Electrochemical and Chemical Reduction of Di-*tert*-butyldiaziridinone[1a]

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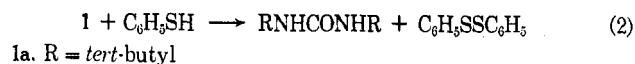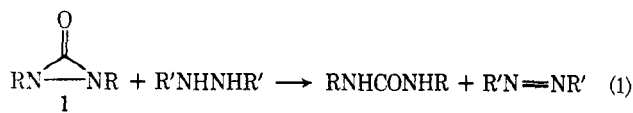FREDRICK D. GREENE* AND J. GRADY PACIFICI

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Di-*tert*-butyldiaziridinone (1a) was reduced both electrochemically and by *tert*-butyllithium and sodium naphthalenide. The product in all three cases was di-*tert*-butylurea, indicating that the preferred mode of reduction of 1a under electron-transfer conditions is cleavage of the N–N single bond. Cyclic voltammetry indicated that, if the radical anion of 1a is an intermediate, its half-life must be less than 2 msec. Mechanisms of the reductions are discussed.

The synthesis and a number of reactions of diaziridinones, 1 (R = *tert*-alkyl), have been described.[2] A property of special interest is the mild oxidizing action (ease of reduction) of 1.[2] We summarize here information on the reduction of diaziridinones.
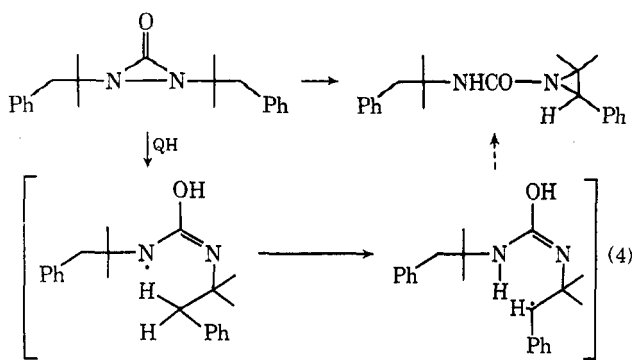
As described earlier, reaction of di-*tert*-butyldiaziridinone (1a) with sodium borohydride leads to cleavage of the C–N bond with formation of 1,2-di-*tert*-butyl-1-formylhydrazine.[2] Reaction of 1a with substituted hydrazines[3] or mercaptans[2] effects reduction of the N–N bond (eq 1 and 2). Results of a detailed study

$$RN\overset{O}{\overbrace{}}NR + R'NHNHR' \longrightarrow RNHCONHR + R'N=NR' \quad (1)$$

$$1 + C_6H_5SH \longrightarrow RNHCONHR + C_6H_5SSC_6H_5 \quad (2)$$

1a. R = *tert*-butyl

of the oxidation–reduction reaction of eq 1[3] led to the suggestion that the reaction proceeded by a free-radical chain reaction involving hydrogen atom transfer to the diaziridinone (eq 3). That study also led to the

$$RN\overset{O}{\overbrace{}}NR \xrightarrow{QH} \left[RN\overset{OH}{\overbrace{}}NR \right] \dashrightarrow RNHCONHR \quad (3)$$
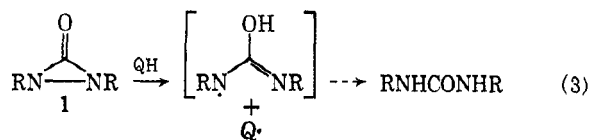
discovery of a rearrangement reaction of diaziridinones to aziridinecarboxamides (eq 4), competitive with the oxidation–reduction reaction of eq 1.

$$(4)$$

Another possible mode of reduction of a diaziridinone (or possible mode of catalysis of the rearrangement reaction of eq 4) would be by electron transfer (eq 5).

$$1 \xrightarrow{e^-} \left[RN\overset{O}{\overbrace{}}NR \right]^{\cdot -} \longrightarrow RN\overset{O^-}{\overbrace{}}NR \quad (5)$$

$$\quad\quad 2 \quad\quad\quad\quad 3$$

In search of species such as **2** and **3**, we have examined the reduction of di-*tert*-butyldiaziridinone by electrochemical and chemical methods.

Electrochemical Reduction.—Diaziridinone 1a exhibits a single diffusion-controlled polarographic wave at −0.76 V (relative to the cadmium amalgam reference electrode of Marple),[4] in dimethyl sulfoxide (DMSO) or dimethylformamide (DMF) containing tetraethylammonium bromide (TEAB). The diffusion current constant, I_d,[5,6] was equal to 4.2 in DMF indicating an overall two-electron reduction process.[6] Tomes' criterion,[5] *i.e.*, $E_{1/4} - E_{3/4}$, was 140 mV, indicating an element of irreversibility to be associated with the reduction. This was confirmed by cyclic voltammetry; no anodic peak was observed upon scan reversal just beyond the cathodic peak, even at the fastest scan rate employed (200 V/sec).[7] Thus any intermediate(s) generated during reduction of the diaziridinone must be too short-lived to be observed under our conditions. The polarographic behavior of 1a was unaffected by the addition of excess phenol, normally an efficient proton donor in DMF and DMSO.[8] Controlled-potential electrolysis of 1a in DMF afforded di-*tert*-butylurea in high yield; integration of the current passed during electrolysis demonstrated that two electrons were consumed per molecule of starting material, in agreement with the observed polarographic diffusion current constant. The solution became dark yellow during electrolysis. When electrolysis was carried out in the
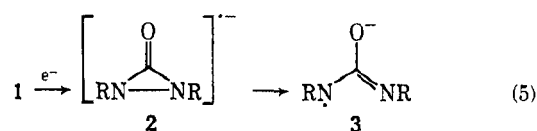
(1) (a) Financial support from the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation is gratefully acknowledged; (b) National Science Foundation trainee.

(2) F. D. Greene, J. C. Stowell, and W. R. Bergmark, *J. Org. Chem.*, **34**, 2254 (1969).

(3) F. D. Greene, W. R. Bergmark, and J. G. Pacifici, *ibid.*, **34**, 2263 (1969).

(4) L. W. Marple, *Anal. Chem.*, **39**, 844 (1967). This electrode is *ca.* −0.7 V relative to sce.

(5) $I_d = 708nD^{1/2} = i_d/Cm^{2/3}t^{1/6}$, using an undamped recorder to measure diffusion currents: L. Meites, "Polarographic Techniques," 2nd ed, Wiley-Interscience, New York, N. Y., 1965.

(6) In DMF, values of I_d of *ca.* 4–6 correspond to a two-electron reduction process: *cf.* (a) Meites, ref 5, pp 678–711; (b) J. L. Sadler and A. J. Bard, *J. Amer. Chem. Soc.*, **90**, 1979 (1968).

(7) The faradaic wave at $E_{p/2} = -0.7$ V was accompanied by two other waves, a cathodic peak at −1.4 V and an anodic peak at 0.4 V. The markedly symmetrical shape of these peaks and the fact that they are relatively much smaller than the wave at −0.7 V at low scan rates or high concentrations of 1 suggest that they are due to adsorption phenomena [see R. H. Wopschall and I. Shain, *Anal. Chem.*, **39**, 1514 (1967)].

(8) J. R. Jezorek and H. B. Mark, Jr., *J. Phys. Chem.*, **74**, 1627 (1970).

presence of added phenol, the solution remained colorless; the product was still the urea.

The principal result is clean reduction of the N–N bond. Several paths are possible (Scheme I).

SCHEME I
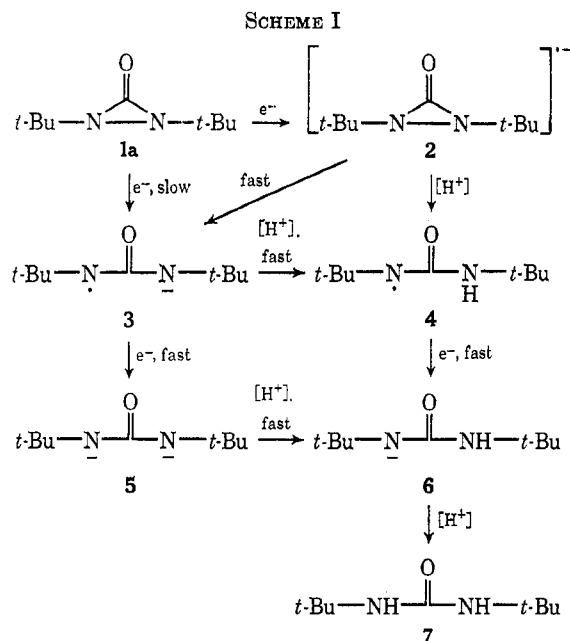
Whether the initial electron-transfer step affords a diaziridinone radical anion (2) as a discrete intermediate, or whether the ring is opened during the first electron-transfer step to afford 3 is not resolvable with the data at hand, other than to note that cyclic voltammetry data indicate that, if 2 is actually a discrete intermediate, it must be short-lived ($t_{1/2} \leq 2$ msec). The dark yellow color observed upon reduction in the absence of any added proton donor might be due to the dianion 5, but is more likely the monoanion 6, since 5 should be sufficiently basic to effect a rapid Hofmann elimination upon the tetraalkylammonium ion used as electrolyte.[9]

The α-lactam, 1,3-di-*tert*-butylaziridinone (8), is not reducible electrochemically even at the most negative potentials accessible in dimethyl sulfoxide (-2.6 V *vs.* see). This indicates that relief of strain cannot alone account for the ease of reduction of 1a. The large (>1.3 V) difference in reduction potentials between 1a and 8 should derive at least in part from a greater strength of the C–N bond in 8 relative to the
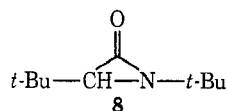

N–N bond in 1a and is suggestive that reduction of 1a does involve breaking of the N–N bond in the transition state for the initial electron transfer.

It is of interest to compare these results with the electrochemical reduction of amides and diaziridines. Reduction of 1a involves cleavage of the N–N bond rather than reduction of the carbonyl group as with amides.[10,11] Also, 1a is considerably easier to reduce

than ordinary amides (DMF was the solvent for preparative scale electrolysis of 1a) or ureas.[12a]

Direct electrochemical reduction of simple aliphatic and aromatic amides occurs only at very negative potentials and in fairly strongly acidic media, where the electroactive species may actually be the protonated amide.[10] It is also possible to reduce amides indirectly, using solvated electrons generated by the electrochemical reduction of lithium ion in methylamine.[11] Both types of reduction apparently proceed *via* the carbinolamine, which has been isolated in several in-

$$R'CONR_2 \xrightarrow[2H^+]{2e^-} \underset{\underset{OH}{|}}{R'CHNR_2} \longrightarrow \text{products}$$
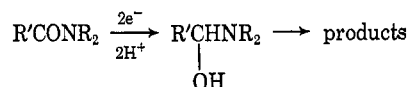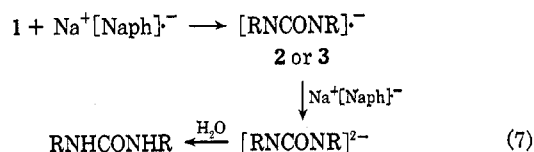
stances.[12b] Probably the most notable feature of the electrochemical reduction of 1a is the fact that it can be carried out under neutral conditions. Hydrazo compounds,[13] including diaziridines, *e.g.*, 9,[14] are inert
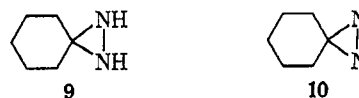
toward electrochemical reduction under neutral or alkaline conditions although the N–N bond can be cleaved in acid. For example, 9 could be prepared in quantitative yield by electrolytic reduction of diazirine, 10 at pH 9, while at pH 6 cyclohexanone was formed, presumably *via* reduction of 9 to the *gem*-diamine, followed by hydrolysis.[14] The pH dependence of the polarographic half-wave potentials of hydrazo compounds and diaziridines is generally ascribed to the fact that the electroactive substance is a protonated species.[13,14] The activated N–N bond of phenylhydrazones and semicarbazones is reduced in acid media (eq 6) but inert in neutral or alkaline media.[13]

$$R_2C{=}\overset{}{N}NHX \xrightarrow[\text{acid}]{2e^-} R_2C{=}\overset{+}{N}H_2 + H_2NX \qquad (6)$$

$$X = C_6H_5 \text{ or } H_2NCO$$
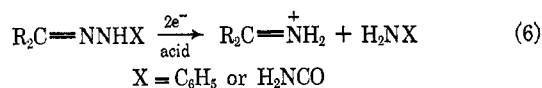
Reduction by Sodium Naphthalenide.—Combination of equimolar amounts of diaziridinone 1a and of sodium naphthalenide in tetrahydrofuran led to the immediate discharge of the color of the naphthalenide radical ion and formation of a precipitate. The reaction mixture, after quenching with water, afforded the urea 7 (46%) and unchanged diaziridinone (48%). Reaction of the diaziridinone with 2 mol of sodium naphthalenide followed by quenching with water afforded the urea in high yield (eq 7). The capability

$$1 + Na^+[Naph]^{\cdot -} \longrightarrow [RNCONR]^{\cdot -}$$
$$\text{2 or 3}$$
$$\downarrow Na^+[Naph]^{\cdot -}$$
$$RNHCONHR \xleftarrow{H_2O} [RNCONR]^{2-} \qquad (7)$$

of sodium naphthalenide to serve as a single-electron transfer agent seems well established.[15] The implica-

(9) A. J. Fry and R. G. Reed, *J. Amer. Chem. Soc.*, **93**, 553 (1971).

(10) S. Swann, Jr., in "Technique of Organic Chemistry," Vol. 2, A. Weissberger, Ed., 1956, pp 502, 503.

(11) R. A. Benkeser, H. Watanabe, S. J. Mels, and M. A. Sabol, *J. Org. Chem.*, **35**, 1210 (1970).

(12) (a) W. E. Bull and R. H. Stonestreet, *J. Electroanal. Chem.*, **12**, 166 (1966); (b) G. Farnia, A. Romanin, G. Capobianco, and F. Torzo, *ibid.*, **33**, 31 (1971).

(13) C. L. Perrin, *Progr. Phys. Org. Chem.*, **3**, 165 (1965).

(14) H. Lund, *Collect. Czech. Chem. Commun.*, **31**, 4175 (1966).

(15) P. W. Ayers, J. F. Garst, and R. C. Lamb, *J. Amer. Chem. Soc.*, **88**, 4266 (1966); G. D. Sargent, J. N. Cron, and S. Bank, *ibid.*, **88**, 5363 (1966).

tion of the above experiment is that either the further reduction of the first-formed radical ion is faster than the initial reduction, or the radical ion disproportionates[16] to diaziridinone and the urea dianion, which precipitates as the disodium salt.

Reaction of sodium naphthalenide with bis(1,1-dimethyl-2-phenylethyl)diaziridinone (**1b**, eq 4) also shows the stoichiometry of eq 7, affording the urea in high yield. Reaction of sodium naphthalenide with an excess of diaziridinone **1b** followed by quenching with water afforded largely unchanged diaziridinone along with a small amount of the corresponding urea. Here, also, the only reaction observed is reduction of the N–N bond.[17]

Reduction by *tert*-Butyllithium.—Reaction of diaziridinones **1a** and **1b** with *tert*-butyllithium in pentane is rapid (eq 8). No products of addition to the car-

$$RN\overline{\qquad}NR + 2t\text{-BuLi} \xrightarrow{\text{pentane}} RNHCONHR \ (\sim 95\%)$$

$$(CH_3)_3CH + (CH_3)_2C{=}CH_2 \quad (8)$$
$$(50\%) \qquad\qquad (50\%)$$
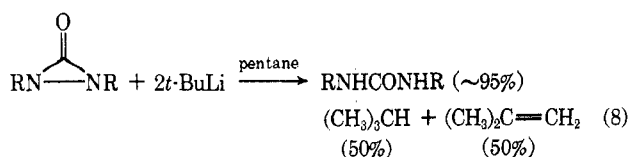
bonyl group (or to nitrogen) were observed. Here, also, the exclusive path, overall, is reduction of the N–N bond of the diaziridinone to the urea dianion, possibly proceeding by electron transfer from *tert*-butyllithium[18] or by a cyclic path (*e.g.*, as in eq 9).

$$[RNCONR]^{2-} + (CH_3)_3CH \quad (9)$$
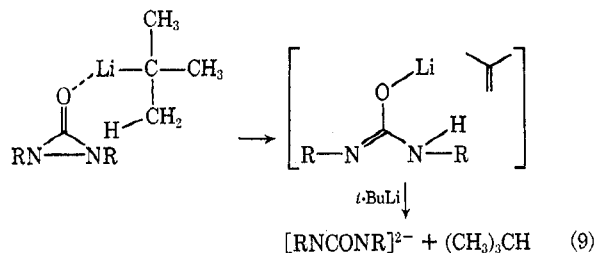
Summary.—Hydride transfer reagents effect reduction of diaziridinones at the C–N bond; hydrogen atom transfer reagents effect reduction at the N–N bond, sometimes accompanied by a rearrangement reaction (eq 3 and 4); electron transfer by electrochemical means or by sodium naphthalenide effects clean reduction of the N–N bond.

Experimental Section

Polarography and cyclic voltammetry were carried out using a Princeton Applied Research Model 170 electrochemistry system. The working electrode for cyclic voltammetry was a mercury drop hanging from a very short (0.1 mm) platinum wire. The reference electrode for all experiments was the cadmium amalgam–cadmium chloride electrode of Marple.[4] Preparative electrolyses were carried out using a potentiostat based upon a Kepco KS-120-2.5 programmable power supply.[19] To obtain coulometric data, the voltage drop across a standard resistor in

series with the cell was measured on a 1-mV strip-chart recorder equipped with Disc integrator and digital printer. The electrochemical cell has been described previously.[20]

Electrochemical Reduction of Di-*tert*-butyldiaziridinone (1).—A 5-ml sample of a 0.1 *M* solution of tetraethylammonium bromide in dimethylformamide was preelectrolyzed at −0.8 V until the current had decayed to a constant value (∼1 mA). A solution of 0.200 g of **1a**[2] in 0.5 ml of dimethylformamide was then injected, and electrolysis was continued until the current had returned to the background value. Integration of the current passed in the electrolysis showed that 2.1 ± 0.2 F had been consumed per mole of **1a**. The dark yellow electrolysis solution was poured into water (whereupon the yellow color disappeared), and the resulting solution was extracted with ether. After the solution was dried over sodium sulfate, the ether was distilled to afford 1,3-di-*tert*-butylurea, 0.190 g [95%], mp (sealed capillary) 238–240° (lit.[2] mp 243–244°).

Reaction of Di-*tert*-butyldiaziridinone with *tert*-Butyllithium.—To a solution of *tert*-butyllithium (6.5 mmol) in 10.0 ml of pentane was added, all at once and under a nitrogen atmosphere, 0.522 g (3.04 mmol) of di-*tert*-butyldiaziridinone in 5.0 ml of pentane. The reaction proceeds rapidly with the evolution of gases and the formation of a white precipitate. Water (5 ml) was added, hydrolyzing the precipitate and forming a white crystalline solid, 0.511 g (2.9 mmol) (95% yield) of di-*tert*-butylurea, mp 240–241°, mmp 240–241°, identical in ir and vpc with an authentic sample. A sample of the pentane solution was removed from the flask and injected into the vpc. The chromatogram showed the presence of isobutane and isobutylene; no di-*tert*-butyl was formed.

To a second solution of *tert*-butyllithium, 3.0 mmol in 2.0 ml of pentane, was added 0.256 g (1.5 mmol) of di-*tert*-butyldiaziridinone in 2.0 ml of pentane by a hypodermic syringe in a closed system. Samples of the gases given off were analyzed by vpc at 25° on SE-30 on Chromosorb W. The gases were identified as isobutane and isobutylene, formed in equal amounts. Yields were determined in a separate experiment by manometric techniques, 0.25 mmol of diaziridinone affording 0.51 mmol of isobutane and isobutene.

The same results (95% yield of the urea) were obtained by reaction at −76°.

Reaction of Sodium Naphthalenide with Diaziridinones.—Preparation of sodium naphthalenide from sodium metal and naphthalene in THF was accomplished by standard vacuum line methods. Samples of the diaziridinone were added all at once by means of a break-seal attached to the reaction vessel. In each case the hydrolysis was carried out by the addition of water to the system by means of a second break-seal. All reactions were carried out at room temperature.

A. Reaction with Di-*tert*-butyldiaziridinone.—To a solution of sodium naphthalenide (1.0 mmol in 8.0 of THF) was added 0.171 g (1.0 mmol) of di-*tert*-butyldiaziridinone. Immediately upon addition a white precipitate was formed with the disappearance of the green color. To the mixture was added 5.0 ml of water which hydrolyzed the precipitate and produced two clear phases. The contents were removed, the two phases were separated, and the ether phase was dried over MgSO4. Removal of the ether left an oily–crystalline residue from which was isolated by trituration with CCl4 0.080 g (0.46 mmol) of di-*tert*-butylurea identified by mp 239–241°, mmp 239–241°, and comparison of infrared spectrum of authentic sample. The filtrate was condensed to a volume of 5.0 ml and analyzed by ir. Comparison to standard solutions indicated that 0.082 g (0.48 mmol) of dizairidinone was present. The spectrum showed no other carbonyl absorption.

To a second solution of sodium naphthalenide (2.0 mmol in 10.0 ml of THF) was added 0.171 g (1.0 mmol) of di-*tert*-butyldiaziridinone. The contents were treated as before, affording 0.160 g (0.93 mmol) of di-*tert*-butylurea.

B. Reaction with Bis(1,1-dimethyl-2-phenylethyl)diaziridinone.—To a solution of sodium naphthalenide (0.05 mmol in 10.0 ml of THF) was added 0.200 g (0.66 mmol) of bis(1,1-dimethyl-2-phenylethyl)diaziridinone.[3] The addition of the diaziridinone rapidly destroys the naphthalenide producing a clear homogeneous solution which was quenched by the addition of 1.0 ml of H2O. The contents of the vial were carefully transferred to a separatory funnel and the two phases separated; the

(16) *E.g.*, see J. J. Silber and H. J. Shine, *J. Org. Chem.*, **36**, 2923 (1971), and J. Marcoux, *J. Amer. Chem. Soc.*, **93**, 537 (1971), and references cited therein.

(17) It is of interest that this reaction did not afford the rearrangement product, aziridinecarboxamide, eq 4. The use of excess diaziridinone was chosen to maximize the opportunity for a possible radical anion path for this isomerization.

(18) R. Waack and M. A. Doran, *J. Organometal. Chem.*, **3**, 92 (1965).

(19) P. Birman, "Power Supply Handbook," Kepco Inc., Flushing, N. Y., 1965, p 129.

(20) A. J. Fry, M. A. Mitnick, and R. G. Reed, *J. Org. Chem.*, **35**, 1232 (1970).

ether solution was dried over magnesium sulfate and the ether removed. A white crystalline residue remained which was diluted to 5.0 ml with CCl₄ and analyzed by ir for unreacted diaziridinone. Comparison of the infrared spectrum to a standard solution revealed that less than 4% of the diaziridinone had been destroyed; a band at 1665 cm⁻¹ of very low intensity indicated the formation of the urea.

A solution of sodium naphthalenide (2.1 mmol in 10.0 ml of THF) was treated with 0.297 g (0.99 mmol) of the diaziridinone under the same conditions as before affording 0.230 g of 1,3-bis-(1,1-dimethyl-2-phenylethyl)urea, mp 180–182°, mmp 180–

182°, and identical in infrared spectrum with an authentic sample.

Seven-Membered Heterocycles. V. Synthesis and Structure of Halogenated 3,4-Dihydro-1-benzothiepin-5(2H)-ones[1a,b]

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Bromination of 3,4-dihydro-1-benzothiepin-5(2H)-one (1) gave 4-bromo-3,4-dihydro-1-benzothiepin-5(2H)-one (2), which was reduced to the bromohydrin 5. Treatment of 5 with base regenerated the starting ketone 1. Chlorination of 1 with N-chlorosuccinimide (NCS) or sulfuryl chloride produced exclusively *cis*-2,4-dichloro-3,4-dihydro-1-benzothiepin-5(2H)-one (6). *trans*-2,4-Dichloro-3,4-dihydro-1-benzothiepin-5(2H)-one (7) was available by the stereoselective ring-opening addition of HCl on 8-chlorocyclopropa[b][1]benzothiopyran-7-one (8). In contrast the reaction of 2 with sulfuryl chloride or NCS provided a mixture of *cis*- (11) and *trans*-4-bromo-2-chloro-3,4-dihydro-1-benzothiepin-5(2H)-one (12) in which the trans isomer was highly predominant. Nucleophilic displacement reactions were used to convert 2 to 4-chloro-3,4-dihydro-1-benzothiepin-5(2H)-one (17) and 4-iodo-3,4-dihydro-1-benzothiepin-5(2H)-one. Sulfones of the above halo ketones were also prepared either by oxidation of the corresponding sulfides or halogenation of keto sulfones. The structural and stereochemical assignments for these compounds were made from interpretation of ir and nmr spectra. The mechanism offered for the stereoselective chlorination of 1 to give *cis*-6 entailed first C₂ chlorination followed by C₄ substitution *via* a transannular chlorination in the chlorosulfonium ion 19 intermediate. Formation of predominantly trans 12 in the sulfuryl chloride reaction with 2 is rationalized by the usual ion pair intermediate 21 proposed for α-chlorination of sulfides by sulfuryl chloride.

Halogenated 3,4-dihydro-1-benzothiepin-5(2H)-ones can serve as potential intermediates for introducing unsaturation into the thiepin ring and thus providing precursors for the synthesis of 1-benzothiepin derivatives. In this paper we emphasize the synthesis and structural assignments for a variety of halogenated 3,4-dihydro-1-benzothiepin-5(2H)-ones and in the subsequent report[2] concentrate on the reactions of these halo ketones with base.

Bromination of 3,4-dihydro-1-benzothiepin-5(2H)-one (1) proceeded readily to form the 4-bromo-3,4-dihydro-1-benzothiepin-5(2H)-one (2),[3] which was characterized as the corresponding sulfone 4 also available by direct bromination of 3. The position of bromination was established by reduction of 2 to the bromohydrin 5, which undergoes base-catalyzed elimination of HBr to form the starting ketone 1. An infrared study of the carbonyl frequencies for ketones 1 and 2 (see Table I) showed a band displacement of 15 cm⁻¹ to higher frequency for the bromo ketone 2, thus favoring the con-
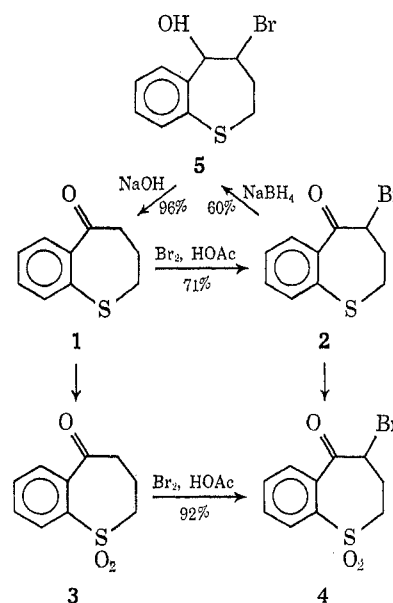
(1) (a) For part IV in this series see V. J. Traynelis and D. M. Borgnaes, *J. Org. Chem.*, **37**, 3824 (1972). (b) Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. (c) Abstracted from a portion of the Ph.D. Dissertation submitted by J. C. S. in Dec 1971 and Y. Y. in May 1973 at West Virginia University. (d) Abstracts from a portion of the Ph.D. Dissertation submitted by R. F. L. in June 1960 and D. M. B. in Aug 1968 at the University of Notre Dame.

(2) V. J. Traynelis, J. C. Sih, and D. M. Borgnaes, *J. Org. Chem.*, **38**, 2629 (1973).

(3) K. Sindelar and M. Protiva, *Collect. Czech. Chem. Commun.*, **33**, 4315 (1968).

formation which places the bromine atom in a quasi-equatorial position[4] and puckers the C₂ and C₃ carbons out of the plane of the ring. The absence of any appreciable bathochromic shift in the uv spectra of 1 and 2 is also consistent with the quasiequatorial assignment

(4) R. N. Jones, D. A. Ramsay, F. Herling, and K. Dobriner, *J. Amer. Chem. Soc.*, **74**, 2828 (1952); E. J. Corey, *ibid.*, **75**, 2301 (1953); N. L. Allinger and J. Allinger, *ibid.*, **80**, 5476 (1958).