Evidence related to the structure of the ether IV was obtained in the following way. The product had the molecular formula $C_{18}H_{12}Cl_2O_3$, and the ultraviolet spectrum suggested olefinic unsaturation conjugated to a benzene ring. The nuclear magnetic resonance spectrum showed peaks at 3.75, 3.09, 2.79, and 2.60 τ (see Experimental), and no absorption in the 5.94- or 7.95-τ region expected for the cyclopropyl ether II.[2] The ether reacted readily with 2,4-dinitrophenylhydrazine reagent to give a hydrazone with the composition calculated for the expected derivative of 2-chloro-3-(2-hydroxyphenyl)propenal.

The ether IV is thought to form as shown in the equations I → II → III → IV. The product, II and/or III, formed prior to addition of water, decomposed upon attempted distillation of chromatography upon alumina. The facile ring expansion of II to III, which occurred either spontaneously in hexane or rapidly upon addition of water, was not unexpected in view of the behavior of related compounds. The corresponding cyclopropane derived from indene[3] underwent ring expansion to give chloronaphthalene when it was dissolved in polar solvents such as alcohol, and the corresponding cyclopropanes derived from dichlorocarbene and 1- or 2-methoxynaphthalene underwent ring expansion[4] in nonpolar solvents at temperatures below 32°.

Although dichlorocarbene does not add appreciably to benzene, the observed addition to benzofuran was expected in view of: (a) the greater nucleophilic character of furan relative to benzene and (b) the known effects of strongly electron-donating substituents as evidenced by the reaction of dichlorocarbene with methoxy-substituted aromatics.[4]

Benzothiophene does not react appreciably with dichlorocarbene even when the latter is in 100% excess. A 92% recovery of aromatic was noted. This observation is consistent with the fact that oxygen can normally[5] enrich the electron density of an attached double bond by utilizing its unshared p-orbital electrons more effectively than can sulfur, and with the greater nucleophilic character of furan relative to thiophene; however, one cannot discount at this time further deactivation of benzothiophene by complex formation between the sulfur atom and dichlorocarbene.[6]

Experimental

Bis[3-chloro-2(3-chromenyl)] Ether (IV).—Ethyl trichloroacetate (53.6 g., 0.281 mole) was added all at once to a cold (ice bath) mixture, under nitrogen, of benzofuran (27.5 g., 0.233 mole), sodium methoxide (16.1 g., 0.298 mole), and pure hexane (200 ml.). The violet color which developed rapidly disappeared. The mixture was kept cold for 6 hr., then allowed to come to room temperature overnight. The resulting solution was divided in two equal parts. Attempts at purification of one part by vacuum distillation and by chromatography on alumina were unsuccessful. In each case decomposition was noted.

Water (100 ml.) was added to the second portion and the resulting mixture was stirred for 3 days at room temperature.[7] The organic layer was separated, dried, and the solvent was removed. The residue was triturated with petroleum ether (b.p. 30–60°), and the solid thus obtained was recrystallized from benzene. There was obtained 3 g. (14.9%) of IV which decomposed at 181–182° with elimination of hydrogen chloride.

Anal. Calcd. for $C_{18}H_{12}Cl_2O_3$: C, 62.35; H, 3.46; Cl, 20.43; mol. wt., 347. Found: C, 62.60; H, 3.68; Cl, 20.89; mol. wt. (Rast), 313.

Infrared (KBr pellet) spectrum: 3068 w, 1638 m, 1606 m, 1575 w, 1489 s, 1460 s, 1206 s, 1194 s, 1124 s, 1083 s, 1008 vs, 962 vs, 925 vs, 756 vs cm.$^{-1}$.

Ultraviolet spectrum (in absolute ether): $\lambda_{\max}$ 263.2 (ϵ 27,200), 273 (ϵ 25,700), and 297 mμ (ϵ 6500).

The nuclear magnetic resonance spectrum of IV as a 10% solution in deuteriochloroform on a Varian A-60 spectrometer using tetramethylsilane as a reference gave: 3.75 τ, singlet assigned to hydrogens alpha to the ether oxygen (calcd.[8] 3.73), 3.09 τ, finely split doublet assigned to the benzyl hydrogen, and 2.79 and 2.60 τ, complex splitting assigned to the aromatic hydrogens.

The 2,4-dinitrophenylhydrazone of 2-chloro-3-(2-hydroxyphenyl)propenal was obtained from IV and the usual reagent. The product was purified by recrystallization from ethyl acetate (m.p. with decomposition 257.5–260°, yield <50%).

Anal. Calcd. for $C_{15}H_{11}ClN_4O_5$: C, 49.66; H, 3.04; N, 15.45. Found: C, 49.59; H, 3.24; N, 15.51.

The reaction of benzothiophene and dichlorocarbene was attempted using the same conditions described above for benzofuran. Benzothiophene (m.p. 29–31°) was recovered (92% recovery).

---

[2] W. E. Parham and L. D. Huestis, *J. Am. Chem. Soc.*, **84**, 813 (1962).

[3] W. E. Parham, H. E. Reiff, and P. Swartzentruber, *ibid.*, **78**, 1437 (1956).

[4] W. E. Parham, D. A. Bolon, and E. E. Schweizer, *ibid.*, **83**, 603 (1961).

[5] It has been suggested that this situation may not obtain in furan relative to thiophene due, primarily, to steric factors; *cf.* M. M. Kreevoy, *ibid.*, **80**, 5543 (1958).

[6] W. E. Parham and R. Koncos, *ibid.*, **83**, 4034 (1961).

(7) In an earlier experiment the mixture was merely extracted with water; the yield of IV was essentially the same.

(8) D. P. Daily and J. N. Schoolery, *J. Am. Chem. Soc.*, **77**, 3977 (1955).

The Reaction of Carbanilides with Sodium Hypochlorite[1]

MARVIN L. OFTEDAHL, ROBERT W. RADUE,
AND MARTIN W. DIETRICH

Research Department, Organic Chemicals Division,
Monsanto Chemical Company, St. Louis 77, Missouri

Received July 13, 1962

Treatment of carbanilide (Ia) with three moles of sodium hypochlorite has been reported by Rosnati[2] to yield 1-phenyl-2-hydroxybenzimidazole (the enol form of IIa). Rosnati also cyclized a number of symmetrically substituted carbanilides (*e.g.*, 4,4′-dimethyl-; 4,4′-dichloro-; 4,4′-dimethoxy-) and demonstrated that the N,N′-dialkylated carbanilides (I. R_3, R_4 = CH_3; R_1, R_2, R_3, R_4 = H) and 2,2′,4,4′,6,6′-hexamethylcarbanilide are inert to alkaline hypochlorite. Because of its biological interest, we deemed it advisable to investigate the behavior of 3,4,4′-trichlorocarbanilide (Ib)[3] upon hypochlorite treatment. Because of the asymmetry involved, ring closure could occur in several directions. Rosnati's work with symmetrical carbanilides does not provide sufficient information for predicting the course of the cyclization.

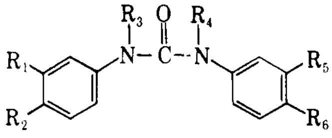
To obtain a reference compound for our work, we repeated Rosnati's experiment with Ia. Following Rosnati's directions,[2] Ia, when treated with three moles

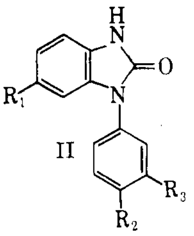
---

(1) Presented before the Division of Organic Chemistry at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., September, 1962.

(2) L. Rosnati, *Gazz. chim. ital.*, **86**, 275 (1956).

(3) D. J. Beaver, D. P. Roman, and P. J. Stoffel, *J. Am. Chem. Soc.*, **79**, 1236 (1957); D. J. Beaver and P. J. Stoffel, U. S. Patent 2,818,390 (December 31, 1957).





II

Ia. R's = H
b. R_1, R_2, R_6 = Cl; R_3, R_4, R_5 = H
c. R_1, R_2 = Cl; R_3, R_4, R_5, R_6 = H
d. R_1, R_2, R_5, R_6 = Cl; R_3, R_4 = H
e. R_1, R_2, R_6 = Cl; R_4 = C_2H_5
R_3, R_5 = H
f. R_1, R_2, R_6 = Cl; R_3 = CH_3
R_4, R_5 = H.
IIa. R_1, R_2, R_3 = H
b. R_1 = Cl. R_2, R_3 = H
c. R_1, R_2, R_3 = Cl

of sodium hypochlorite, in our hands afforded 1-phenyl-6-chloro-2-benzimidazolinone (IIb). To obtain the unchlorinated product (IIa), it was necessary to employ one mole of hypochlorite. The chlorination providing IIb appears to have taken place during the acidic work-up, whereby hypochlorite, in the presence of hydrochloric acid, generates chlorine. We are unable to account for the fact that Rosnati did not observe this result under the conditions he describes.

The infrared spectra of these cyclized carbanilides revealed them to be in the keto form rather than the hydroxy form,[4] exhibiting a strong carbonyl band at 5.8 μ and no —OH absorption. The increase in frequency of the carbonyl absorption from about 1660 cm.$^{-1}$ for the carbanilides to 1725–1750 cm.$^{-1}$ for the benzimidazolinones is consistent with the cyclic amide structure.[5]

When 3,4,4'-trichlorocarbanilide (Ib)[3] was treated with three moles of sodium hypochlorite, it cyclized to provide 1-(3,4-dichlorophenyl)-6-chloro-2-benzimidazolinone (IIc). No further chlorination occurred, presumably due to ring deactivation by the initial chlorine substituent. Treatment of 3,4-dichlorocarbanilide (Ic)[3] with hypochlorite under the same conditions also gave IIc, supporting this conclusion as well as providing evidence for the structure of IIc. Where either urea nitrogen was alkylated (Ie, If), or where each aryl ring was substituted with more than one chlorine atom (Id), the cyclization failed to occur under the experimental conditions employed.

Comparison of the infrared spectra of IIb and c with the spectrum of the Rosnati compound[2] established the similarities of the ring systems. The positions of the chlorine atoms in IIb and c were deduced by analysis of their n.m.r. spectra and those of their monoacetate derivatives. The chemical shift[6] of ring A[7] was established by examination of 2-benzimidazolinone itself, and of a series of chlorinated 2-benzimidazolinones (0.50 *M* dimethylacetamide). The aromatic proton region of the n.m.r. spectrum of each compound examined contained a single peak at 410 ± 4 c.p.s. The chemical shift of ring B[7] was established by examination of IIa. The aromatic portion of the n.m.r. spectrum of this compound (0.50 *M* dimethylacetamide) contained two peaks at 412 and 440 c.p.s., with an area ratio of 3.9:5.0. The peak at 412 c.p.s. was assigned to ring A; the peak at 440 c.p.s. to ring B.

The aromatic portion of the n.m.r. spectrum of IIb (0.50 *M* dimethylacetamide) contained two peaks at 413 and 443 c.p.s., with an area ratio of 3.1:5.0. The peak at 413 c.p.s. was assigned to ring A; the peak at 443 c.p.s. to ring B. The observed area ratio established that the chlorine atom was in ring A. Similarly, the aromatic portion of the n.m.r. spectrum of IIc (0.50 *M* dimethylacetamide) contained three peaks centered at 414, 450, and 462 c.p.s. with an area ratio of 3.0:2.0:0.9. The peak at 414 c.p.s was assigned to ring A and the remaining complex peaks to ring B The observed area ratio established the presence of one chlorine atom in ring A and two in ring B. In both cases, the lack of sufficient resolved multiplet detail made it impossible to assign the precise location of the chlorines in either structure.

To determine the positions of the chlorine atoms in IIb and c, derivatives of these compounds were prepared in which the various proton positions in each ring no longer had approximately equal chemical shifts. The monoacetate derivatives were chosen. The literature[3,8] is not clear as to whether acetylation of a 2-benzimidazolinone will lead to the N-acetyl or O-acetyl derivative since the evidence available is at times contradictory. In any event, formation of either the O or N-acetyl derivative of IIb and c, would introduce unsaturation into the heterocyclic ring system, causing a concommitant non-equivalency of the various ring positions.[9] In particular, the absorption from the 4-position, which is nearest the unsaturation, can be expected to be appreciably shifted to lower field.

The aromatic portion of the n.m.r. spectrum of the monoacetate of IIb (0.50 *M* dimethylacetamide) contained a single complex peak centered at 440 c.p.s. for the protons in ring B and a simple first-order spectrum for the protons in ring A. Analysis of this pattern established IIb as 1-phenyl-6-chloro-2-benzimidazolinone. Chemical shifts and coupling constants determined from this analysis are for ring A of the monoacetate: $\tau_4 = 2.08$, $\tau_5 = 3.06$, $\tau_7 = 3.31$, $J_{45} = 8.7$ c.p.s., and $J_{57} = 1.8$ c.p.s.

The n.m.r. spectrum of the monoacetate of IIc (0.50 *M* dimethylacetamide) contained a complex pattern in the aromatic proton region. Rather than attempt an analysis of this spectrum, solvent effects upon the relative chemical shifts of the various aromatic protons were utilized.[10] The aromatic proton region in the n.m.r. spectrum of the monoacetate of IIc (0.7 *M* dioxane) was a well resolved pattern which could be easily analyzed by first-order methods, establishing IIc as 1-(3,4-dichlorophenyl)-6-chloro-2-benzimidazolinone. Chemical shifts and coupling constants determined

---

[4] For a general discussion of this question, see A. R. Katritsky and R. A. Y. Jones, *Chem. Ind.* (London), 722 (1961).

[5] L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p. 223; R. Gompper and H. Herlinger, *Chem. Ber.*, **89**, 2825 (1956).

[6] Chemical shifts are reported in τ units; if no spectral analysis was made, peak positions are reported in c.p.s. referred to internal tetramethylsilane.

[7] Ring A = 2-benzimidazolinone ring; ring B = phenyl substituent in 1-position of the 2-benzimidazolinone ring.

[8] D. Harrison and A. C. B. Smith, *J. Chem. Soc.*, 4827 (1961).

[9] For numerous examples of the effect of unsaturated substituents on the chemical shift of aromatic protons, see N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "Varian High Resolution NMR Spectra Catalog," Varian Associates, Palo Alto, Calif., 1962.

[10] T. Schaefer and W. T. Schneider, *J. Chem. Phys.*, **32**, 1218 (1960).

from this analysis are for ring A of the monoacetate: $\tau_4 = 2.01$, $\tau_5 = 3.03$, $\tau_7 = 3.10$, $J_{45} = 8.9$ c.p.s., $J_{57} = 2.0$ c.p.s., $J_{47} \simeq 0.9$ c.p.s.; and for ring B: $\tau_2 = 2.43$, $\tau_5 = 2.45$, $\tau_6 = 2.76$, $J_{56} = 8.7$ c.p.s., and $J_{26} = 2.3$ c.p.s.

The direction of ring closure of both Ib and c suggests that the cyclization proceeds *via* intramolecular attack of an electrophilic nitrogen upon the most electron rich aryl ring available. Failure of Id to cyclize can be explained by reduction of the electron density of both aryl rings, thus preventing attack by electrophilic nitrogen. Alkylation of one urea nitrogen (Ie, f) could prevent the cyclization from taking place either by interference with the formation of the electrophilic nitrogen (*e.g.*, N-chlorination by hypochlorite) or by electronic interference with the ring closure.

Experimental

Melting points are uncorrected. All n.m.r. measurements were made on a Varian V-4300 B n.m.r. spectrometer operating at 60 Mc./sec. Spectra were calibrated by the audiofrequency side band technique,[11] a frequency counter being employed. Hypochlorite cyclizations were all run following the same general procedure described by Rosnati,[2] the preparation of 1-phenyl-6-chloro-2-benzimidazolinone serving as an example. The sodium hypochlorite employed was a commercially available 12% aqueous solution which was analyzed just prior to use.

Reaction of Carbanilide (Ia) with Three Moles of Hypochlorite.—To a slurry of 10.6 g. (0.05 mole) of carbanilide in 300 ml. of methanol was added a solution of 4.0 g. of sodium hydroxide in 15 ml. of water. After cooling in an ice bath, the mixture was treated with 110 ml. of 1.36 *M* (0.15 mole) sodium hypochlorite. The hypochlorite addition was conducted such that the solution temperature did not exceed 35°. As the addition proceeded, most of the carbanilide passed into solution, and the solution darkened in color. A half hour after the completion of the addition, a strong positive test for hypochlorite ion was noted with starch–iodide test paper. The reaction mixture was neutralized with dilute hydrochloric acid, the methanol removed by evaporation at reduced pressure, and the residue diluted with 500 ml. of water. The residue was collected by filtration, dissolved in 400 ml. of hot 10% aqueous sodium hydroxide, decolorized, and precipitated once more by acidification. The resultant residue (10 g.) was recrystallized from toluene to afford 6.0 g. (49%) of 1-phenyl-6-chloro-2-benzimidazolinone (IIb), m.p. 232–238°. Recrystallization once more from toluene afforded the pure material as white needles, m.p. 246–247°. Mixture melting point with carbanilide (m.p. 240–241°) showed 202–214°. The infrared spectrum had characteristic bands at 5.8 μ (C=O) and 3.15 μ (N—H).

Anal. Calcd. for $C_{13}H_9ClN_2O$: C, 63.8; H, 3.71; Cl, 14.5; N, 11.4. Found: C, 63.6; H, 3.97; Cl, 14.5; N, 11.3.

Acetylation of the above compound (1.0 g.) with acetic anhydride (10 ml.) and powdered, fused sodium acetate (0.5 g.) at steam bath temperatures provided the monoacetate, m.p. 160.0–160.5°, in 70% yield.

Anal. Calcd. for $C_{15}H_{11}ClN_2O_2$: C, 62.8; H, 3.87. Found: C, 63.0; H, 3.98.

Reaction of Carbanilide (Ia) with One Mole of Hypochlorite.—Carbanilide (10.6 g., 0.05 mole), when treated with 45 ml. of 1.23 *M* (0.055 mole) of sodium hypochlorite, provided 1-phenyl-2-benzimidazolinone, (IIa), m.p. 203.5–204°, in 71% yield. Rosnati[2] reported m.p. 201–202° for his compound. The infrared spectrum shows absorption characteristic of the amide structure[5] with bands at 5.9 μ (C=O) and at 2.9, 3.2, and 3.5–3.7 μ (N—H). Acetylation and recrystallization from absolute ethanol afforded the monoacetate in 90% yield, m.p. 134–135°. Rosnati[2] reported m.p. 134–135° for his monoacetate derivative.

Reaction of 3,4,4′-Trichlorocarbanilide (Ib)[3] with Three Moles of Hypochlorite.—Treatment of the trichlorocarbanilide as described above provided 1-(3,4-dichlorophenyl)-6-chloro-2-benzimidazolinone (IIc) in 39% yield, m.p. 259–260°. Mixture melting point with 3,4,4′-trichlorocarbanilide (m.p. 254–256°) showed 219–228°.

Anal. Calcd. for $C_{13}H_7Cl_3N_2O$: C, 49.8; H, 2.25; Cl, 33.9; N, 8.93. Found: C, 50.0; H, 2.32; Cl, 34.1; N, 9.12.

Acetylation of IIc as described previously provided the monoacetate in 65% yield, m.p. 164–165°.

Anal. Calcd. for $C_{15}H_9Cl_3N_2O_2$: C, 50.6; H, 2.55; Cl, 29.9; N, 7.87. Found: C, 50.6; H, 2.62; Cl, 29.9; N, 8.00.

Reaction of 3,4-Dichlorocarbanilide (Ic)[3] with Three Moles of Hypochlorite.—Treatment of the dichlorocarbanilide as previously described, provided IIc in 13.7% yield. The sample was demonstrated as identical with the product obtained by cyclization of 3,4,4′-trichlorocarbanilide by m.p., mixture m.p., mp. and mixture m.p. of the monoacetate derivatives, and comparison of infrared spectra of the monoacetates, which were superimposeable.

Reaction of 3,3′,4,4′-Tetrachlorocarbanilide (Id),[3] 1-Ethyl-1-(4-chlorophenyl)-3-(3,4-dichlorophenyl)urea (Ie),[3] and 1-Methyl-1-(3,4-dichlorophenyl)-3-(4-chlorophenyl)urea (If) with Three Moles of Hypochlorite.—The N-methylated urea (If) was prepared by a standard reaction[3] of N-methyl-3,4-dichloroaniline with *p*-chlorophenyl isocyanate in ether to give the product, m.p. 159–160°.

Anal. Calcd. for $C_{14}H_{11}Cl_3N_2O$: C, 51.0; H, 3.36. Found: C, 51.0; H, 3.57.

The tetrachlorocarbanilide (Id), when treated as described earlier, was recovered unchanged in a yield of 75%. The N-alkylated ureas, treated similarly, were recovered unchanged in yields of 80% (Ie) and 86% (If) from the reaction mixtures.

Acknowledgment.—The authors gratefully acknowledge the assistance of Mr. O. E. Kinast in the infrared determinations.

---

[11] J. T. Arnold and M. E. Packard, *J. Chem. Phys.*, **19**, 1608 (1951).

The Reaction of N,N-Bis(2-chloroethyl)amines with Hydrazine[1]

FRANK D. POPP[2]

Departments of Chemistry, University of Miami,
Coral Gables, Florida, and Clarkson College of Technology
Potsdam, New York

Received August 7, 1962

The reaction of a number of aromatic nitrogen mustards with hydrazine under mild conditions has been reported. For example, the reaction of *p*-[N,N-bis(2-chloroethyl)amino]benzaldehyde with hydrazine in ethanol gave the azine,[3] and the reaction of *p*-[N,N-bis(2-chloroethyl)amino]benzoyl chloride with hydrazine in dioxane–water gave the hydrazide.[4] In neither case did the mustard function react with the hydrazine. As indicated[4] his failure is noteworthy and it is also somewhat surprising in view of the ease in which certain bis(2-haloethyl)amines react with amines.[5]

We have now found that certain aromatic nitrogen mustards do react with hydrazine, *but under much more severe conditions*, to give 1-aminopiperazines. Thus refluxing ethyl *p*-[N,N-bis(2-chloroethyl)amino]benzoate in a large excess of 95% hydrazine gave the aminopiperazine hydrazide I. That the reaction led to an aminopiperazine and not a diazepine or bishydrazine

---

[1] Supported in part by a research grant (CY 4814C2) from the National Institutes of Health.

[2] Present address: Department of Chemistry, Clarkson College of Technology, Potsdam, N.Y.

[3] R. H. Wiley and G. Irick, *J. Org. Chem.*, **26**, 593 (1961).

[4] R. C. Elderfield and T.-K. Liao, *ibid.*, **26**, 4996 (1961).

[5] See for example: W. Davis and W. C. J. Ross, *J. Chem. Soc.*, 2831 (1949).