solution was cooled and the precipitated solid was collected by filtration. The methiodide (81.3 g, 99%) was recrystallized from aqueous ethanol to give pure white crystals, mp 305–307°.

*Anal.* Calcd for $C_9H_{16}INO$: C, 38.45; H, 5.74; N, 4.98. Found: C, 38.64; H, 5.83; N, 5.16.

**5-Dimethylamino-7-oxa-1,3-cyclooctadiene (7).**—A solution of 18.0 g (0.064 mole) of **6** in water was eluted through a column of Amberlite IRA-400 in its basic form. The alkaline eluate was evaporated *in vacuo* below 45°. The residual quaternary methohydroxide was decomposed by heating at 45–50° under a nitrogen atmosphere at 6 mm for 2 hr. The liquid which formed was taken up in ether, dried over anhydrous magnesium sulfate, and evaporated to give 7.2 g (73.2%) of yellow liquid, $\lambda_{max}^{EtOH}$ 227 mμ (ε 5330). Because this material could not be distilled without rearrangement,[18] it was hydrogenated without further purification.

**3-Dimethylaminooxocane (8).**—A solution of 400 mg (2.6 mmoles) of **7** in 40 ml of ethyl acetate was hydrogenated at atmospheric pressure in ethyl acetate solution over Adams catalyst. Hydrogen uptake ceased after the uptake of 2 moles. The solution was filtered and evaporated and the residual liquid was distilled to give **8** as a colorless liquid, bp 97–98° (16 mm), $n^{25}D$ 1.4653. The corresponding methiodide was prepared in the usual manner and was obtained as white crystals from ethanol–ether: mp 147–148°.

*Anal.* Calcd for $C_{10}H_{22}INO$: C, 40.14; H, 7.41; N, 4.68. Found: C, 40.19; H, 7.18; N, 4.55.

**3,4,5,6-Tetrahydro-2H-oxocin (9).**—An aqueous solution of 15.0 g (0.050 mole) of the above methiodide was eluted through a column of Amberlite IRA-400 in its basic form. The alkaline eluate was concentrated under reduced pressure and the residue was distilled (with elimination beginning at *ca.* 150°) to give 1.87 g (33.4%) of **9** as a colorless liquid: bp 75–80° (15 mm); $n^{25}D$ 1.4612; $\nu_{max}^{CCl_4}$ 1650 cm$^{-1}$ (vinyl ether); $\lambda_{max}^{EtOH}$ end absorption; $\delta_{TMS}^{CCl_4}$ 1.70 (broad absorption, 6 H, H-3,4,5), *ca.* 2.16 (multiplet, 2 H, H-6), *ca.* 3.80 (multiplet, 2 H, H-2), *ca.* 4.88 (multiplet, 1 H, H-7), and 6.00 (doublet of doublets, $J$ = 6 and 1 cps, 1 H, H-8). A sample purified by preparative gas chromatography (10 ft × 0.25 in. stainless steel column packed with 15% Carbowax 20 M on Chromosorb W, 60–80 mesh) at 118° and microredistillation was submitted for analysis.

*Anal.* Calcd for $C_7H_{12}O$: C, 74.95; H, 10.78. Found: C, 75.03; H, 10.76.

**Oxocane (11). A. Catalytic Hydrogenation of 9.**—A solution of 850 mg (7.6 mmoles) of **9** in 100 ml of anhydrous ether was hydrogenated at atmospheric pressure over Adams catalyst. Hydrogen (1 mole equiv) was absorbed. The solution was filtered and the ether was carefully removed. The remaining liquid was purified by preparative gas chromatography (same column as used for **9**) and microredistillation to give 380 mg (44%) of oxocane: $n^{25}D$ 1.4486; $\delta_{TMS}^{CCl_4}$ 1.62 (broad absorption, 10 H, methylene protons) and 3.56 (broad absorption, 4 H, $-CH_2OCH_2-$).

*Anal.* Calcd for $C_7H_{14}O$: C, 73.63; H, 12.36. Found: C, 73.43; H, 12.29.

**B. Catalytic Hydrogenation of 10.**—The methiodide **10** was prepared in the usual manner. From 6.0 g (0.039 mole) of **7**, there was obtained 9.8 g (90.5%) of **10**, mp 170–171°, $\lambda_{max}^{EtOH}$ 220 mμ (ε 17,100).

*Anal.* Calcd for $C_{10}H_{18}INO$: C, 40.69; H, 6.15. Found: C, 40.38; H, 6.45.

A solution of 885 mg (3.0 mmoles) of **10** in 30 ml of methanol was hydrogenated at atmospheric pressure over Adams catalyst. Hydrogen (~3 mole equiv) was absorbed. The solution was filtered and the methanol was carefully evaporated under reduced pressure. Ether was added to the residual oil and 330 mg of trimethylammonium iodide, mp 262–263°, was precipitated. The filtrate was evaporated to give 150 mg of oxocane (**11**) which proved to display an infrared spectrum and vpc retention times identical with those derived from the sample of part A.

**Low-Temperature Nmr Spectra.**—These spectra were recorded at Northwestern University with a Varian HR-60 instrument equipped with a low-temperature probe. The oxocane spectra were obtained on approximately 10% solutions of **11** in vinyl chloride with TMS as the internal standard.

**Registry No.**—**4**, 13145-99-8; **5**, 13146-00-4; hydrochloride salt of **5**, 13146-01-5; **6**, 13146-02-6; **7**, 13146-03-7; **8**, 13146-04-8; **9**, 13146-05-9; **11**, 6572-98-1; methiodide of **8**, 13146-17-1.

(18) This rearrangement will be described in full in a subsequent paper.

# The Chlorination of Conjugated Dienamides. A New Application of the Principle of Least Motion[1,2]

LEO A. PAQUETTE[3] AND WILLIAM C. FARLEY[4]

*Department of Chemistry, The Ohio State University, Columbus, Ohio 43210*

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The monochlorination of some 1,3-dihydro-2H-azepin-2-ones with several reagents, *e.g.*, N-chlorosuccinimide, *t*-butyl hypochlorite, chloramine, and chlorine, is described. Chemical and spectroscopic methods reveal the site of chlorination in these cyclic dienamides to be $C_4$ or $C_6$ depending upon the substitution at N, $C_3$, or $C_7$. For example, whereas 1,3-dihydro-3,7-dimethyl-2H-azepin-2-one, 1,3-dihydro-3-*t*-butyl-7-methyl-2H-azepin-2-one, and 1,3-dihydro-1,3,7-trimethyl-2H-azepin-2-one afford exclusively the corresponding 6-chloro derivatives, 1,3-dihydro-3,5,7-trimethyl-2H-azepin-2-one leads, upon chlorination, to the 4-chloro derivative as the major product (58% yield) in combination with a lesser quantity (6%) of the 6-chloro isomer. Two related dienamides, 2-pyridone and N-methyl-2-pyridone, yield the 5-chloro pyridones in good yield. A theoretical interpretation of the observed results on the basis of the principle of least motion is advanced.

In previous publications,[5] we have described the remarkable ring enlargement which is obtained upon the addition of cold ethereal chloramine to solutions of sodio 2,6-dialkylphenoxides in molten 2,6-dialkylphenols at 125–150°. Apart from the unusual nature of the ring expansion, the 1,3-dihydro-2H-azepin-2-ones which result are interesting in their own right because they embody the conjugated dienamide chromophore, >C=CC=CNC=O, an infrequently encountered and little-studied functionality. In this paper we describe the results of studies performed with the intent of investigating the mode of reaction of the conjugated dienamide unit toward chlorinating agents.

## Results

To this end, treatment of 1,3-dihydro-3,7-dimethyl-2H-azepin-2-one (**1**) with a dilute solution of chlorine in carbon tetrachloride for 16 hr at 25° resulted in tar

(1) Unsaturated Heterocyclic Systems. XXIX. For XXVIII of this series, refer to L. A. Paquette and M. Rosen, *J. Am. Chem. Soc.*, **89**, 4102 (1967).

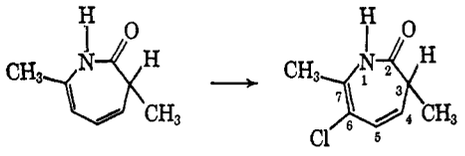
(2) Support of this work by the National Science Foundation, Grant GP-2939, is gratefully acknowledged.

(3) Alfred P. Sloan Foundation Research Fellow.

(4) Sinclair Oil Fellow, 1965–1966; Esso Summer Fellow, 1964.

(5) (a) L. A. Paquette, *J. Am. Chem. Soc.*, **85**, 3288 (1963); (b) *ibid.*, **84**, 4987 (1962); (c) L. A. Paquette and W. C. Farley, *ibid.*, **89**, 3595 (1967).

formation. In contrast, however, exposure of **1** to 1 equiv of N-chlorosuccinimide in refluxing methylene chloride solution resulted in the formation of a monochlorinated derivative in near-quantitative yield. In



**1** **2**

parallel experiments, **1** was likewise subjected to the action of *t*-butyl hypochlorite and chloramine; monochlorination was again observed but in much less satisfactory yield (see Table I).

TABLE I

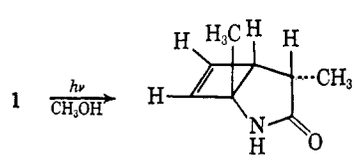
CHLORINATION OF 1,3-DIHYDRO-3,7-DIMETHYL-2H-AZEPIN-2-ONE (1)

| Chlorinating agent | Solvent | Conditions | Product (%) |
|---|---|---|---|
| N-Chlorosuccinimide | $CH_2Cl_2$ | Reflux, 24 hr | **2** (97)[a] |
| *t*-Butyl hypochlorite | $CCl_4$ | Reflux, 24 hr | **2** (27)[a] |
| Chloramine | Cumene | Temp maintained at 120–130° during addition of ethereal $NH_2Cl$ | **2** (3)[a] |
| Chlorine | $CCl_4$ | 25°, 16 hr | Tar formation |

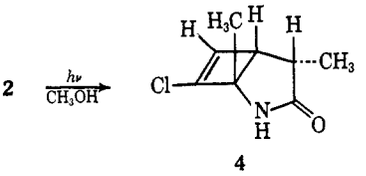
[a] The only other major component observed upon gas chromatography of the crude reaction product was unreacted **1**.

In agreement with structure **2**, this monochloro derivative exhibited infrared peaks (in $CCl_4$) at 3450 and 1675 $cm^{-1}$ and ultraviolet absorption (in EtOH) at 257 m$\mu$ ($\epsilon$ 5100). The nmr spectrum of **2** was compatible with the proposed formulation; a low-field doublet ($J$ = 10 cps) at $\delta$ 6.05 was assigned to the vinyl proton at $C_5$ and a doublet of doublets ($J$ = 10 and 6 cps) centered at 5.18 to the $C_4$ vinyl hydrogen. A complex multiplet at 2.50 was attributed to the proton at $C_3$, the pattern suggesting splitting with an adjacent methyl group and proton. In addition, the absorption peaks of the two methyl groups were located at 2.15 (singlet, 7-$CH_3$) and 1.36 (doublet, $J$ = 7 cps, 3-$CH_3$).

Conclusive proof for this structural assignment was derived from an examination of the photoisomerization of **1** and **2**. Thus, irradiation of these dihydroazepi-



**3**



**4**

nones in methanol solution with an unfiltered 200-w Hanovia lamp for 48 hr at room temperature gave the

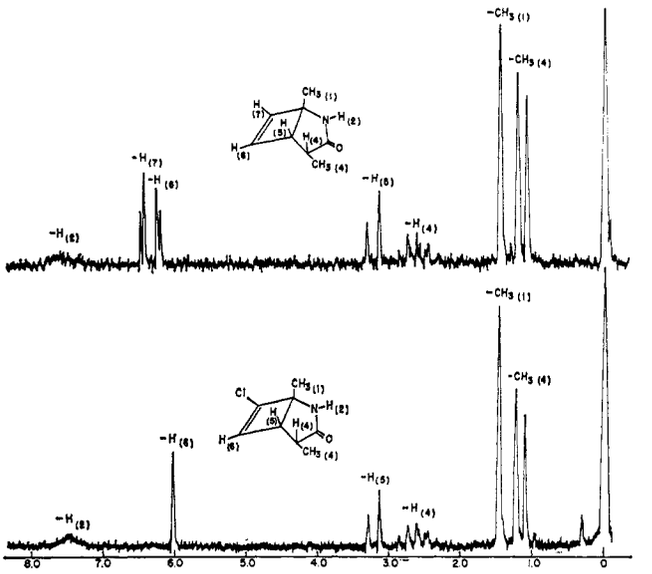
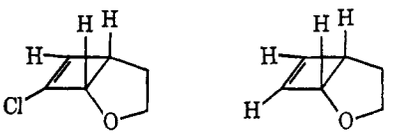


Figure 1.—Nmr spectra of compounds **3** (top) and **4** (bottom).

expected[6] 2-azabicyclo[3.2.0]hept-6-enes **3** and **4**, respectively. Of particular relevance to the argument at issue are the nmr spectra of **3** and **4** which are illustrated in Figure 1. Initially, it will be observed that the spectrum of **4** displays but a lone vinyl proton signal thereby indicating that the chlorine substituent in **2** must be affixed to either $C_5$ or $C_6$. Inherently more significant, however, is the fact that this sole vinyl proton in **4** resonates at slightly higher field than the analogous proton in **3**. In the present instance, this phenomenon is uniquely attributable to the anisotropy effect of the neighboring carbon–chlorine bond. Paquette and co-workers[7] have previously calculated the magnitude of the chlorine neighbor-anisotropy effect in chlorocyclobutene **5** to be $\delta$ −0.13 relative to the same proton in its nonchlorinated counterpart (**6**).



**5** **6**

The correspondence between the calculated and observed ($\delta$ −0.14) chemical shift differences was found to be excellent. Since the anisotropy effect of the carbon–chlorine bond is a function of the internal C–H and C–Cl bond angles[8] and because the geometry of the $CH_2$=CHCl part structures of **4** and **5** is expected to be virtually identical, the values of $R$ (distance from the vinyl cyclobutene proton to the center of the C–Cl bond) and $\gamma$ (the internal angle made by this line) should be the same for both systems.[7] In other words

$$\frac{\Delta\sigma_{2,3\text{-Cl}_2\text{-1-propene}}}{\Delta\sigma_4} = \frac{(2.92)^3(+0.427)}{(2.32)^3(-0.245)} = -3.51$$

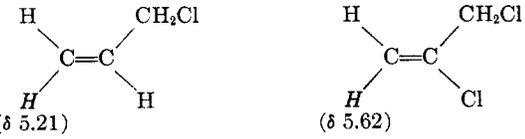
In the present situation, however, **4** proved to be insoluble in carbon tetrachloride (the previously em-

(6) L. A. Paquette, *J. Am. Chem. Soc.*, **86**, 500 (1964); O. L. Chapman and E. D. Hoganson, *ibid.*, **86**, 498 (1964).

(7) L. A. Paquette, J. H. Barrett, R. P. Spitz, and R. Pitcher, *ibid.*, **87**, 3417 (1965).

(8) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High-Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, pp 176–179.

ployed[7] standard solvent), thereby requiring recalibration in deuteriochloroform. The chemical shifts of the appropriate vinyl protons of allyl chloride and 2,3-dichloro-1-propene in this medium (illustrated below)




indicate that the $\Delta\sigma$ for the acyclic case equals 0.41. Therefore

$$\Delta\sigma_4 = \frac{-0.41}{3.51} = \delta\ -0.117 \text{ (calcd)}$$

$$\Delta\sigma_4 \text{ (obsd)} = \delta\ -0.16$$

It is obvious that the observed shift difference in this example is again in very good agreement with theory. The above considerations, in conjunction with the singlet vinyl proton signal,[9,15] can only be reconciled with structure **4** (and therefore also structure **2**) Of added importance, this result further indicates the validity of the cos² approximation in the prediction of chemical shifts.[7]

Dihydroazepinone **7** was similarly subjected to the action of various chlorinating agents (see Table II).

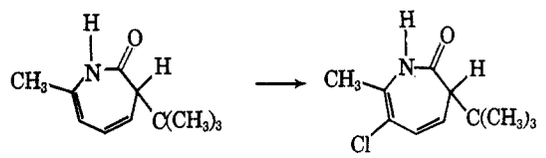
TABLE II

CHLORINATION OF 1,3-DIHYDRO-3-*t*-BUTYL-7-METHYL-2H-AZEPIN-2-ONE (**7**)

| Chlorinating agent | Solvent | Conditions | Product (%) |
|---|---|---|---|
| N-Chloro-succinimide | $CH_2Cl_2$ | Reflux, 24 hr | **8** (88)[a] |
| *t*-Butyl hypochlorite | $CCl_4$ | Reflux, 24 hr | **8** (39)[a] |
| Chloramine | Cumene | Temp maintained at 120–130° during addition of ethereal $NH_2Cl$ | **8** (7)[a] |
| Chlorine | $CCl_4$ | 25°, 16 hr | **8** (3)[b] |

[a] The only other major component observed upon gas chromatography of the crude product was unreacted **7**. [b] In addition to much tar formation, there was present approximately 5% of an unknown substance.

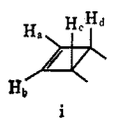
In this particular example, direct chlorination with elemental chlorine did afford a monochloro derivative in low yield, although tar formation was still prevalent.




**7** **8**

The substitution pattern in the halogenated product (**8**) was shown to be identical with that in **2** on the basis of its spectral properties (*cf.* Experimental Section).

(9) It has recently been demonstrated in a number of examples that in bent bicyclic structures such as i there is little obvious coupling between

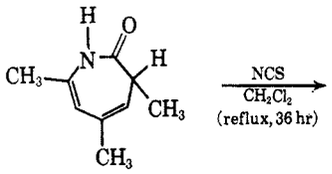



i

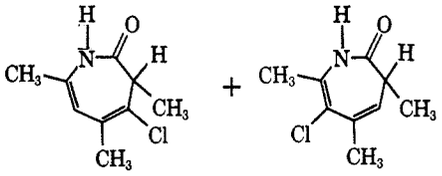
$H_a$–$H_d$ and $H_b$–$H_c$, presumably because the dihedral angles involved approximate 90°.[6,7,10] In contrast, allylic coupling of the $H_a$–$H_c$ and $H_b$–$H_d$ variety is easily detectable under normal operating conditions ($J$ = 1.5–2.8 cps).

(10) L. A. Paquette and J. H. Barrett, *J. Am. Chem. Soc.*, **88**, 1718 (1966).

With 1,3-dihydro-3,5,7-trimethyl-2H-azepin-2-one (**9**), however, reaction with N-chlorosuccimide in refluxing methylene chloride solution proceeded more slowly and afforded the 4-chloro derivative (**10**) as the major product (58% yield); the 6-chloro derivative



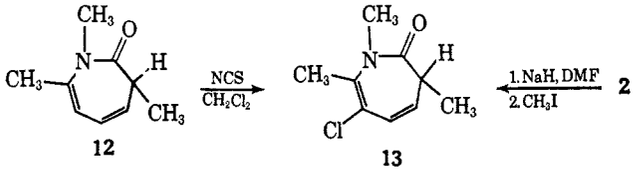

**9**




**10** **11**

(**11**) was formed to the extent of only 6%. Careful scrutiny of the progress of the reaction by vapor phase chromatography (vpc) of small aliquots demonstrated that **10** was formed directly from **9** and was not resulting from an unprecedented rearrangement of **11**. The infrared, ultraviolet, and nmr evidence (*cf.* Experimental Section) was in agreement with the assigned structures of **10** and **11**.

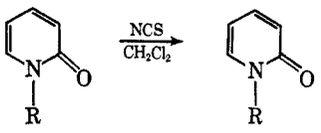
It was deemed important to evaluate the propensity of an N-substituted conjugated dienamide toward substitution and 1,3-dihydro-1,3,7-trimethyl-2H-azepin-2-one (**12**) was selected for this purpose. Thus, treating **12** with N-chlorosuccinimide under conditions identical with those employed earlier for **1** and again following the course of the reaction by vpc resulted in the interesting, and undoubtedly significant, observation that the rate of chlorination in this instance was much slower than in the case of **1**. However, the




**12** **13**

ability of the dienamide system to direct substitution to position 6 was not lost because of alkyl substitution on nitrogen. The chlorinated dihydroazepinones were chemically interrelated by means of the standard[5c] amide methylation procedure.

During the course of this work we have also observed that 2-pyridone reacts readily with N-chlorosuccinimide




**14a**, R = H
**b**, R = $CH_3$

to give 5-chloro-2-pyridone (**14a**) in high yield. None of the 3 isomer could be detected by nmr analysis.[11]

(11) This conclusion was reached after comparison with the nmr spectrum of an authentic sample of 3-chloro-2-pyridone generously provided by Professor M. P. Cava.

This result lies in direct contrast to reports that the halogenation of 2-pyridone is difficult to control and results in the production of 3,5-dihalogeno-2-pyridones.[12,13] Also, as in the case of **12**, chlorination of N-methyl-2-pyridone did not proceed so rapidly as with the parent heterocycle.

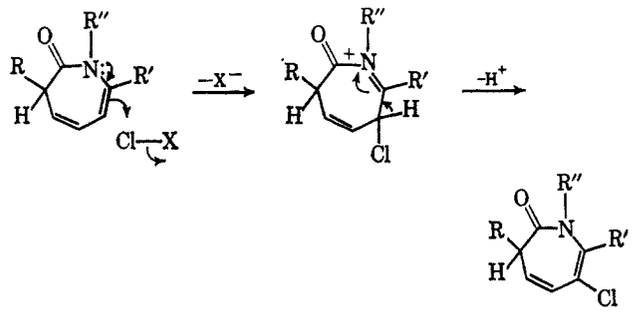
## Discussion

The mechanistic import of the directive effects observed in these chlorination reactions need now be considered. *A priori* at least, more than one mechanistic rationale can be envisioned.

First, one can entertain the possibility that the halogenation is free radical in nature. However, the available evidence strongly suggests that radicals are not involved. For example, if such conditions were operative it is quite likely that substantial chlorination of the allylic methyl groups could be expected and this phenomenon was not observed. Furthermore, no evidence of radicals could be detected when the progress of the chlorination was followed by esr spectroscopy. In addition, chloramine has been found not to undergo homolytic cleavage in cumene at 150°.[5a] An attempt to brominate 1-methyl-2-pyridone with N-bromosuccinimide in the presence of benzoyl peroxide has been reported to give no product.[14]

Second, it is possible in the case of the secondary lactams that the products of kinetic control are the N-chlorolactams, which intermediates would be capable of facile rearrangement to the observed products. The initial step of this reaction pathway would be analogous to the formation of other N-chloramides, although under somewhat differing conditions, reported by a number of investigators.[15] Presumably, the requisite rearrangement would derive from N–Cl bond heterolysis to give chloronium ion and the conjugate base of the dienamide, to be followed by electrophilic attack and prototropic shift. Alternatively, the chlorination could be proceeding by direct formation of the conjugate base (in the case of secondary amides) which is subsequently attacked by the concomitantly generated chloronium ion. If either of these mechanistic pathways were operative, then this would require that the tertiary N-alkyl dienamides react by an alternative route which must eventuate in an identical substitution pattern. In connection with this mechanism, it is cogent to question the degree of steric inhibition which can be reasonably expected to affect the relatively nonbulky chloronium ion to an extent sufficient to disfavor almost totally normal $C_6$ substitution in **9**. This point will be discussed in more detail below.

Last, a direct electrophilic substitution upon the unsaturated dienamide system by the route outlined below may very likely be the preferred pathway. In other words, this last proposal states that the action of weak electrophiles upon the dienamide group leads to kinetically controlled product by electrophilic attack



at the central position of this conjugated system. Appropriately, the capability of N-chlorosuccinimide,[16] *t*-butyl hypochlorite,[17] and chloramines[18,19] to function as electrophilic agents has been documented in a number of instances. Although the available evidence does not completely rule out the intervention of the first three mechanistic alternatives, the direct electrophilic chlorination pathway is presently in best agreement with all of the accumulated data. For example, the relatively large N-chlorosuccinimide molecule would be expected to find the 6 position in **9** quite inaccessible because of the two flanking methyl groups which are both bonded to trigonally hybridized carbon atoms. In this case, the rate of attack at this site would be greatly retarded and the kinetically favored process becomes attack at $C_4$. It is to be noted that this position is less hindered than $C_6$ because one of the neighboring methyl groups is bonded to an $sp^3$ hybridized carbon and this substituent has been found to prefer the quasiequatorial conformation.[20]

The corresponding slower rates of chlorination of the N-methyl derivatives are also explicable in terms of this mechanism. Thus, the result of introducing a methyl substituent onto the amide nitrogen is effectively to twist the $-N(CH_3)CO-$ linkage from its normally planar configuration because of the newly generated steric interference between N-methyl and carbonyl oxygen. In the approach to the transition state leading to chlorination, however, the generation of the immonium intermediate demands that the methyl substituent and the carbonyl oxygen regain the coplanar arrangement. The resulting steric compression can be expected to raise the energy of activation of such chlorination reactions relative to the unsubstituted counterparts. Because of the greater flexibility of the seven-membered ring, this effect would be expected to be larger in the dihydroazepinones than in the 2-pyridones as observed. Several examples of the dramatic effect of N-methyl substitution in cyclic

(12) H. Meislich in "Pyridine and Its Derivatives," Part 3, E. Klingsberg, Ed., Interscience Publishers, Inc., New York, N. Y., 1961, pp 509–896.

(13) R. A. Abramovitch and J. G. Saha, *Advan. Heterocyclic Chem.*, **6**, 229 (1966).

(14) D. J. Cook, R. E. Bowen, P. Sorter, and E. Daniels, *J. Org. Chem.*, **26**, 4949 (1961).

(15) See, for example, H. W. Baumgarten, R. L. Zey, and V. Krolls, *J. Am. Chem. Soc.*, **83**, 4469 (1961); H. Zimmer and L. F. Audrieth, *ibid.*, **76**, 3856 (1954).

(16) Consult, for example, (a) F. L. Lambert, W. D. Ellis, and R. J. Parry, *J. Org. Chem.*, **30**, 304 (1965); (b) A. G. Anderson and L. R. Replogle, *ibid.*, **28**, 2578 (1963).

(17) Refer, for example, to (a) D. Ginsburg, *J. Am. Chem. Soc.*, **73**, 2723 (1951); (b) M. Anbar and D. Ginsburg, *Chem. Rev.*, **54**, 925 (1954); (c) E. Tobler, D. E. Battin, and D. J. Foster, *J. Org. Chem.*, **29**, 2834 (1964); (d) C. R. Johnson, C. J. Cheer, and D. J. Goldsmith, *ibid.*, **29**, 3320 (1964).

(18) (a) R. S. Neale and R. L. Hinman, *J. Am. Chem. Soc.*, **85**, 2666 (1963); (b) R. S. Neale, *ibid.*, **86**, 5340 (1964); (c) R. S. Neale, *Tetrahedron Letters*, 483 (1966).

(19) Aromatic halogenation by N-halo compounds has ample precedent: (a) G. H. Coleman and W. A. Noyes, *J. Am. Chem. Soc.*, **43**, 2211 (1921); (b) N. Stoll, *Bull. Soc. Chim. Belges*, **38**, 71 (1929); *Chem. Abstr.*, **23**, 4456 (1929); (c) T. W. J. Taylor and W. Baker in "The Organic Chemistry of Nitrogen," Sidgwick, Ed., Clarendon Press, Oxford, 1937, p 67; (d) L. O. Brown and F. G. Soper, *J. Chem. Soc.*, 3576 (1953); (e) M. D. Carr and B. D. England, *Proc. Chem. Soc.*, 350 (1958); P. Haberfield and D. Paul, *J. Am. Chem. Soc.*, **87**, 5502 (1965).

(20) L. A. Paquette, *ibid.*, **86**, 4096 (1964).

amides on the reactivity of such molecules have been documented.[21a] In addition to steric inhibition of resonance, the lower reactivity of the N-methyl compounds may possibly be attributed in part to the anticipated less effective hyperconjugative capability of the N-methyl group when compared to the N–H function.[21b]

Of considerable interest is the fact that the position of chlorination of the dienamides is predictable on the basis of the principle of least motion.[22] This principle states that "those elementary reactions will be favored that involve the least change in atomic position and electronic configuration." From a qualitative point of view, the energy needed to effect internal geometric changes has been shown to be approximately proportional to the sum of the squares of the changes in bond numbers.[22] In the case of the dienamide system, contributing structures of unequal weight are involved; as before, however, the greater (or lesser) importance of these structures can be recognized by assigning a value of $n$ (larger or smaller than 1) to such entities; this innovation does not disrupt the qualitative application of the principle. Calculation of the geometric changes involved in electrophilic chlorination at the three possible sites of a typical dienamide (see Table III) shows that reaction at the central atom of the dienamide system should be favored. Although the results in section B of Table III indicate that N-chloroamides may form in the case of the secondary lactams, such are not isolated because of the strong product stability disadvantage which they possess.

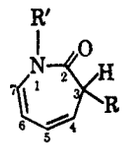
The calculations in section A of Table III also apply to conjugated dienamines; therefore, kinetically controlled protonation of such systems with weak acids is predicted to result in proton attack at the central position of the dienamine. This conclusion has been verified by a number of research groups.[23–25] The preference of **9** to undergo chlorination at $C_4$ and the failure of 1,3-disubstituted 1,6-dihydropyridines to undergo further borohydride reduction[26] are both explainable on the basis of the operation of steric effects which inhibit attack of the electrophile at the center of the conjugated system.

## Experimental Section[27]

**6-Chloro-1,3-dihydro-3,7-dimethyl-2H-azepin-2-one (2). A. N-Chlorosuccinimide.**—A solution of 13.6 g (0.10 mole) of 1,3-dihydro-3,7-dimethyl-2H-azepin-2-one (1)[5] and 14.7 g (0.11 mole) of N-chlorosuccinimide in 150 ml of methylene chloride

TABLE III

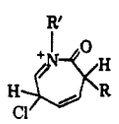
APPLICATION OF THE PRINCIPLE OF LEAST MOTION TO THE 1,3-DIHYDRO-2H-AZEPIN-2-ONE NUCLEUS



A. Dienamide Considered as Resonance Hybrid

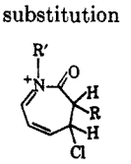
Bond numbers in starting material: $C_4$–$C_5$: $\frac{2n+3}{n+2}$; $C_5$–$C_6$: $\frac{n+3}{n+2}$; $C_6$–$C_7$: $\frac{2n+2}{n+2}$; $C_7$–N: $\frac{n+4}{n+2}$

6 substitution



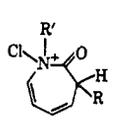
$$\left(\frac{2n+3}{n+2}-2\right)^2+\left(\frac{n+3}{n+2}-1\right)^2+\left(\frac{2n+2}{n+2}-1\right)^2+\left(\frac{n+4}{n+2}-2\right)^2=\frac{2n^2+2}{(n+2)^2}$$

4 substitution



$$\left(\frac{2n+3}{n+2}-1\right)^2+\left(\frac{n+3}{n+2}-2\right)^2+\left(\frac{2n+2}{n+2}-1\right)^2+\left(\frac{n+4}{n+2}-1\right)^2=\frac{4n^2+4n+2}{(n+2)^2}$$

1 substitution



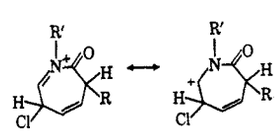
$$\left(\frac{2n+3}{n+2}-2\right)^2+\left(\frac{n+3}{n+2}-1\right)^2+\left(\frac{2n+2}{n+2}-2\right)^2+\left(\frac{n+4}{n+2}-1\right)^2=\frac{10}{(n+2)^2}$$

| $n$ | Position of substitution: 6 | 4 | 1 |
|---|---|---|---|
| $^1/_2$ | 2.5 | 5 | 10 |
| | $^{25}/_4$ | $^{25}/_4$ | $^{25}/_4$ |
| 1 | $^4/_{16}$ | $^{10}/_{16}$ | $^{10}/_{16}$ |
| 2 | $^{10}/_{16}$ | $^{26}/_{16}$ | $^{10}/_{16}$ |

B. Reaction Intermediates Considered as Resonance Hybrids

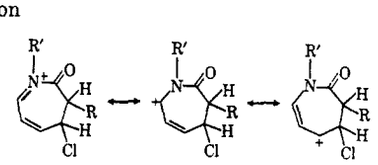
Bond numbers in starting material: $C_4$–$C_5$: 2; $C_5$–$C_6$: 1; $C_6$–$C_7$: 2; $C_7$–N: 1

6 substitution



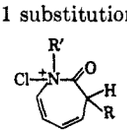
$$\left(1-\frac{2n+1}{n+1}\right)^2+\left(2-\frac{n+1}{n+1}\right)^2=\frac{n^2}{(n+1)^2}+1$$

4 substitution



$$\left(1-\frac{2n+2}{n+2}\right)^2+\left(2-\frac{n+3}{n+2}\right)^2+\left(1-\frac{2n+3}{n+2}\right)^2+\left(2-\frac{n+2}{n+2}\right)^2=\frac{3n^2+4n+2}{(n+2)^2}+1$$

1 substitution



No geometric changes

| $n$ | Position of substitution: 6 | 4 | 1 |
|---|---|---|---|
| $^1/_2$ | $^{10}/_9$ | $^{44}/_{25}$ | 0 |
| 1 | $^5/_4$ | 2 | 0 |
| 2 | $^{13}/_9$ | $^{19}/_8$ | 0 |

(21) (a) L. A. Paquette and L. D. Wise, *J. Am. Chem. Soc.*, **87**, 1561 (1965). (b) P. B. D. de la Mare, *Tetrahedron*, **5**, 107 (1959); P. B. D. de la Mare, O. M. H. el Dusouqui, J. G. Tillett, and M. Zeltner, *J. Chem. Soc.*, 5306 (1964).

(22) J. Hine, *J. Org. Chem.*, **31**, 1236 (1966).

(23) P. S. Anderson and R. E. Lyle, *Tetrahedron Letters*, 153 (1964); R. E. Lyle, D. A. Nelson, and P. S. Anderson, *ibid.*, 553 (1962).

(24) J. A. Marshall and W. S. Johnson, *J. Org. Chem.*, **28**, 421 (1963); W. S. Johnson, V. J. Bauer, and R. W. Franck, *Tetrahedron Letters*, 72 (1962).

(25) G. Opitz and W. Merz, *Ann. Chem.*, **652**, 139, 158, 163 (1962).

(26) K. Schenker and J. Druey, *Helv. Chim. Acta*, **42**, 1960 (1959); N. Kinoshita, M. Hamana, and T. Kawasaki, *Chem. Pharm. Bull.* (Tokyo), **10**, 753 (1962).

(27) Melting points and boiling points are uncorrected. The microanalyses were determined by the Scandinavian Microanalytical Laboratory, Herlev, Denmark, and the Galbraith Laboratories, Inc., Knoxville, Tenn. The infrared spectra were obtained with a Perkin-Elmer Model 237 Infracord spectrometer fitted with sodium chloride prisms. Ultraviolet measurements were made with a Cary Model 14 recording spectrometer. The nmr spectra were determined with a Varian A-60 spectrometer purchased with funds made available from the National Science Foundation.

was refluxed for 24 hr. At the end of this time, the solvent was removed under reduced pressure. The residue was slurried in ether and filtered. The ether filtrate was washed with water, dried over magnesium sulfate, and concentrated. The residue was sublimed to give 16.5 g (97%) of white solid, mp 156–158°. Vpc analysis[28] of this sample (180°) indicated it to be pure **2**. Recrystallization of the sublimate from ligroin gave white crystals: mp 158–158.5°; $\nu_{max}^{CCl_4}$ 3450 (N–H) and 1675 cm$^{-1}$ (amide carbonyl); $\lambda_{max}^{EtOH}$ 257 mμ (ε 5100); $\delta_{max}^{CDCl_3}$ 1.36 (doublet, $J$ = 7 cps, 3 H, 3-methyl), 2.15 (singlet, 3 H, 7-methyl), 2.50 (multiplet, 1 H, $C_3$ proton), 5.18 (doublet of doublets, $J$ = 10 and 6 cps, 1 H, $C_4$ proton), and 6.05 (doublet, $J$ = 10 cps, 1 H, $C_5$ proton).

*Anal.* Calcd for $C_8H_{10}ClNO$: C, 55.86; H, 5.49; Cl, 20.66; N, 8.16. Found: C, 56.01; H, 5.94; Cl, 20.84; N, 8.20.

**B. *t*-Butyl Hypochlorite.**—A solution of 2.0 g (0.015 mole) of **1** and 1.85 g (0.017 mole) of *t*-butyl hypochlorite in 20 ml of carbon tetrachloride was refluxed for 24 hr. The solvent was removed under reduced pressure and the residue was sublimed at 120° (0.05 mm) to afford 1.12 g of crystalline solid. Vpc analysis of this material at 170° [28] indicated it to be composed of 52% of **2** and 48% of **1**; thus the yield of **2** was 27%. Preparative vpc of the mixture[28] gave pure **2** as a white solid, mp 158–158.5°, identical in all respects with the sample prepared in A.

**C. Chloramine.**—A stirred solution of 2.0 g (0.015 mole) of **1** in 15 ml of cumene was heated to reflux and a cold (−70°) ethereal solution of chloramine containing approximately 0.10 mole of active ingredient[29] was added in a thin stream at such a rate that the internal temperature did not fall below 120°. When the addition was completed, the solvent was removed under reduced pressure and the residue was sublimed at 100° (0.05 mm) to give 1.95 g of white solid. Vpc analysis at 170° [28] denoted the presence of 96% of **1** and 4% of **2**. The yield of **2** was therefore 3%.

**1,4-Dimethyl-2-azabicyclo[3.2.0]hept-6-en-3-one (3).**[30]—A solution of 8.0 g (0.06 mole) of **1** in 300 ml of anhydrous methanol was irradiated with a 200-w Hanovia mercury arc in Pyrex for 72 hr. The solution was concentrated *in vacuo* and the residue was chromatographed on Florisil. Elution with hexane–acetone (9:1) gave 2.3 g (29%) of recovered **1**, while elution with hexane–acetone (1:1) afforded 1.2 g (21% based on recovered **1**) of **3** after recrystallization from hexane–ether. Further recrystallization from this solvent and sublimation at 45° (0.2 mm) gave pure **3** as white crystals: mp 84.5–86°; $\nu_{max}^{CCl_4}$ 3180 (N–H) and 1680 cm$^{-1}$ (amide carbonyl).

*Anal.* Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.77; H, 8.17; N, 10.10.

**7-Chloro-1,4-dimethyl-2-azabicyclo[3.2.0]hept-6-en-3-one (4).**—A solution of 2.0 g (0.012 mole) of **2** in 300 ml of methanol was irradiated as above for 48 hr. Chromatography of the crude product on Florisil and elution with hexane–acetone (4:1) gave 0.84 g (42%) of a white solid, mp 136–139°. Recrystallization of this material from ligroin gave pure **4**: mp 139–140°; $\nu_{max}^{CCl_4}$ 3200 (N–H) and 1690 cm$^{-1}$ (amide carbonyl).

*Anal.* Calcd for $C_8H_{10}ClNO$: C, 55.86; H, 5.87; N, 8.16. Found: C, 56.02; H, 6.02; N, 7.85.

**3-*t*-Butyl-6-chloro-1,3-dihydro-7-methyl-2H-azepin-2-one (8). A. N-Chlorosuccinimide.**—A 2.0-g (0.011 mole) sample of **7**[5] was treated with 1.75 g (0.013 mole) of N-chlorosuccinimide in 25 ml of methylene chloride as described above. The isolated product (2.23 g) was found by vpc analysis at 180° [28] to consist of 92% of **8** and 8% of unreacted **7**. The yield of **8** was therefore 88%. Pure **8** was isolated by preparative vpc and was obtained as a white solid; mp 183.5–184° (from ethanol); $\nu_{max}^{CCl_4}$ 3200 (N–H) and 1675 cm$^{-1}$ (amide carbonyl); $\lambda_{max}^{EtOH}$ 257 mμ (ε 3400); $\delta_{TMS}^{CDCl_3}$ 1.15 (singlet, 9 H, $-C(CH_3)_3$), 2.05 (multiplet (partially hidden), 1 H, $C_3$ proton), 2.12 (singlet, 3 H, methyl group), 5.48 (doublet of doublets, $J$ = 10 and 6 cps, $C_4$ proton), and 6.16 (doublet, $J$ = 10 cps, 1 H, $C_5$ proton).

*Anal.* Calcd for $C_{11}H_{16}ClNO$: C, 61.81; H, 7.54; N, 6.55. Found: C, 61.61; H, 7.59; N, 6.41.

**B. *t*-Butyl Hypochlorite.**—A solution of 2.0 g (0.011 mole) of **7** and 1.3 g (0.012 mole) of *t*-butyl hypochlorite in 20 ml of carbon tetrachloride was treated as above. The isolated solid (1.12 g) was found by vpc[28] to consist of **8** and **7** in an 81:19 ratio. The yield of **8** was therefore 39%.

**C. Chloramine.**—A solution of 3.0 g (0.017 mole) of **7** in 15 ml of refluxing cumene was treated with a solution of approximately 0.10 mole of chloramine in cold ether as described above. The sublimate (3.0 g) was found by vpc[28] to contain 7% of **8** and 93% of unreacted **7**. The yield of **8** was thus 5%.

**D. Chlorine.**—A solution of 1.4 g (0.02 mole) of chlorine in 10 ml of carbon tetrachloride was added to a solution of 1.4 g (0.02 mole) of **7** in 20 ml of the same solvent. The reaction mixture was stirred overnight at room temperature. The solvent was removed under reduced pressure and the residue was chromatographed on Florisil. Elution with ether yielded 0.87 g of a light brown viscous oil, which was found by vpc[28] to contain 66% of **8** and 25% of an unknown substance which was not investigated further. The chloroazepinone (14%) was subjected to preparative vpc, mp 183–184°.

**Chlorination of 1,3-Dihydro-3,5,7-trimethyl-2H-azepin-2-one (9).**—A solution of 3.0 g (0.02 mole) of **9** and 2.94 g (0.022 mole) of N-chlorosuccinimide in 50 ml of methylene chloride was treated as above. The crude sublimate (3.65 g) was found to consist of 21% of unreacted **9**, 58% of the 4-chloro isomer (**10**), 6% of the 6-chloro isomer, and a total of 15% of three unidentified components. Pure **10** was obtained by chromatography on alumina (elution with hexane–ether (9:1)). After several recrystallizations from ethanol and ligroin, **10** was obtained as fluffy white needles: mp 174.5–175°; $\nu_{max}^{CCl_4}$ 3250 (N–H) and 1675 cm$^{-1}$ (amide carbonyl); $\lambda_{max}^{EtOH}$ 257 mμ (ε 7000); $\delta_{TMS}^{CDCl_3}$ 1.38 (doublet, $J$ = 7 cps, 3 H, $C_3$ methyl), 1.86 and 1.98 (singlets, 3 H each, other methyl groups), *ca.* 2.75 (multiplet, 1 H, $C_3$ proton), 5.52 (singlet, 1 H, $C_6$ proton).

*Anal.* Calcd for $C_9H_{12}ClNO$: C, 58.22; H, 6.52; N, 7.54. Found: C, 58.50; H, 6.64; N, 7.71.

The 6-chloro isomer (**11**) was isolated in approximately 90% purity by preparative vpc. After recrystallization from ethanol, slightly impure **11** was obtained as a fluffy white solid: mp 141–143°; $\nu_{max}^{CCl_4}$ 3250 (N–H) and 1675 cm$^{-1}$ (amide carbonyl); $\delta_{TMS}^{CDCl_3}$ 1.38 (doublet, $J$ = 7 cps, 3 H, $C_3$ methyl), 1.87 and 2.15 (singlets, 3 H each, other methyl groups), *ca.* 2.50 (multiplet, 1 H, $C_3$ proton), 5.08 (doublet, $J$ = 7 cps, 1 H, $C_4$ proton). Attempted isolation of the three remaining components led to oils which darkened rapidly upon exposure to air. Furthermore, these components appeared to be altered or decomposed in the course of the attempted vpc separation.

**6-Chloro-1,3-dihydro-1,3,7-trimethyl-2H-azepin-2-one. A. N-Chlorosuccinimide on 12.**—A solution of 0.75 g (5.0 mmoles) of **12**[5] and 0.8 g (6.0 mmoles) of N-chlorosuccinimide in 20 ml of methylene chloride was treated as above. The residual oil was submitted to molecular distillation and afforded 0.68 g of product. This material was shown by vpc[31] to consist of 26% of the 6-chloro derivative **13** and 74% of unreacted **12**. After isolation by preparative vpc, **13** was obtained as a colorless oil with spectral characteristics identical with those of an authentic sample prepared in the manner described below.

**B. Methylation of 2.**—To a solution of 1.0 g (6.0 mmoles) of **2** in 10 ml of dry dimethylformamide was added 300 mg (6.0 mmoles) of 51.5% sodium hydride–mineral oil dispersion. The mixture was heated at 50° for 1 hr with stirring, cooled, and treated with 1.7 g (0.012 mole) of methyl iodide. After stirring at room temperature for 1 hr, the mixture was treated with 50 ml of ether and the precipitated solid was separated by filtration. The filtrate was concentrated and the residue was molecular distilled to give 0.80 g (73%) of a pale yellow liquid. Purification of this material by preparative vpc[31] and redistillation afforded a colorless liquid: $\nu_{max}^{CCl_4}$ 1675 cm$^{-}$ (amide carbonyl); $\lambda_{max}^{EtOH}$ 258 mμ (ε 6150); $\delta_{TMS}^{CCl_4}$ 1.32 (doublet, $J$ = 7 cps, 3 H, $C_3$ methyl), 2.20 (singlet, 3 H, $C_7$ methyl), *ca.* 2.45 (multiplet, 1 H, $C_3$ proton), 3.02 (singlet, 3 H, N-methyl), 5.35 (doublets of doublets, $J$ = 10 and 6 cps, 1 H, $C_4$ proton), and 5.99 (doublet, $J$ = 10 cps, 1 H, $C_5$ proton).

*Anal.* Calcd for $C_9H_{12}ClNO$: C, 58.22; H, 6.52. Found: C, 58.62; H, 6.75.

**5-Chloro-2-pyridone (14a).**—A solution of 4.75 g (0.05 mole) of 2-pyridone and 8.0 g (0.06 mole) of N-chlorosuccinimide in 50 ml of methylene chloride was refluxed for 24 hr and treated as above. There was obtained after one recrystallization from

(28) A 0.25 in. × 15 ft aluminum column packed with 1% Carbowax 20 M on Chromosorb P was employed. The vpc analyses were performed on a Varian-Aerograph A90-P3 instrument.

(29) G. H. Coleman and H. L. Johnson, *Inorg. Syn.*, **1**, 59 (1939).

(30) The authors wish to thank M. L. Wise for carrying out this experiment.

(31) A 0.25 in. × 5 ft aluminum column packed with 20% SF-96 on Chromosorb W was employed in conjunction with an Aerograph A90-P3 (thermal conductivity) gas chromatograph.

tetrahydrofuran 6.2 g (95%) of **14a** as white needles, mp 162–164° (lit.[32] mp 163°).

**5-Chloro-1-methyl-2-pyridone (14b).**—A solution of 2.0 g (0.018 mole) of N-methyl-2-pyridone and 2.7 g (0.02 mole) of N-chlorosuccinimide in 20 ml of methylene chloride was refluxed for 24 hr and treated as above. The residue was distilled to give 0.85 g of pale yellow liquid, bp 100° (0.05 mm). Vpc analysis[31] of this material indicated it to be composed of 78% of **14b** and 22% of unreacted starting material. The product after isolation by preparative vpc had a melting point (44–46°) and infrared spectrum identical with those of an authentic sample.[33]

**Registry No.**—2, 13118-80-4; **3**, 13118-81-5; **4**, 13118-82-6; **8**, 13118-83-7; **10**, 13118-84-8; **11**, 13118-85-9; **13**, 13118-86-0.

**Acknowledgment.**—The authors wish to express their gratitude to Professor Jack Hine for generously reading and commenting upon this manuscript.

(32) M. P. Cava and N. K. Bhattacharyya, *J. Org. Chem.*, **23**, 1287 (1958).

(33) A. Binz and C. Rath, *Ann. Chem.*, **486**, 71 (1931).

# The Preparation and Reactions of 2-(Trichloromethyl)benzothiazoline and Some Related Compounds

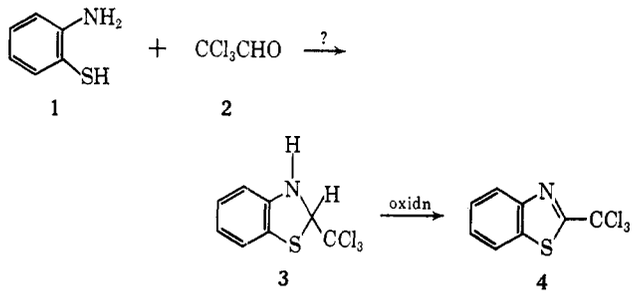
DAVID T. MANNING AND C. B. STROW, JR.

*Research and Development Department, Union Carbide Corporation, Chemicals and Plastics, South Charleston, West Virginia*

*Received April 14, 1967*

Reaction of chloral with *o*-aminobenzenethiol produced a crystalline compound, $C_8H_6Cl_3NS$, shown by chemical and spectral studies to be the novel 2-(trichloromethyl)benzothiazoline (**3**). Isolation of **3** revealed a minor, dimeric coproduct found by nuclear magnetic resonance and other studies to be 2,7-bis(trichloromethyl)-2,3,7,8-tetrahydrodibenzo[*d,i*][1,3,6,8]dithiadiazecine (**9**). Gentle pyrolysis of either **3** or of **9** effects dehydrochlorination with formation of 2-(dichloromethyl)benzothiazole (**5**). Compound **5** is also formed from **3** by treatment of the latter with ferric chloride while mild acidic permanganate oxidation of the benzothiazoline (**3**) afforded 2-(trichloromethyl)benzothiazole (**4**). Attempted ring chlorination of **5** produced only the trichloromethyl compound (**4**) in high yield, although action of a nitric–sulfuric acid mixture on **5** gave a ring-nitrated product. Cupric acetate catalyzed oxidation of **3** with gaseous oxygen proceeds exothermically with loss of hydrogen chloride and formation of a high molecular weight product of unknown structure.

Our interest in 2-(trichloromethyl)benzothiazoline (**3**) as an intermediate prompted a study of its preparation by condensation of *o*-aminobenzenethiol (**1**) with chloral (**2**), a procedure which apparently has not been described. The benzothiazoline (**3**) appeared to be an obvious intermediate for oxidative conversion to 2-(trichloromethyl)benzothiazole (**4**), reported earlier by Japanese workers[1] (in crude form) and, quite recently, by Holan, *et al.*[2] In addition, **3**, if obtainable, was considered as a possible source of a carbene resulting from thermal chloroform elimination in the manner previously described by Wanzlick.[3] Although the




formation of benzothiazolines by reaction of **1** with aldehydes appears to be fairly general,[4] the reported reactions of chloral with certain aromatic amines bearing a YH (Y = O, S, or NH) substituent at the *ortho* position suggested possible acyclic Schiff-base formation as a complicating alternative.[5,6] Thus Stephens and Bower[5] have reported the synthesis of such a Schiff base from chloral and *o*-aminophenol, while Dunn, *et. al.*, have recently suggested the existence of similar Schiff bases as precursors of the corresponding benzothiazoles in a lead tetraacetate oxidation.[6] On the other hand, Sumerford and Dalton noted that reaction of chloral with aromatic amines failed to produce aldimines but led instead to both 2,2,2-trichloro-1-hydroxyethyl adducts and stable bisanilino derivatives.[7]

## Results

Anhydrous chloral reacted vigorously with *o*-aminobenzenethiol (**1**) to give 71–96% yields of a crystalline compound $C_8H_6Cl_3NS$ whose infrared and nmr spectra were in accord with 2-(trichloromethyl)benzothiazoline (**3**) as the structure. On recrystallization of the crude product, it was found that a second product, constituting a dimer of **3**, was present to the extent of about 4–10% (by weight) of the crude material. Compound **3** melted with vigorous HCl evolution. Unlike the reported behavior of the Schiff bases of Stephens and Bower, **3** was insoluble in aqueous alkali at 25°.

With all evidence indicating **3** to be the structure of the condensation product, its oxidation to **4** was attempted. One of the most characteristic reactions of benzothiazolines is facile oxidation to the corresponding

(1) Y. Mizuno, K. Adachi, and S. Kanda, *Yakugaku Zasshi*, **72**, 1268 (1952).

(2) G. Holan, E. L. Samuel, B. C. Ennis, and R. W. Hinde, *J. Chem. Soc.*, 20 (1967).

(3) H. W. Wanzlick, *Angew. Chem. Intern. Ed. Engl.*, **1** (No. 2) 75 (1962).

(4) H. P. Lankelma and P. X. Sharnoff, *J. Am. Chem. Soc.*, **53**, 2654 (1931); **54**, 379 (1932).

(5) F. F. Stephens and J. D. Bower, *J. Chem. Soc.*, 1722 (1950).

(6) G. L. Dunn, P. Actor, and V. J. Di Pasquo, *J. Med. Chem.*, **9**, 751 (1966).

(7) W. T. Sumerford and D. N. Dalton, *J. Org. Chem.*, **9**, 81 (1944). An interesting example cited by these authors was the formation of a 2,2,2-trichloro-1-hydroxyethyl adduct from 2-amino-5-methoxycarbonylphenol which possesses an *ortho* hydroxy group available for ring closure.