, respectively.

When the original distillation residue was taken up in anhydrous ether it was noticed that a solid remained. This solid was recrystallized from a chloroform-ether mixture and identified as N-methylbenzamidine hydrochloride, m.p. 224–225°; picrate, m.p. 131–123°; Pyman[23] reports 222–223° and 130–132°, respectively.

Part B of the residue was treated with 10% sodium hydroxide until the solution was definitely basic, cooled in an icebath and filtered. The solid obtained was recrystallized twice from an ethanol-ether mixture to give N-methylbenzamide, m.p. 78.5–80.5°. A mixed m.p. with the starting amide of m.p. 78.5–80.0° was 79–81°. The infrared spectrum of this product was identical with that of the starting amide.

N-Benzylbenzamide and Thionyl Chloride.—The amide (21 g., 0.10 mole) was dissolved in 150 ml. of nitromethane and the solution distilled until the distillation temperature remained at 100° for 10 min. The solution was cooled to below room temperature and thionyl chloride (46 g., 0.38 mole) added. The reaction mixture was allowed to stand at room temperature and then heated on the steam-bath for 1.5 hr. The excess thionyl chloride was distilled off at atmospheric pressure and the nitromethane at water-pump pressure from the steam-bath. The residue was then distilled at reduced pressure. A forerun and five reactions were collected; A, 120–122° (0.3 mm.); B, 122–128° (0.3 mm.); C, 128° (0.3 mm.); D, 124–128° (0.2–0.3 mm.); and E, 124° (0.2 mm.), Lander[9] reports of 80–160° (12 mm.) for N-benzylbenzimidoyl chloride produced from the reaction of phosphorus pentachloride with N-benzylbenzamide. Lander also reports that his material was not pure, and although the compound had been reported earlier, it had never been isolated in the pure state.

Fraction A (2 g.) was dissolved in 15 ml. of acetone and 5 ml. of water added. The resulting solution was heated on the steam-bath for 3 hr., most of the solvent evaporated, and the residue cooled in an ice-bath. The solid which separated was recrystallized twice from absolute ethanol to give N-benzylbenzamide, m.p. 104.2–106.2°. When mixed with the starting amide of m.p. 105.5–106.5° the m.p. was 105.5–107.0°. The infrared spectrum of this material was identical with that of the starting amide.

Fraction B (1.8 g.) was dissolved in 15 ml. of anhydrous ether and a solution of aniline (1.2 g.) in 15 ml. of anhydrous ether slowly added. The reaction mixture was allowed to stand at room temperature for 1 hr. and then warmed on the steam-bath. The solid which had separated was filtered off and 10% sodium hydroxide added to this solid until the mixture was definitely basic. This mixture was steam distilled to remove aniline, the residue cooled and the solid which separated filtered off and recrystallized three times from absolute ethanol to give N-benzyl-N'-phenylbenzamidine, m.p. 99.5–100.5°; Strain[24] reports 99–100°.

A small amount of this amidine was treated with *p*-toluenesulfonyl chloride in 10% sodium hydroxide. The solid which separated was filtered off and recrystallized from absolute ethanol and from a chloroform-ether mixture to give the sulfonamide, m.p. 148–149°; Strain[24] reports 148°.

Fractions C and D (5.5 g.) were mixed and distilled at atmospheric pressure. Two fractions were obtained, but both were a mixture of benzyl chloride and benzonitrile (infrared). On redistillation, a fraction b.p. 172–177°, $n^{22.8}$D 1.5351, was obtained. Charlton and Hughes[25] report benzyl chloride b.p. 66° (13.5 mm.) and n^{25}D 1.5360. The infrared spectrum of this fraction showed the presence of a small amount of benzonitrile. Another fraction, b.p. 177–180° and $n^{22.8}$D 1.5320, was obtained. The infrared spectrum of this fraction corresponded quite well to that of authentic benzonitrile, but the liquid showed the presence of chlorine when treated with silver nitrate.

A solid was isolated from the residue of the original distillation, which when recrystallized from a chloroform-ether mixture was identified as cyaphenine, m.p. 234–236°[22]; *vide supra.*

(19) W. R. Vaughan, M. V. Andersen, Jr., H. S. Blanchard, D. I. McCane and W. L. Meyer, *J. Org. Chem.*, **20**, 819 (1955).

(20) G. H. Coleman and R. E. Pyle, *J. Am. Chem. Soc.*, **68**, 2007 (1946).

(21) A. W. Chapman, *J. Chem. Soc.*, **123**, 1150 (1923).

(22) A. H. Cook and D. G. Jones, *ibid.*, 278 (1941).

(23) F. L. Pyman, *ibid.*, **123**, 3359 (1923).

(24) H. H. Strain, *J. Am. Chem. Soc.*, **50**, 2218 (1928).

(25) J. C. Charlton and E. D. Hughes, *J. Chem. Soc.*, 850 (1956).

Fraction E (2 g.) was dissolved in 200 ml. of anhydrous ether and intermittently shaken with 25 ml. of a saturated aqueous solution of sodium benzoate for 18 hr. The layers were separated, the ether layer evaporated to dryness, and the residue recrystallized three times from absolute ethanol to give N,N-dibenzoylbenzylamine, m.p. 109–110°; Mumm, Hesse and Volquartz[26] report 108°. When mixed with the starting amide, m.p. 105.5–106.5°, the m.p. was 80–100°.

α-p-Dimethylbenzyl Chloride.—The products from the von Braun reactions of N-α,p-dimethylacetamide, propionamide and benzamide were identical (infrared spectra). The following b.p. data were obtained: 65° (2.5 mm.), 67° (3.5 mm.), 65–70° (4.5 mm.), 88–90° (12.5 mm.); n^{22}D 1.5250, n^{25}D 1.5240.

Anal. Calcd. for $C_9H_{11}Cl$: C, 69.91; H, 7.17; Cl, 22.93. Found: C, 70.04; H, 7.25; Cl, 22.66.

In the propionamide reaction p-methylstyrene, b.p. 60–61° (12.5 mm.), n^{22}D 1.5394, dibromide m.p. 44.5–45.5° (reported[27] b.p. 81°) (41 mm.), n^{20}D 1.5420, dibromide m.p. 44.0–44.5°) was isolated.

α-Cyclopentylbenzyl Chloride.—The products from the von Braun reactions of N-α-cyclopentylbenzylacetamide

(26) O. Mumm, H. Hesse and H. Volquartz, *Ber.*, **48**, 379 (1915).

(27) L. H. Schwartzman and B. B. Corson, *J. Am. Chem. Soc.*, **78**, 322 (1956).

and benzamide were identical (infrared spectra). The following b.p. data were obtained; 103–104° (2.5 mm.), 112–114° (4 mm.), n^{25}D 1.5380.

Anal. Calcd. for $C_{12}H_{15}Cl$: C, 74.01; H, 7.77; Cl, 18.21. Found: C, 74.12; H, 7.73; Cl, 18.31.

The structure of this chloride was confirmed in the following manner. A 1.40-g. (0.007 mole) sample was dissolved in 30 ml. of a 50% aqueous solution of triethanolamine and then heated on the steam-bath for 48 hr. The resulting solution was extracted with benzene and the benzene extracts were washed twice with 10% hydrochloric acid and once with water, dried and evaporated in an air stream on the steam-bath leaving 1.0 g. of slightly yellow oil. The oil was dissolved in 2.5 ml. of glacial acetic acid, and this solution was added with shaking to a cooled mixture of 0.7 g. (0.007 mole) of chromic oxide in 2.5 ml. of 80% acetic acid. After standing at room temperature for 48 hr., the reaction mixture was poured into 10 ml. of ice-water and extracted with benzene. The benzene extract was washed twice with 10% sodium bicarbonate solution and once with water, dried and evaporated on the steam-bath. The residual oil possessed an infrared spectrum identical with that of authentic phenylcyclopentyl ketone,[28] and the 2,4-dinitrophenylhydrozone melted at 142.0–143.5°, reported[29] 144.5–145.5°.

(28) P. A. Smith, D. R. Baer and S. N. Ege, *ibid.*, **76**, 4564 (1954).

(29) D. V. Nightingale and M. Maienthal, *ibid.*, **72**, 4823 (1950).

Copper Salt-catalyzed Reaction of Butenes with Peresters[1a]

BY JAY K. KOCHI[1b]

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The mechanism of the copper salt-catalyzed reactions of peresters has been studied. The role of copper salts in these free radical reactions is described by a series of one-electron oxidation–reduction steps: first, the oxidation of cuprous ion by perester to alkoxy radical and cupric carboxylate; and second, reduction of the cupric salt by a free radical generated by the chain transfer reaction between the alkoxy radical and an hydrogen donor compound. With butenes, butenyl radical intermediates are shown to equilibrate to produce a mixture of α-methallyl and crotyl esters independent of the reactant normal butene isomer. The effect of solvent and foreign nucleophiles is examined. The nature of the oxidation of allylic radicals by cupric species is elaborated.

Introduction

The copper salt-catalyzed reactions of peroxides and hydrogen donor substrates have been extensively described by Kharasch and co-workers.[2,3] The reaction can be delineated in its most general form as

$$XOOY + RH \xrightarrow{Cu^I} ROX + HOY \quad (1)$$

Peroxides which have been employed include benzoyl peroxide, t-butyl peracetate and perbenzoate, t-butyl hydroperoxide, di-t-butyl peroxide and related compounds. The hydrogen donor substrates include olefins, ethers, aldehydes, aralkanes and generally compounds possessing hydrogen atoms labile to free radical abstraction processes.

The mechanism originally[2] postulated for this versatile reaction involves a termolecular complex of substrate, peroxide and copper salt. Subsequently, Denney, *et al.*,[4] have presented corrobora-

tive evidence for this mechanism. An important part of this mechanism is its ability to account for the *non-rearrangement* of olefinic bonds during substitution. Thus, Kharasch and Sosnovsky and Yang[2b] reported that octene-1 with t-butyl perbenzoate yielded exclusively 3-benzoxyoctene-1. Denney, *et al.*,[4] also reported non-rearrangements in the cases of allylbenzene and propenylbenzene with t-butyl peresters. Some earlier work[2] with benzoyl peroxide, however, showed appreciable amounts of rearrangement products.

Studies[5] on the reactions of free radicals and metal ions demonstrated the facile oxidation–reduction reactions between free radicals and metal ions. With copper salts these reactions are described by the generalized equations[5a]

$$R\cdot + Cu^{II} \xrightarrow{SH} RS + Cu^I + H^+ \quad (2)$$

$$R\cdot + Cu^{II} \longrightarrow \text{olefin} + Cu_I + H^+ \quad (3)$$
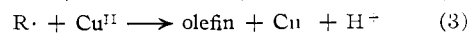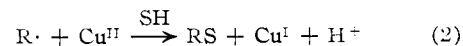
SH is a protic solvent

In particular, allylic radicals were oxidized by cupric salts to a *mixture* of two isomeric allylic

(2) M. Kharasch, *et al.*, (a) *J. Am. Chem. Soc.*, **80**, 756 (1958); (b) **81**, 5819 (1959); (c) *J. Org. Chem.*, **23**, 324 (1958); (d) **24**, 72, 606, (1959).

(3) (a) G. Sosnovsky and N. Yang, *J. Org. Chem.*, **25**, 899 (1960); (b) G. Sosnovsky, *ibid.*, **25**, 874 (1960); **26**, 281 (1961).

(4) D. Denney, *et al.*, *Tetrahedron Letters*, **No. 15**, 19 (1959).

(5) (a) H. De La Mare, J. Kochi and F. Rust, *J. Am. Chem. Soc.*, **83**, 2013 (1961); (b) J. Kochi, *ibid.*, **78**, 4815 (1956); **79**, 2942 (1957); (c) J. Kumamoto, H. De La Mare and F. Rust, *ibid.*, **82**, 1935 (1960); (d) E. Collinson, F. S. Dainton, D. R. Smith, G. J. Trudel and S. Tazuké, *Faraday Soc. Dis.*, **29**, 188 (1960); (e) R. M. Haines and W. A. Waters. *J. Chem. Soc.*, 4256 (1955); (f) C. Bamford, A. Jenkins and R. Johnston, *Nature*, **177**, 992 (1956).