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Oxidative Reactions of Hydrazines. IV. Elimination of Nitrogen from 1,1-Disubstituted-2-arenesulfonhydrazides[1-4]

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Alkaline degradation of 1,1-dibenzyl-2-benzenesulfonhydrazides leads to the formation of bibenzyls. The reaction is represented as proceeding through an intermediate formed by α-elimination of the elements of benzenesulfinic acid. A new method of introducing the very conveniently removed carbo-*t*-butoxy group is described involving acylation by *t*-butyl azidoformate.

Generally, the oxidation of 1,1-disubstituted hydrazines leads to the formation of the corresponding tetrazenes (eq. 1).[5] However, in several cases,

$$R_2NNH_2 \xrightarrow{[O]} R_2NN{=}NNR_2 \qquad (1)$$

as yet relatively unexplored, other products have been obtained. Oxidation of 1,1-dibenzylhydrazine with mercuric oxide was first noted by Busch and Weiss[6] to yield bibenzyl, and recently Overberger and Marks achieved the same result using bromine in ethanol or *t*-butyl hypochlorite as oxidizing agents. Busch and Lang[7] studied the mercuric oxide oxidation of numerous 1-aryl-1-benzylhydrazines and obtained either the tetrazenes or substituted benzaldehyde arylhydrazones. Kenner and Knight[8] postulated that the Busch–Weiss reaction involved the formation of the intermediate Ia which subsequently underwent decomposition

$$(C_6H_5CH_2)_2NNH_2 \xrightarrow{[O]} \underset{\text{Ia}}{[(C_6H_5CH_2)_2\ddot{N}{-}\ddot{N}\!:]} \longleftrightarrow$$

$$\underset{\text{Ib}}{(C_6H_5CH_2)_2\overset{+}{N}{=}\overset{-}{\ddot{N}}\!:] \longrightarrow C_6H_5CH_2CH_2C_6H_5 + N_2} \qquad (2)$$

to bibenzyl (eq. 2). Intermediates such as I[9] are clearly analogous to the aliphatic diazo compounds except that they lack the resonance stabilization possible with the latter. The present study is designed to obtain evidence relative to the postulation of Kenner and Knight. In view of the analogy between the postulated intermediates such as I and aliphatic diazo compounds it would appear that many of the syntheses of the latter could be modified to provide new routes to bibenzyls and to shed more light on this novel and potentially useful reaction. The first such process to be examined was that of Bamford and Stevens[10] who found that phenyldiazomethane was obtained by treatment of the benzenesulfonhydrazone of benzaldehyde with alkali (eq. 3, Z = CH). As an α-elimination[11] of the elements of benzenesulfinic acid this reaction is related to the conversion of the corresponding triazene to the azide[12] (eq. 3, Z = N). These results suggested that alkaline degradation of 1,1-dibenzyl-2-benzenesulfonhydrazide should yield bibenzyl if the postulation of Kenner and Knight is correct (eq. 4). This reaction did, in fact, yield bibenzyl in 85% yield suggesting that the same intermediates might intervene in the two cases.[13]

$$C_6H_5Z{=}NNHSO_2C_6H_5 \xrightarrow{OH^-} C_6H_5Z{=}\overset{+}{N}{=}\overset{-}{N} \quad Z = N, CH \qquad (3)$$

$$(C_6H_5CH_2)_2NNHSO_2C_6H_5 \xrightarrow{OH^-} \overset{+\quad -}{(C_6H_5CH_2)_2NNSO_2C_6H_5} \longrightarrow [(C_6H_5CH_2)_2N{=}N] \longrightarrow C_6H_5CH_2CH_2C_6H_5 \qquad (4)$$

(1) This work was supported in part (see Experimental section) by the following organizations: (a) Research Corporation, New York, N. Y.; (b) the United States Air Force through the Air Force Office of Scientific Research of the Air Research and Development Command under contract number 18(603)-114; (c) The Office of Ordnance Research, United States Army, under contract number DA-19-059-ORD-2468.

(2) Paper III, L. A. Carpino, *Chemistry & Industry*, 172 (1957).

(3) Paper II, L. A. Carpino, THIS JOURNAL, **79**, 98 (1957).

(4) Presented at the 130th National Meeting of the American Chemical Society, Sept. 18, 1956, Atlantic City, N. J. (Abstracts, p. 18-O).

(5) See C. G. Overberger and B. S. Marks, THIS JOURNAL, **77**, 4104 (1955).

(6) M. Busch and B. Weiss, *Ber.*, **33**, 270 (1900). A preliminary account of an investigation of the scope of the Busch–Weiss reaction has been given by R. L. Hinman and K. L. Hamm, Abstracts of the 130th National Meeting of the American Chemical Society, Sept. 18, 1956, p. 17-O. The reaction has seen only limited use as a preparative method [see J. Kenner and J. Wilson, *J. Chem. Soc.*, 1108 (1927), and F. G. Mann, I. T. Miller and B. B. Smith, *ibid.*, 1130 (1953)].

(7) M. Busch and K. Lang, *J. prakt. Chem.*, [2] **144**, 291 (1936). References to other anomalous results are given by Overberger and Marks.[5]

(8) J. Kenner and E. C. Knight, *Ber.*, **69**, 341 (1936).

(9) The name *azamine* has been suggested for the parent substance, $H_2N^+{=}N^-$ (ref. 4 and reference cited therein). Recently W. R. McBride and H. W. Kruse [THIS JOURNAL, **79**, 572 (1957)] have presented evidence for the existence of stable azaminiun salts, $[R_2N{=}NH]X$, obtained through the oxidation of 1,1-disubstituted hydrazines.

(10) W. R. Bamford and T. S. Stevens, *J. Chem. Soc.*, 4335 (1952).

(11) Most α-eliminations yield unstable substances which either react with the environment or achieve stabilization by rearrangement. For leading references to such postulated cases of α-elimination see S. J. Cristol and R. F. Helmreich, THIS JOURNAL, **77**, 5034 (1955); J. Hine, *ibid.*, **72**, 2438 (1950); R. L. Letsinger and D. F. Pollart, *ibid.*, **78**, 6079 (1956). While α-elimination of the elements of benzenesulfinic acid is rare the corresponding β-elimination is relatively common. For examples see O. Piloty, *Ber.*, **29**, 1565 (1896); A. Hantzsch and R. Glogauer, *ibid.*, **30**, 2555 (1897); E. L. Holmes and C. K. Ingold, *J. Chem. Soc.*, 1305 (1926); A. Michael and A. M. Comey, *Am. Chem. J*, **5**, 116 (1883). When there is a choice between α- or β-elimination of HX from alkyl halides, reaction rarely, if ever, goes by the former route. The possibility exists that this preference may be reversed in the sulfonhydrazide series due to the acidity of the α-hydrogen and the presence of an unshared electron pair on the atom beta to the leaving group. The implications of this possibility are being pursued further. There does not appear to be any evidence as to whether labile 3-ring intermediates (gamma elimination) intervene in the formation of the diazo and azido groups by reactions such as 3. The diazo and azido groups are known to be linear (see K. Clusius and H. Hürzeler, *Helv. Chim. Acta*, **37**, 383 (1954), and earlier work by these authors and others).

(12) A. Key and P. K. Dutt, *J. Chem. Soc.*, 2053 (1928).

(13) Alkaline degradation of 1-phenyl-2-benzenesulfonhydrazide has been postulated [M. L. Dhar, E. D. Hughes, C. K. Ingold, A. M. M. Mandour, G. A. Maw and L. I. Woolf, *J. Chem. Soc.*, 2093 (1948)] to involve β-elimination to yield phenyldiimide ($C_6H_5N{=}NH$) which subsequently decomposes to benzene and nitrogen. The results reported in the present paper suggest that α-elimination with the formation of the azamine ($C_6H_5\overset{+}{N}H{=}\overset{-}{N}$) may represent a second possibility

TABLE I

1,1-DIBENZYL-2-ARENESULFONHYDRAZIDES,[a,b,d] p-$RC_6H_4SO_2NHN(CH_2C_6H_4R')_2$

R	R'	M.p., °C.	Yield,[c] %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
F	H	115–117	57 (92)	$C_{20}H_{19}O_2N_2SF$	64.84	65.19	5.17	5.34
Br	H	128–129 dec.	68 (82)	$C_{20}H_{19}O_2N_2SBr$	55.68	55.65	4.44	4.48
CH_3O	H	123–125	27 (57)	$C_{21}H_{22}O_3N_2S$	65.94	66.21	5.80	5.60
H	p-NO_2	160–162 dec.	56 (69)	$C_{20}H_{18}O_6N_4S$	54.29	54.23	4.10	4.13
CH_3	o-Br	124.5–126.5	53 (83)	$C_{21}H_{20}N_2SO_2Br_2$	48.10	48.22	3.85	3.61

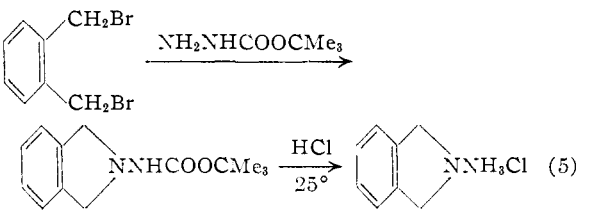
[a] Nitromethane was used as recrystallization solvent for all of the hydrazides. [b] 1,1-Bis-(o-bromobenzyl)-hydrazine was prepared by the method of Kenner and Wilson, ref. 6. [c] Yield of crude product is given in parentheses. [d] Alkaline degradation of the sulfohydrazides appeared to proceed equally as well with 5% as with 20% aqueous alkali. With the p-bromo and p-methoxy derivatives use of the more concentrated alkali caused separation of a solid, presumably the sodium sulfinate, which hindered further reaction.

Nitrogen elimination and coupling of benzyl groups also proceeds readily with the sulfonyl derivatives of 1,1-bis-(p-nitrobenzyl)- and 1,1-bis-(o-bromobenzyl)-hydrazine. By utilizing the cyclic hydrazide, 1-p-toluenesulfonamido-2,7-dihydro-3,4,5,7-dibenzazepine, 9,10-dihydrophenanthrene may be obtained in 95% yield (final step).[14] The synthetic usefulness of this reaction has been reported previously.[2] As yet no non-benzyl 1,1-disubstituted hydrazines have been found to undergo the reaction.

A brief study has been made of the effect of substitution in the benzenesulfonyl moiety on the decomposition–rearrangement since ease of loss of the benzenesulfinate anion might be expected to parallel the acidity of the corresponding sulfinic acid.[15,16] No gross differences were observed in the decomposition when 1,1-dibenzyl-2-p-bromo-, p-fluoro- or p-methoxybenzenesulfonhydrazides were compared with the unsubstituted compound. However, a marked effect was observed in the case of the o- and p-nitrobenzenesulfonhydrazides. When the reaction between p-nitrobenzenesulfonyl chloride and 1,1-bis-(p-nitrobenzyl)-hydrazine was carried out at ice-bath temperatures an unstable solid was obtained which decomposed with gaseous evolution on repeated crystallization yielding 4,4'-dinitrobibenzyl. A nitro-substituted hydrazide was isolated in a state of analytical purity by reaction of o-nitrobenzenesulfonyl chloride with 1,1-dibenzylhydrazine. Addition of either p- or o-nitrobenzenesulfonyl chloride to 1,1-dibenzylhydrazine at room temperature in the presence of triethylamine resulted in immediate gas evolution and direct formation of bibenzyl (55 and 16.5%, respectively).

Trichloromethanesulfonyl chloride similarly converted, 1,1-bis-(p-nitrobenzyl)-hydrazine directly to the bibenzyl (25–35% yield) and operation at low temperatures did not serve to yield an intermediate hydrazide.[17] For general synthetic work the p-toluenesulfonyl derivatives are preferred since these usually crystallize more readily than the benzenesulfonyl compounds.

The 1,1-disubstituted hydrazines have in general been prepared by alkylation of hydrazine or substituted hydrazines. Because of the possibility of polysubstitution, it has been found convenient in some cases to employ t-butyl carbazate in place of hydrazine. For example, N-t-butyloxycarbonylaminodihydroisoindole was prepared readily from α,α'-dibromo-o-xylene and t-butyl carbazate in 57% yield (eq. 5) whereas N-aminodihydroisoindole could not be isolated from the reaction of the dibromide and hydrazine hydrate or free hydrazine although a variety of experimental procedures were examined; resins appeared to be formed. Removal of the carbo-t-butoxy group occurred in a few minutes when the carbazate was added to concentrated hydrochloric acid. The use of the t-butyl compound proved decidedly superior to the use of benzyl carbazate,[18] both from the point of view of the initial condensation and the subsequent cleavage to the N-amino compound.[19]



which should be considered. Work is underway by which we hope to distinguish between these two processes. It also has been suggested [F. Raschig, *Z. angew. Chem.*, **23**, 972 (1910)] that benzenesulfonhydrazide itself undergoes β-elimination of benzenesulfinic acid under alkaline conditions yielding diimide which then undergoes decomposition to equimolar amounts of nitrogen and hydrogen.

A variety of other reactions have been postulated to yield diimide as an intermediate followed by subsequent decomposition to (a) nitrogen and hydrazine and (b) ammonia and hydrazoic acid [A. Angeli and Z. Jolles, *Ber.*, **62**, 2099 (1929); F. O. Rice and M. Freamo, THIS JOURNAL, **73**, 5529 (1951), **75**, 548 (1953); R. E. Kirk and A. W. Browne, *ibid.*, **50**, 337 (1928); J. Thiele, *Ann.*, **271**, 127 (1892)]. Conclusive evidence for the occurrence of diimide in any of these reactions is not available and the contradictory results suggest that other intermediates may be involved.

(14) Reference 2; experimental details are included in the present paper.

(15) Hydrazides which have been prepared but are not covered in the Experimental section are listed in Table I. The method of preparation followed that given for 1,1-dibenzyl-2-benzenesulfonhydrazide.

(16) The acidity constants of only a few benzenesulfinic acids have been determined. The unsubstituted compound has an ionization constant of approximately 3×10^{-2} [R. R. Coats and D. T. Gibson, *J. Chem. Soc.*, 442 (1940)].

(17) This reaction may proceed not through the hydrazide but rather by virtue of the oxidizing properties associated with "positive halogen" compounds. According to M. Battegay and W. Kern [*Bull. soc. chim. France*, **41**, 34 (1927)] this chloride acts as an oxidizing agent even toward ammonia and other amines. Recently trifluoromethanesulfonyl chloride has been prepared and found to react normally with amines [T. Gramstad and R. N. Haszeldine, *J. Chem. Soc.*, 173 (1956); R. N. Haszeldine and J. M. Kidd, *ibid.*, 2901 (1955); 4228 (1954)]. This compound was not available at the time of our work although trifluoromethanesulfonhydrazides would be of considerable interest since the corresponding sulfinic acid would undoubtedly be comparable to a mineral acid in strength.

(18) See the Experimental section.

(19) Mercuric oxide oxidation of N-aminodhydroisoindole as well as alkaline degradation of the corresponding p-toluenesulfonhydrazide will be the subject of a future communication.

In this and the previous paper[3] the very conveniently removed carbo-*t*-butoxy group[20] has been introduced indirectly by means of isocyanate or carbazate reactions. However, it was recorded[3] that *t*-butyl hydrazodiformate could be obtained through use of a crude sample of *t*-butyl azidoformate.[21] In view of the relative instability of *t*-butyl chloroformate and the lack of knowledge concerning the acylating power of azidoformates, representative amino compounds have been treated with the azide, which has now been obtained pure by vacuum distillation. The azide reacts readily with aqueous ammonia, hydrazine, phenylhydrazine, *t*-butyl carbazate and benzylamine yielding the expected carbamates. The reaction with aniline is more sluggish, requiring about two weeks standing in pyridine in order to give a 50–60% conversion to the carbanilate. These results suggest that the azide will be generally useful for the acylation of amino derivatives which are at least as basic as aniline. Attempted acylation of acetamide under the conditions described for aniline gave no isolable acylation product. We have not examined the acylation products of amino acids or their esters although these probably would be useful in peptide synthesis. No studies in these areas are contemplated.

$$Me_3COCON_3 \xrightarrow{RNH_2} RNHCOOCMe_3$$

Experimental[22,23]

1,1-Dibenzyl-2-benzenesulfonhydrazide.[1a]—A solution of 10.6 g. of 1,1-dibenzylhydrazine in 40 ml. of dimethylformamide and 6.95 ml. of triethylamine was cooled in an ice-bath and treated dropwise with 6.4 ml. of benzenesulfonyl chloride. After the mixture had stood for 15–20 min. it was diluted with water and acidified with hydrochloric acid. The oil which separated solidified in a few minutes and was dried prior to recrystallization from nitromethane which gave 13.2 g. (75%) of small yellowish needles, m.p. 138–140° dec. For analysis, see ref. 2.

An attempt to prepare this compound by the action of benzyl chloride on benzenesulfonhydrazide in the presence of triethylamine in hot dimethylformamide gave an alkali-stable solid which was recrystallized from nitromethane, m.p. 149–150.5°. This appeared to be benzyl phenyl sulfone (lit.[24] m.p. 148°) as would be expected if the unsubstituted hydrazine were first converted to the triethylamine salt of benzenesulfinic acid. The yield was 70–80%.

Anal. Calcd. for $C_{13}H_{12}SO_2$: C, 67.24; H, 5.18. Found: C, 67.40; H, 4.98.

Alkaline Decomposition of 1,1-Dibenzyl-2-benzenesulfonhydrazide.[1a]—A solution of 25 ml. of 20% sodium hydroxide was warmed to 70–80° and 5 g. of 1,1-dibenzyl-2-benzenesulfonhydrazide was added in 2–3 portions. When the evolution of nitrogen slowed down the mixture was warmed to 90° for a few minutes until the evolution stopped. The mixture was diluted with 75 ml. of water and cooled whereupon the oil solidified and was filtered and recrystallized from methanol which yielded 2.2 g. (85%) of tiny white crystals, m.p. 51–52.5°. A second recrystallization from ethanol raised the melting point to 51.5–53.5°. A mixed melting point with an authentic sample of bibenzyl showed no depression. The 1,3,5-trinitrobenzene complex melted at 100–102° (lit.[25] m.p. 102°). From the aqueous alkaline filtrate after filtration of the bibenzyl there was isolated a crystalline white solid, m.p. 80–83° (lit.[26] m.p. of benzenesulfinic acid 85°).

1,1-Dibenzyl-2-*o*-nitrobenzenesulfonhydrazide.[1a]—A solution of 2.21 g. of 1,1-dibenzylhydrazine in 10 ml. of dimethylformamide and 1.39 ml. of triethylamine was cooled in an ice-bath and a similarly cooled solution of 2.22 g. of *o*-nitrobenzenesulfonyl chloride[27] in 2.5 ml. of dimethylformamide was added dropwise. After allowing the mixture to stand for four hours, 50 ml. of water was added and the resulting mixture stored in an ice-box for five days whereupon partial solidification occurred and was completed by trituration with ethanol. Recrystallization from methanol yielded 2.2 g. (55.4%) of yellow solid which softened at 88° and melted at 91–92° dec. After three further recrystallizations from methanol the powder softened at 92° and had m.p. 95–97° dec.

Anal. Calcd. for $C_{20}H_{19}N_3O_4S$: C, 60.44; H, 4.82. Found: C, 60.30; H, 4.99.

The hydrazide evolved gas on contact with aqueous sodium hydroxide at room temperature or by heating alone in solvents such as dimethylformamide. A similar reaction was run with *p*-nitrobenzenesulfonyl chloride but the crude hydrazide (m.p. 88–92° dec.) was decomposed on attempted recrystallization from methyl ethyl ketone.

1,1-Bis-(*p*-nitrobenzyl)-hydrazine.[1a]—A modification of the method of Busch and Weiss[6] was used. A solution of 35 g. of α-chloro-*p*-nitrotoluene and 4.6 g. of 64% hydrazine in 250 ml. of warm ethanol was treated all at once with 37.8 ml. of triethylamine. A solid began to precipitate after two hours and was filtered after two days standing. The crude product amounted to 20 g. (66.3%), m.p. 115–117°. Recrystallization from nitromethane gave 12 g. (39.8%) of tiny bright yellow crystals, m.p. 135–137° (lit.[6] m.p. 137–138°).

Thermal Decomposition of 1,1-Bis-(*p*-nitrobenzyl)-2-methanesulfonhydrazide.[1a]—The hydrazide (crude, 79.5%, m.p. 139–149°) was prepared as given for the dibenzyl compound and recrystallized from nitromethane which gave tiny yellow crystals, m.p. 154–155° dec., yield 58%.

Anal. Calcd. for $C_{15}H_{16}N_4SO_6$: C, 47.36; H, 4.24. Found: C, 47.48; H, 4.46.

Heating of this hydrazide for 1–2 min. at 145–150° in ethylene glycol gave 4,4′-dinitrobibenzyl (70%), m.p. 182–184° (lit.[6] m.p. 179°). Treatment of the corresponding benzenesulfonhydrazide with 20% aqueous sodium hydroxide gave only 40% of the bibenzyl, possibly because of decomposition due to the nitro groups.

Reaction between 1,1-Dibenzylhydrazine and *p*-Nitrobenzenesulfonyl Chloride.[1a]—A solution of 2.12 g. of 1,1-dibenzylhydrazine in 10 ml. of dimethylformamide and 2.8 ml. of triethylamine was treated over a period of 3–4 minutes with 2.2 g. of *p*-nitrobenzenesulfonyl chloride (Eastman Kodak Co.) while allowing the reaction mixture to warm up spontaneously. The mixture was then held at a temperature just below its boiling point for 5 minutes, diluted with 250 ml. of water, acidified with phosphoric acid and steam-distilled. The yield of bibenzyl collected in 1 liter of distillate was 1.0 g. (54.9%), m.p. 50–51°. The same procedure applied to *o*-nitrobenzenesulfonyl chloride gave only 16.5% of bibenzyl.

(20) Observations to be published shortly in coöperation with Mr. Paul J. Crowley indicate that a wide spectrum of protective groups of the carboalkoxy and thiocarboalkoxy types is available which can be cleaved selectively under anhydrous conditions by acids of varying strengths.

(21) Repetition of the acylation of *t*-butyl carbazate using a distilled sample of the azide led to the isolation (80%) of a white solid, m.p. 124.5–125.5° (see Experimental section), which had the correct analysis for the expected hydrazo compound. The compound previously obtained, m.p. 103–105°, which also gave a correct analysis, has not been obtained since. The compound, m.p. 124.5–125.5°, was characterized by N-bromosuccinimide oxidation to the azo derivative and reconversion of the latter by reduction with hydrazine to the hydrazide. Unfortunately at the time of preparation of the compound m.p. 124.5–125.5°, none of the lower melting substance was available for direct comparison although it was noted that an attempt to oxidize the compound m.p. 103–105°, by exactly the same procedure used for the higher melting compound was not successful.

(22) All boiling and melting points are uncorrected.

(23) Analyses are by Geller Laboratories, Hackensack, N. J., and Drs. Weiler and Strauss, Oxford, England.

(24) E. Knoevenagel, *Ber.*, **21**, 1349 (1888).

(25) J. J. Sudborough, *J. Chem. Soc.*, **109**, 1344 (1916).

(26) S. Krishna and H. Singh, THIS JOURNAL, **50**, 792 (1928).

(27) H. E. Fierz, E. Schlitter and H. Waldman, *Helv. Chim. Acta*, **12**, 663 (1929).

Preparation of N-(*t*-Butyloxycarbonylamino)-dihydroisoindole.[1b]—A solution of 39.6 g. of *o*-xylylene dibromide[28] and 19.8 g. of *t*-butyl carbazate in 100 ml. of dimethylformamide was warmed to 50° and 41.7 ml. of triethylamine was added during 5–8 minutes while maintaining the temperature at 50–60° by slight tap-water cooling, if necessary. After complete addition the mixture was allowed to stand at room temperature for three hours and diluted with water to a final volume of 400 ml. After standing for one hour the amorphous white solid was filtered and on air-drying amounted to 31 g. (88.5%), m.p. 103–113° (previous softening at 98°). Recrystallization from the minimum amount of nitromethane gave 20 g. (56.9%) of tiny crystals, m.p. 115.5–117.5° (very slight previous softening at 110°). The analytical sample (from nitromethane) melted at 119–120°.

Anal. Calcd. for $C_{13}H_{16}N_2O_2$: C, 66.64; H, 7.74. Found: C, 66.35; H, 7.77.

Preparation of N-Aminodihydroisoindole Hydrochloride.[1b]—At room temperature 4.6 g. of N-(*t*-butyloxycarbonylamino)-dihydroisoindole was added during 1–2 minutes to 6 ml. of concentrated hydrochloric acid (d. 1.18). After standing for one hour the mixture, from which the crystalline hydrochloride had begun to separate, was evaporated with a water aspirator (17 mm.) from a water-bath (65–70°) until the residue was dry (1.5–2 hours). The crystalline hydrochloride (3.32 g., 62.6%, m.p. 150–180°) was washed onto a funnel with ether and recrystallized twice by solution in the minimum amount of hot ethanol followed by precipitation with ether: I, amount 2.77 g. (52.3%), m.p. 185–195° after previous softening at 160°; II, amount 2.55 g. (48%), m.p. 203–205.5° (lit.[29] m.p. 190–194°). The benzal derivative melted at 129.5–131° (lit.[29] m.p. 127–129°).

N-Benzyloxycarbonylaminodihydroisoindole.[1b]—This compound was obtained as indicated above for the corresponding *t*-butyl derivative by substituting benzyl carbazate[30] for *t*-butyl carbazate except that after addition of the triethylamine the mixture was heated for two hours on a steam-bath prior to precipitation with water. The product, which was difficult to purify, was recrystallized from dimethylformamide and then nitromethane, yield 31%, m.p. 134–135°.

Anal. Calcd. for $C_{16}H_{16}O_2N_2$: C, 71.62; H, 6.01. Found: C, 71.52; H, 5.84.

Cleavage by means of hydrogen bromide in nitromethane gave a tacky brown solid which was not easily purified although it gave a benzal derivative, m.p. 129.5–131°.

N-*p*-Toluenesulfonamidodihydroisoindole.[1b]—A solution of 1.35 g. of the hydrochloride of N-aminodihydroisoindole in 5 ml. of warm dimethylformamide was treated with 1.4 ml. of triethylamine and the resulting mixture cooled in an ice-bath and treated during 1–2 minutes with 0.95 g. of *p*-toluenesulfonyl chloride. After 15 minutes standing in the ice-bath, dilution with water gave a tan-colored solid which was recrystallized at once by solution in hot acetone and precipitation with water. The yield was 1.3 g. (67%), m.p. 130–132° dec. (previous darkening at 126°). A second recrystallization in the same way gave 0.9 g. (46.4%) of yellow crystals, m.p. 135–136° dec. The analytical sample, m.p. 136–138° dec., was recrystallized from acetone. Recrystallization from higher-boiling solvents caused considerable decomposition.

Anal. Calcd. for $C_{15}H_{16}N_2SO_2$: C, 62.47; H, 5.59. Found: C, 62.50; H, 5.54.

1-Amino-2,7-dihydro-3,4,5,7-dibenzazepine Hydrochloride.[1b]—*o*-Bitolyl was prepared and converted to *o,o'*-bis-(bromomethyl)-biphenyl according to the procedures of Wenner.[31] The *m*-tolidine used was a commercial sample[32] of a salt having "54% contained amine." A warm solution (50–60°) of 4.15 g. of *o,o'*-bis-(bromomethyl)-biphenyl and 1.61 g. of *t*-butyl carbazate in 10 ml. of dimethylformamide was treated slowly (2–3 minutes) with 3.42 ml. of triethylamine. After standing for 3–4 hours the solution was diluted with water and the oily semi-solid extracted with methylene chloride. Removal of solvent from the dried ($MgSO_4$) solution by means of a water aspirator yielded an oil which would not crystallize and was cleaved by addition of 10 ml. of concd. hydrochloric acid. The remainder of the procedure followed that given for the corresponding dihydroisoindole. The crude hydrochloride, after one precipitation from ethanol by means of ether, amounted to 1.8 g. (60%), m.p. 213–220° A second precipitation gave 1.5 g. (50%), m.p. 226–228°. The analytical sample[2] was recrystallized from nitromethane–ethanol (1:1), m.p. 230–231°.

1-*p*-Toluenesulfonamido-2,7-dihydro-3,4,5,7-dibenzazepine.[1b]—This derivative was prepared as indicated for the corresponding dihydroisoindole compound. The yield of pure hydrazide, m.p. 149.5–151.5° dec., recrystallized from ethanol–nitromethane (2:1), was 50%. For analysis, see ref. 2.

9,10-Dihydrophenanthrene.[1b]—The azepine described directly above was decomposed as given for the 1,1-dibenzyl compound. The crude product (m.p. 33–35°, 94.5%) was recrystallized from methanol, yield 67.5%, m.p. 34.5–35.5° (lit.[33] m.p. 34.5–35°).

***t*-Butyl Azidoformate.**[1c]—*t*-Butyl phenyl carbonate was prepared as indicated previously[3] except that tap-water cooling of the reaction mixture was dispensed with, the acid chloride being added at a rate such that the temperature remained between 38–41°. *t*-Butyl carbazate was prepared in the manner previously reported[3] although the yield was 89–94% rather than 68.3% as previously indicated. Conversion of the carbazate to the azide followed the earlier method except that the water-washed, $NaHCO_3$-washed ether extracts were dried (magnesium sulfate) and the solvent removed from a water-bath at 40–45° with a water aspirator pressure of 140–150° mm. The azide was then distilled by raising the bath temperature to 90° and lowering the pressure to 70 mm. where the azide collected as a water-white liquid, b.p. 73–74° (70 mm.), yield 80%.[34]

Anal.[35] Calcd. for $C_5H_9N_3O_2$: C, 41.95; H, 6.34. Found: C, 41.90; H, 6.29.

***t*-Butyl 2-Phenylcarbazate.**[1c]—A mixture of 2.86 g. of *t*-butyl azidoformate, 2.16 g. of phenylhydrazine, 2.78 ml. of triethylamine and 5 ml. of water was placed on a continuous shaking machine for 40 hours. Filtration gave 3.2 g. (80.4%) of yellow-orange solid which was washed with water and air-dried, m.p. 85–91°. Recrystallization from ligroin (60–90°) gave 2.75 g. (69.1%) of cream-colored crystals, m.p. 91–93°. The analytical sample, recrystallized from the same solvent, melted at 92–93.5°.

Anal. Calcd. for $C_{11}H_{16}O_2N_2$: C, 63.44; H, 7.75. Found: C, 63.56; H, 7.56.

Other Acylations Using *t*-Butyl Azidoformate.[1c]—*t*-Butyl 2-phenylcarbazate also was prepared by allowing a solution of the reactants in methylene chloride to stand overnight, although the product was less easily purified (yield 40–50%). *t*-Butyl carbamate[36] was prepared by allowing the azide to stand in contact with concd. aqueous ammonia for 16 hours with occasional shaking. The yield was 80%, m.p. 108–109.5° (1:1, 60–90° ligroin–benzene). Hydrazine (64%) converted the azide back to *t*-butyl carbazate with spontaneous warming (yield 83.3%). Acylation of benzylamine occurred with spontaneous warming when 2.86 g. of the azide, 4.28 g. of the amine and 5 ml. of pyridine were mixed and allowed to stand overnight. Precipitation with water gave 3.8 g. (91.8%) of white solid, m.p. 54–57°. Recrystallization from ligroin (b.p. 60–90°) gave 3.5 g. (84.6%) of *t*-butyl N-benzylcarbamate, m.p. 57–58°.

Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.53; H, 8.27. Found: C, 69.30; H, 8.20.

Acylation of aniline by means of the azide was more difficult to achieve than that of more basic amino compounds. The method used for the acylation of phenylhydrazine gave

(28) A. C. Cope and S. W. Fenton, THIS JOURNAL, **73**, 1668 (1951).

(29) K. Frankel, *Ber.*, **33**, 2808 (1900).

(30) N. Rabjohn, THIS JOURNAL, **70**, 240 (1948).

(31) W. Wenner, *J. Org. Chem.*, **17**, 523 (1952).

(32) We wish to acknowledge a generous gift of this material from the Carwin Co., North Haven, Conn.

(33) G. Schroeter, H. Muller and J. Y. S. Huang, *Ber.*, **62**, 649 (1929).

(34) The azide should be handled with adequate ventilation. Careless handling of the azide was always accompanied by development of a painful throbbing headache which, however, disappeared within several hours. In large doses the azide also affects the nasal passages in a manner similar to the action of the common cold.

(35) Prepared by Mr. C. A. Giza.

(36) A. R. Choppin and J. W. Rogers, THIS JOURNAL, **70**, 2967 (1948).

only a trace of *t*-butyl carbanilate, m.p. 135–137°. By allowing equimolar amounts of the azide and aniline to stand in pyridine solution for two weeks followed by precipitation with water, a 50–60% yield, m.p. 135–137°, was obtained (lit.[36] m.p. 136.3–136.5).

t-Butyl **Hydrazodiformate**[1c,21]—A solution of 2.86 g. of distilled *t*-butyl azidoformate, 2.64 g. of *t*-butyl carbazate in 6 ml. of pyridine was allowed to stand for one week (if allowed to stand for two weeks the yield was only 3–5% greater) and then diluted with 75 ml. of water. The snow-white solid which precipitated amounted to 3.7 g. (80.1%), m.p. 124–126°. The analytical sample was recrystallized from ligroin (60–90°)–benzene (1:1) as tiny needles, m.p. 124–125.5°.

Anal. Calcd. for $C_{10}H_{20}O_4N_2$: C, 51.71; H, 8.70. Found: C, 52.00; H, 8.77.

AMHERST, MASS.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA]

Mechanism of Trimethylene Oxide Formation from 3-Chloropropyl Acetate

BY DONALD C. DITTMER, WALTER R. HERTLER AND HERBERT WINICOV

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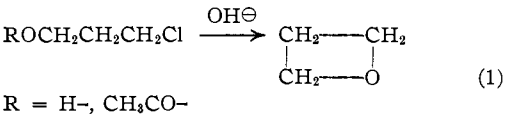
Evidence has been obtained that the better yields of trimethylene oxide from 3-chloropropyl acetate than from 3-chloropropanol may be caused by a protective effect of the acetate group and not by a fundamentally different mechanism. Oxide prepared from carbonyl O^{18}-labeled ester contained no excess O^{18}; this result rules out any mechanism for trimethylene oxide formation in which the two acetate oxygens are equivalent. Trimethylsilyl 3-chloropropyl ether gave as high a yield of oxide as the acetate, and 3-chloropropyl thiolacetate gave only trimethylene sulfide.

Yields of trimethylene oxide obtained by treatment of 3-chloropropyl acetate with strong base have been reported to be much greater than yields from 3-chloropropanol.[1] A similar result has been reported for the preparation of ethylene oxide from 2-chloroethyl acetate.[2]

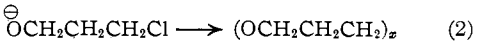


$$ROCH_2CH_2CH_2Cl \xrightarrow{OH^\ominus} \begin{matrix} CH_2 & CH_2 \\ | & | \\ CH_2 & O \end{matrix} \qquad (1)$$

R = H–, CH_3CO–

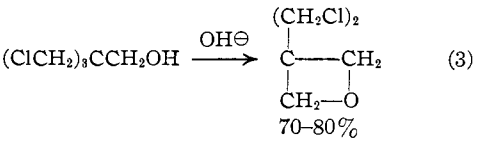
Since in the concentrated base used the acetate presumably would be hydrolyzed to the same chlorohydrin anion, $\ominus OCH_2CH_2CH_2Cl$, as the one formed from 3-chloropropanol, the yields of trimethylene oxide, if they proceeded from this alkoxide, would not be expected to be as different as they are between acetate and chlorohydrin.

To explain the disparity in yields between chlorohydrin and chloroacetate, a protective effect of the acetate group or a different mechanism may be invoked. The chloroacetate may yield the chlorohydrin anion at a slower rate than it is produced from the chlorohydrin. Since the concentration of alkoxide from chloroacetate at any time would be smaller than from chlorohydrin, conditions might be more favorable for intramolecular cyclization than for intermolecular reaction which would produce a polymeric ether. In other types of ring closure, high dilution of the reactants is necessary to prevent intermolecular reactions since the extent of intermolecular reaction depends on the concentration of the reactants while that of the intramolecular reaction does not.[3]



$$\ominus OCH_2CH_2CH_2Cl \longrightarrow (OCH_2CH_2CH_2)_x \qquad (2)$$

Indeed, a linear polymeric ether, $(C_3H_6O)_x$, has been isolated as a by-product in the preparation of trimethylene oxide from 3-chloropropanol.[4] Excellent yields (70–80%) of 3,3-dichloromethyloxetane have been reported from trichloropentaerythritol and potassium hydroxide.[5] Here, the intermolecular reaction involves a displacement reaction on a neopentyl-type system which would be expected to be very slow.

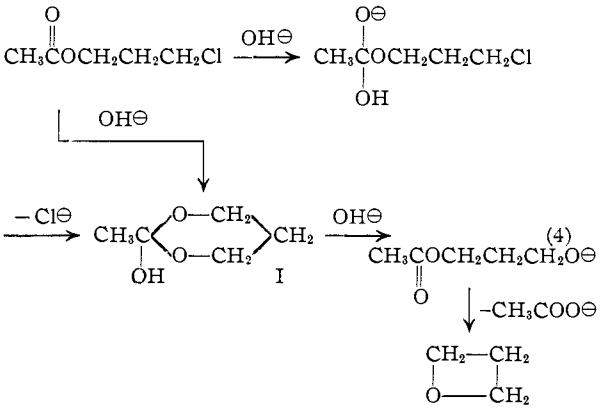


$$(ClCH_2)_3CCH_2OH \xrightarrow{OH^\ominus} \begin{matrix} (CH_2Cl)_2 \\ | \\ C & CH_2 \\ | & | \\ CH_2 & O \end{matrix} \qquad (3)$$

70–80%

Other side products from 3-chloropropanol were said to be allyl alcohol and allyl chloride.[1a] It is not expected that acetylation of the hydroxyl group would have much effect on these olefin-producing side reactions.

If the production of trimethylene oxide from 3-chloropropyl acetate involved a different mechanism other than the straightforward intramolecular displacement of chloride ion by the alkoxide part of the molecule,[6] higher yields of oxide might be expected if the free energy of activation for the new mechanism were less than that for the old



$$CH_3COCH_2CH_2CH_2Cl \xrightarrow{OH^\ominus} CH_3C(O^\ominus)(OH)CH_2CH_2CH_2Cl$$

$$\xrightarrow{OH^\ominus} \xrightarrow{-Cl^\ominus} CH_3C\begin{matrix} O-CH_2 \\ O-CH_2 \end{matrix}CH_2 \quad (OH) \quad I$$

$$\xrightarrow{OH^\ominus} CH_3COCH_2CH_2CH_2O^\ominus \qquad (4)$$

$$\downarrow -CH_3COO^\ominus$$

$$\begin{matrix} CH_2 & CH_2 \\ | & | \\ O & CH_2 \end{matrix}$$

(1) (a) C. G. Derick and D. W. Bissell, THIS JOURNAL, **38**, 2478 (1916); (b) C. R. Noller, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 835.

(2) E. Demole, *Ann.*, **173**, 125 (1874).

(3) P. Ruggli, *ibid.*, **392**, 92 (1912); G. M. Bennett, *Trans. Faraday Soc.*, **37**, 794 (1941); K. Ziegler, H. Eberle and H. Ohlinger, *Ann.*, **504**, 94 (1933)

(4) M. Reboul, *Ann. chim.*, [5] **14**, 497 (1878).

(5) F. Govaert and M. Beyaert, *Natuur. Tijdschr.*, **22**, 73 (1940); *C. A.*, **37**, 3054 (1943).

(6) S. Winstein and H. J. Lucas, THIS JOURNAL, **61**, 1576 (1939).