2210 (1962).
(10) The IR spectra were determined with a Perkin-Elmer Model 237B and a Beckmann Model IR-9 infrared recording spectrophotometers. The NMR spectra were determined at 60 MHz with a Varian Associates Model T-60 and at 100 MHz with a Varian Associates Model HA-100 NMR spectrometers. The chemical shifts are expressed in δ values (parts per million) relative to a Me_4Si internal standard. The mass spectra were obtained with a Consolidated Electronics Corp. Model 110-21B and a Varian Associates Model CH5 mass spectrometer. Gas chromatographic analyses (GLC) were performed on a Hewlett-Packard Model 402 high-efficiency chromatograph with a flame-ionization detector attached to a Hewlett-Packard Model 3380A integrator.
(11) M. J. Mintz and C. Walling, *Org. Synth.*, **49**, 9 (1969).
(12) Washed in dilute NaOH solution, rinsed three times with distilled water, and oven dried immediately prior to use.
(13) Refluxing **7b** in methanol for 3 h yielded 5-chloro-6,6-dimethoxy-2-hexanone (89%): IR (film) 1717 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 4.36 (1 H, d, J = 6 Hz), 4.13–3.77 (1 H, complex m), 3.49 (6 H, s), 2.97–2.44 (2 H, complex m), 2.20 (3 H, s) superimposed on 2.44–1.46 (2 H, complex m); mass spectrum *m/e* (rel intensity) 165 (4), 164 (2), 163 (14), 162 (5), 127 (15), 107 (19), 105 (53), 75 (100), 47 (46), 43 (62).
(14) D. Jentzsch, "Gas Chromatographie", Franckh'sche Verlagshandlung, Stuttgart, 1968, pp 61–62 and 98.
(15) This mixture is rather unstable. A refrigerated methanolic solution of **8a** and **8b** slowly decomposed to *m*-cresol in a few weeks. A stirred mixture of **8a** and **8b** in methanol at 25 °C for 4 days yielded 3-chloro-2,6-heptadione (83%): IR (film) 1725 cm^{-1}; NMR (60 MHz, $CDCl_3$) δ 4.33 (1 H, d of d, J = 8, 5.5 Hz), 2.9–2.4 (2 H, m), 2.35 (3 H, s) and 2.18 (3 H, s) superimposed on 2.4–1.7 (2 H, m), which after 24 h storage neat in a refrigerator had also decomposed to *m*-cresol.

Isoquinolines. 7.[1] Reaction of Ethylene Oxide with Isoquinolines. Novel Isoquinolone and Oxazolidine Formation

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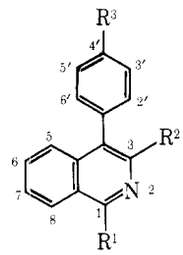
Aprotic deamination of 3-amino-1-bromo-4-nitrophenylisoquinoline (**6**) followed by partial reduction yielded 4-aminophenyl-1-bromoisoquinoline (**8**), and complete reduction yielded 4-aminophenylisoquinoline (**9**). Isoquinolines **8** and **9** when treated with excess ethylene oxide in acetic acid afforded 4-[*p*-bis(2-hydroxyethyl)amino]phenyl-2-(2-hydroxyethyl)-1-isoquinolone (**15a**) and 2-(2-acetoxyethyl)-4-[*p*-bis(2-hydroxyethyl)amino]phenyl-1-isoquinolone (**15b**). Evidence for a mechanism involving an oxazolidine intermediate is presented. When isoquinoline (**17**) was similarly treated with ethylene oxide, 2,3-dihydro-10b*H*-oxazolo[2,3-*a*]isoquinoline (**19**) was obtained.

In the course of preparing potential CNS antitumor agents, we recently reported that amine **1** afforded diol **2**, whereas amine **3** yielded a mixture of diol **4** and triol **5** when treated with excess ethylene oxide.[1] In continuation of this



Compd	R^1	R^2	R^3
1	Br	$NHCOCH_3$	NH_2
2	Br	$NHCOCH_3$	$N(CH_2CH_2OH)_2$
3	H	$NHCOCH_3$	NH_2
4	H	$NHCOCH_3$	$N(CH_2CH_2OH)_2$
5	H	$NH(CH_2)_2OH$	$N(CH_2CH_2OH)_2$
6	Br	NH_2	NO_2
7	Br	H	NO_2
8	Br	H	NH_2
9	H	H	NH_2
10a	Br	H	$N(CH_2CH_2OH)_2$
10b	Br	H	$NHCH_2CH_2OH$
10c	H	H	$N(CH_2CH_2OH)_2$

program we required isoquinolines lacking the 3-amino group. The deamination of **6**[2a] with isoamyl nitrite in dry THF yielded **7** (27–43%).[2b] Stannous chloride reduction of **7** yielded **8** (81%), and catalytic hydrogenation of **8** gave **9** (90%). Treatment of either **8** or **9** with excess ethylene oxide in acetic acid overnight at room temperature did not yield the expected isoquinoline diols **10a** or **10c** but gave isoquinolones **15a** and **15b** as shown in Scheme I. In particular, **8** afforded a mixture of **15a** and **15b** in 51 and 25% yield, respectively. The yield of **15a** from **9** was somewhat lower (34%). The reaction between isoquinolines and related compounds with epoxides has been previously observed,[3a–d] but only in one instance was isoquinolone formation noted.[4]

With the addition of excess sodium acetate to the reaction, monoacetate **15b** constituted as much as 50% of the product mixture. Compound **15b** could not be chromatographed on silica gel without extensive (50%) hydrolysis to **15a** and appeared thermally labile toward intermolecular acylation. Evidence for the intermolecular acylation was provided by the mass spectrum of **15b** which at 60 °C showed the expected molecular ion (*m/e* 410) and $M^+ - CH_2OH$ (*m/e* 379) as prominent peaks, but at 110 °C peaks assignable to a diacetate (*m/e* 452 M^+, *m/e* 421 $M^+ - CH_2OH$) and triacetate (*m/e* 494 M^+) of **15a** were also observed. In view of the instability of **15b**, mixtures of **15a** and **15b** were gently saponified to **15a** and treated with $SOCl_2$ in CH_3CN to give mustard **16** (49%) as shown in Scheme I.

A suggested mechanism for the transformation of **8** (X = Br) and **9** (X = H) to isoquinolones **15a** and **15b** is incorporated in Scheme I. Pertinent to the mechanism are the following observations: Diol **10a** can be isolated as the initial product in the reaction of **8** and ethylene oxide after short (2 h) reaction times. Prior to this study, solvent incorporation into isoquinolone products had not been reported, but the isolation and characterization of isoquinolone **15b** implicates intermediates **12–14** in the mechanism and precludes consideration of **11** as an intermediate in isoquinolone formation. Although a hydride transfer (X = H) has been suggested as the penultimate step in the reaction of **9** and ethylene oxide, the observation that no isoquinolone products are formed under conditions that rigorously exclude oxygen would argue for an oxidation step (X = OH or OOH) prior to oxazolinium

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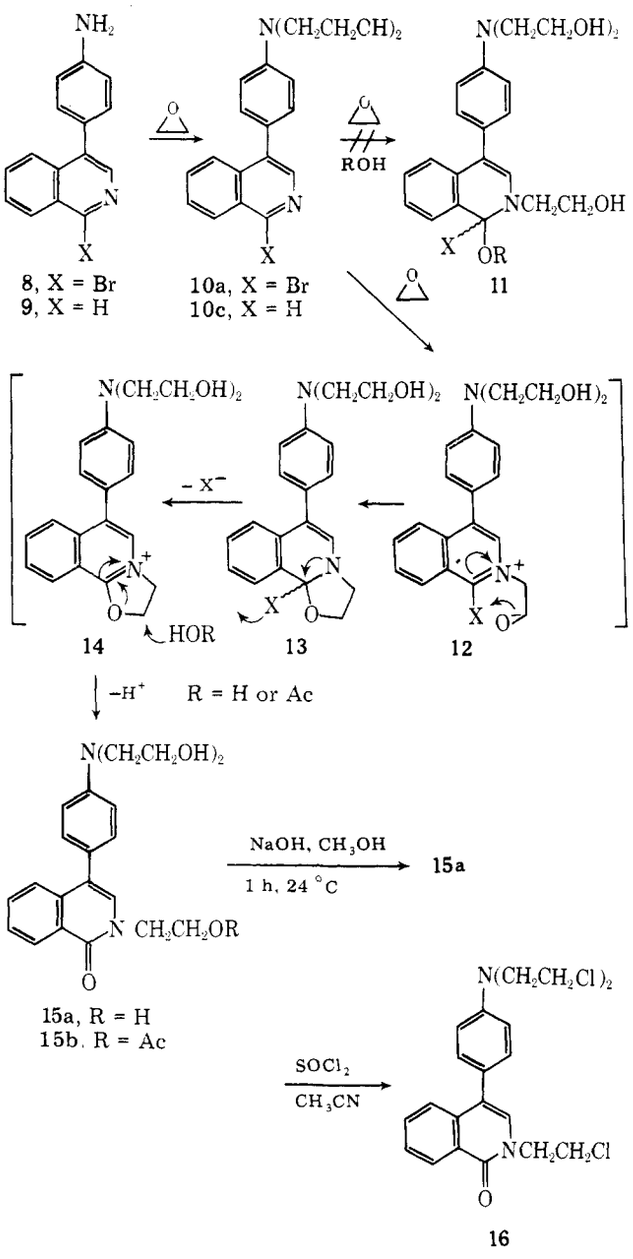
Scheme I



salt (**14**) formation.[5] The regiospecific attack of available nucleophile (H_2O or HOAc) on oxazolinium salt **14** at the methylene carbon adjacent to oxygen is precedented in analogous systems.[6a-c] Treatment of **8** in anhydrous CH_3OH with 30–60 equiv of ethylene oxide, with and without acid catalyst (TsOH), for 1–2 days led to a mixture of **10a** (26%) and **10b** (41%). No isoquinolone formation was noted.

Treatment of 3,4-dihydroisoquinoline with ethylene oxide has been shown by Schneider and Müller to yield an oxazolidine.[7] In our hands, the reaction of isoquinoline (**17**) and excess ethylene oxide at room temperature in acetic acid yielded transient intermediate **18** of undetermined structure which rapidly converted to oxazolidine **19** in 35% yield. No isoquinolone formation was observed. Compound **19** was stable for several days at room temperature in $CDCl_3$ solution, but while standing in air overnight it decomposed to a violet TLC (silical gel) immobile residue.[8] The structure of oxazolidine **19** as displayed in Scheme II is compatible with ^1H and ^{13}C NMR (Table I), IR, UV, and high- and low-resolution mass spectra.

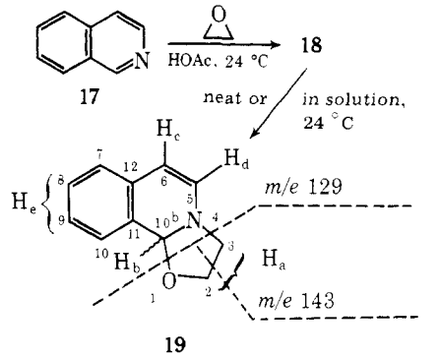
Analogues of **19** with substitution at positions 2 and 3 have been reported by the reaction of *N*-benzylisoquinolinium halides with aldehydes.[9a,b] Furthermore, several methods of preparing more stable 5,6-dihydro analogues of **19** have been described.[7,10a-f] The present method represents an example of oxazolidine formation via epoxide insertion into an aromatic C=N bond. Unlike the reaction of isoquinoline and ethylene oxide, no oxazolidine was isolated from the reaction of **8** or **9** and ethylene oxide. The presence of the 4-phenyl group in putative oxazolidine intermediate **13** may promote oxazolinium salt (**14**) formation by facilitating leaving group (X) explusion. The lack of either isoquinolone or oxazolidine products when **1** or **3** is treated with ethylene oxide may reflect the decreased isoquinoline nitrogen nucleophilicity of **1** and **3**. In view of these observations, we are currently measuring pK_a values for this series of compounds.

Table I. NMR Spectra of 19[a]

^1H NMR	^{13}C NMR[b]
H_a 3.60 (m, 4)	C_2 62.307
H_b 5.25 (d, 1, $J_{b,d}$ = 0.5 Hz)	C_3 59.297
H_c 5.65 (d, 1, $J_{c,d}$ = 7.0 Hz)	C_5 130.486
H_d 6.30 (dd, 1, $J_{b,d}$ = 0.5 Hz, $J_{c,d}$ = 7.0 Hz)	C_6 102.529
H_e 7.50–7.00 (m, 4)	C_7 123.664[c]
	C_8 128.945
	C_9 124.842[c]
	C_{10} 133.899
	C_{10b} 76.122
	C_{11} 121.329
	C_{12} 134.441

[a] In $CDCl_3$. Chemical-shift values in parts per million downfield from internal $(CH_3)_4Si$. Proton and carbon assignments are shown in Scheme II. [b] Carbon assignments are based on both noise-decoupled and gated spectra with H irradiation applied during 0.33-s pulse delay after data acquisition. [c] The chemical-shift assignments for C_7 and C_9 are ambiguous and may be reversed.

Scheme II



Experimental Section

General Methods. Evaporations were carried out in a Büchi rotary evaporator in vacuo at temperatures below 50 °C. Melting points were determined on a Thomas-Hoover apparatus (capillary method) and are uncorrected. Analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Samples for analysis were dried at 10^{-2} mm over silica gel at 55 °C. Thin-layer chromatography (TLC) was performed on 7 × 3 cm precoated silica gel 13179 poly(ethylene terephthalate) foils (Eastman Kodak, Rochester, N.Y.). Preparative TLC was carried out on silica gel plates (Analtech, 20 × 20 cm, 2000 μm). Detection was done by UV light (mineral light) or with iodine vapors. The IR spectra were measured in $CHCl_3$ or KBr on a Perkin-Elmer Model 700 spectrophotometer. The ^1H NMR spectra were obtained using a Varian T-60 spectrometer in $CDCl_3$ or CD_3SOCD_3 using $(CH_3)_4Si$ as an internal standard. The ^{13}C NMR spectra were obtained using a Varian XL-100 spectrometer with a Varian 620-I data system in $CDCl_3$ using $(CH_3)_4Si$ as an internal standard. The UV spectra were measured in EtOH using a Beckman DB-G grating spectrophotometer. Mass spectra were determined on a 12-90-G Nuclide (low resolution) mass spectrometer and a Dupont CEC-110 (high resolution) mass spec-

Table II. High-Resolution MS Data for 19

Peak (rel intensity)		Empirical	
Calcd	Found	formula	Assignment
174.09188	174.09349 (2)	$C_{11}H_{12}NO$	$M^+ + 1$
173.08406	173.08787 (3)	$C_{11}H_{11}NO$	M^+
172.07623	172.08023 (4)	$C_{11}H_{10}NO$	$M^+ - 1$
143.07349	143.07539 (20)	$C_{10}H_9N$	$M^+ - CH_2O$
129.05784	129.05969 (100)	C_9H_7N	$M^+ - CH_2CH_2O$

trometer. Tetrahydrofuran (THF) and acetonitrile (CH_3CN) were distilled and dried over Linde molecular sieves prior to use.

1-Bromo-4-*p*-nitrophenylisoquinoline (7). A solution of 1.0 g (2.90 mmol) of amine 6[2a] in 60 mL of dry THF was added to a refluxing solution of 1.0 mL (872 mg, 7.5 mmol) of isoamyl nitrite (Aldrich 99%) in 20 mL of dry THF dropwise over the course of 1 h under N_2. The solution was stirred and refluxed under N_2 for 36 h and then cooled and stripped of excess solvent to yield 1.0 g of a yellow solid. The solid was recrystallized from 40 mL of CH_3CN, yielding 200 mg (21%) of **7** as a yellow solid, mp 216–219 °C. Concentration of the mother liquor to 20 mL and cooling to 4 °C yielded an additional 60 mg (6%) of **7**, mp 216–219 °C. Yields of recrystallized **7** varied from 27 to 43%. Preparative TLC (silica gel eluted with $CHCl_3$–Et_2O–hexane, 1:1:1) afforded an analytical sample of **7** (R_f 0.50): mp 222–224 °C; NMR ($CDCl_3$) δ 8.35 (m, 4), 7.70 (m, 5); IR ($CHCl_3$) 3000, 1600, 1550, 1525, 1355 cm^{-1}; UV_{max} (EtOH) 219 nm (log ϵ 4.47); MS *m/e* (rel intensity) 328 (100) M^+, 330 (96) $M^+ + 2$.

Anal. Calcd for $C_{15}H_9N_2O_2Br \cdot 0.5H_2O$: C, 53.27; H, 2.98; N, 8.29; Br, 23.63. Found: C, 53.50; H, 2.98; N, 8.19; Br, 23.48.

4-*p*-Aminophenyl-1-bromoisoquinoline (8). To a solution of 500 mg (1.5 mmol) of **7** in 10 mL of HOAc and 1.5 mL of concentrated HCl was added 2.0 g (9 mmol) of $SnCl_2 \cdot 2H_2O$ in 2 mL of concentrated HCl dropwise. The reaction was stirred at room temperature overnight and then cooled to 0 °C and filtered free of a yellow precipitate. The precipitate was dissolved in 25 mL of H_2O and the pH was adjusted to 11 with 20% aqueous NaOH. The aqueous solution was extracted with $CHCl_3$. Drying (Na_2SO_4), filtration, and evaporation of the $CHCl_3$ solution yielded 220 mg (49%) of **8** as a yellow solid. Basification and $CHCl_3$ extraction of the original acidic reaction filtrate yielded an additional 150 mg (33%) of amine **8**. Preparative TLC (silica gel eluted with $CHCl_3$–Et_2O–hexane, 1:1:1) afforded an analytical sample of **8** as an off-white amorphous solid (R_f 0.30): mp 152–154 °C; NMR ($CDCl_3$) δ 8.35 (m, 1, 8 H), 8.20 (s, 1, 3 H), 8.00–7.40 (m, 3), 7.30 (d, 2, J = 7 Hz), 6.80 (d, 2, J = 7 Hz), 3.90 (s, 2, NH_2, D_2O exchanges); IR ($CHCl_3$) 3450, 3350, 3000, 1620, 1550, 1520 cm^{-1}; UV λ_{max} (EtOH) 210 (log ϵ 4.46), 221 (4.56), 253 (4.33) nm; MS *m/e* (rel intensity) 298 (98) M^+, 300 (99) $M^+ + 2$.

Anal. Calcd for $C_{15}H_{11}N_2Br \cdot 0.5H_2O$: C, 58.45; H, 3.90; N, 9.09; Br, 25.93. Found: C, 58.71; H, 3.79; N, 8.99; Br, 25.80.

4-*p*-Aminophenylisoquinoline (9). A solution of 100 mg (0.33 mmol) of amine **8** and 100 mg (1 mmol) of Et_3N in 20 mL of absolute EtOH was Parr hydrogenated using 10 mg of 10% Pd/C at 40 psi of H_2 for 2 h (larger runs required longer periods of time and often catalyst change). The reaction was then gravity filtered and stripped of excess solvent. The residue was taken up in $CHCl_3$, washed with H_2O and brine, dried (Na_2SO_4), filtered, and evaporated to yield 66 mg (90%) of amine **9** as a glassy solid. Preparative TLC (silica gel eluted with EtOAc) provided an analytical sample of amine **9** (R_f 0.75): mp 45–55 °C; NMR ($CDCl_3$) δ 9.20 (s, 1, 1 H), 8.50 (s, 1, 3 H), 8.10–7.40 (m, 4), 7.30 (d, 2, J = 7 Hz), 6.80 (d, 2, J = 7 Hz), 4.00 (s, 2, NH_2, D_2O exchanges); IR ($CHCl_3$) 3450, 3350, 3000, 1620, 1570, 1520, 1495 cm^{-1}; UV λ_{max} (EtOH) 219 (log ϵ 4.73), 251 (4.18) nm; MS *m/e* (rel intensity) 220 (100) M^+.

Anal. Calcd for $C_{15}H_{12}N_2 \cdot 0.5H_2O$: C, 78.58; H, 5.71; N, 12.22. Found: C, 78.80; H, 5.30; N, 12.20.

4-[*p*-Bis(2-hydroxyethyl)amino]phenyl-1-bromoisoquinoline (10a) and 1-Bromo-4-*p*-(2-hydroxyethylamino)phenylisoquinoline (10b). A solution of 300 mg (1 mmol) of amine **8** in 10 mL of dry [distilled from $Mg(OCH_3)_2$] CH_3OH and 1.5 mL (30 mmol) of ethylene oxide was allowed to sit at room temperature overnight. After this time solvent evaporation yielded 300 mg of a residue which was purified by preparative TLC (silica gel eluted with EtOAc) to yield 100 mg (25.8%) of diol **10a** (R_f 0.29): mp 73–78 °C; NMR ($CDCl_3$) δ 8.30 (m, 1, 8 H), 8.10 (s, 1, 3 H), 8.00–6.60 (m, 7), 4.50 (s, 2, OH, D_2O exchanges), 3.70 (m, 8); IR ($CHCl_3$) 3300, 3000, 1600, 1550, 1518, 1440, 1400 cm^{-1}; UV λ_{max} (EtOH) 213 (log ϵ 4.58), 221 (4.61), 266 (4.31) nm; MS *m/e* (rel intensity) 386 (52) M^+, 388 (41) $M^+ + 2$, 355 (100) $M^+ - CH_2OH$, 357 (69) $M^+ + 2 - CH_2OH$.

Anal. (molecular ion) calcd for $C_{19}H_{19}N_2O_2Br$: 386.06298, 388.06094. Found: 386.06288, 388.05888.

Alcohol **10b** (R_f 0.58) was isolated as a bright-yellow solid (140 mg, 40.8%): mp 149–152 °C; NMR ($CDCl_3$, CD_3SOCD_3) δ 8.30 (m, 1, 8 H), 8.15 (s, 1, 3 H), 8.00–6.70 (m, 7), 5.0 (s, 1, NH, D_2O exchanges), 4.50 (t, 1, J = 6 Hz, OH, D_2O exchanges), 3.80 (t, 2, J = 5 Hz, CH_2OH), 3.35 (t, 2, J = 5 Hz, CH_2NH); IR (KBr) 3250, 1600, 1520, 1440 cm^{-1}; UV λ_{max} (EtOH) 213 (log ϵ 4.55), 220 (4.61), 2.59 (4.25) nm; MS *m/e* (rel intensity) 342 (42) M^+, 344 (42) $M^+ + 2$, 311 (100) $M^+ - CH_2OH$, 313 (99) $M^+ + 2 - CH_2OH$.

Anal. Calcd for $C_{17}H_{15}N_2OBr$: C, 59.48; H, 4.41; N, 8.16; Br, 23.28. Found: C, 59.54; H, 4.60; N, 8.03; Br, 23.05.

4-[*p*-Bis(2-hydroxyethyl)amino]phenyl-2-(2-hydroxyethyl)-1-isoquinolone (15a) and Monoacetate (15b). From Amine 8. To 1.0 g (3.33 mmol) of amine **8** in 20 mL of glacial HOAc was added all at once 5 mL (100 mmol) of ethylene oxide at room temperature. After standing overnight at room temperature, the reaction was poured into 100 mL of ice water and basified with excess 20% aqueous NaOH. The solution was then extracted with $CHCl_3$. The $CHCl_3$ solution was washed with brine, dried (Na_2SO_4), filtered, and evaporated to yield 1.50 g of a froth. Purification by preparative TLC (silica gel eluted with 10% CH_3OH in EtOAc) yielded 620 mg (51%) of **15a** as a major product (R_f 0.30), negative Beilstein test: mp 75–80 °C; NMR (CD_3SOCD_3) δ 8.25 (m, 1, 8 H), 7.60–6.60 (m, 8), 4.40 (s, 3, D_2O exchanges), 4.10 (t, 2, J = 5 Hz, $CONCH_2$–), 3.60 (m, 10); IR ($CHCl_3$) 3350, 3000, 1639 (lactam C=O), 1610, 1590, 1520 cm^{-1}; UV λ_{max} (EtOH) 210 (log ϵ 4.54), 224 (4.31), 266 (4.31) nm; MS *m/e* (rel intensity) 368 (72) M^+, 366 (20) $M^+ - 2$ H, 337 (100) $M^+ - CH_2OH$. Anal. (molecular ion) Calcd for $C_{21}H_{24}N_2O_4$: 368.17360. Found: 368.17601.

Anal. Calcd for $C_{21}H_{24}N_2O_4 \cdot H_2O$: C, 65.27; H, 6.78; N, 7.25. Found: C, 65.55; H. 6.40; N, 7.18.

Monoacetate **15b** (R_f 0.60) was isolated as an oil (340 mg, 25%) contaminated with a small amount of **15a**. Spectra of monoacetate **15b**: NMR ($CDCl_3$) δ 8.50 (m, 1, 8 H), 7.60–6.60 (m, 8), 4.50–4.10 (m, 4), 4.00–3.50 (m, 8), 2.05 (s, 3, $COCH_3$); IR ($CHCl_3$) 3400, 3000, 1740 (acetate C=O), 1645 (lactam C=O), 1620, 1520 cm^{-1}; MS *m/e* (rel intensity) 410 (17) M^+, 379 (44) $M^+ - CH_2OH$. Anal. (molecular ion − 1) Calcd for $C_{23}H_{26}N_2O_5$: 409.17634. Found: 409.17856.

Mixtures of **15a** and **15b** were gently saponified with 1 equiv of NaOH in aqueous CH_3OH at room temperature for 2 h, yielding pure **15a**.

Diol **10a** could be isolated as the initial product of amine **8** and ethylene oxide after short (2 h) reaction times. In particular, 200 mg (0.66 mmol) of **8** yielded after workup and purification by preparative TLC (silica gel eluted with EtOAc) 70 mg (27%) of a froth (R_f 0.30), mp 73–78 °C, whose TLC mobility and IR and NMR spectra were identical to that of an authentic sample of **10a**.

From Amine 9. A solution of 700 mg (3.20 mmol) of amine **9** and 4.0 mL (80 mmol) of ethylene oxide in 20 mL of HOAc was allowed to sit at room temperature overnight. Workup in the usual fashion yielded 960 mg of a crude froth whose TLC (silica gel eluted with 10% CH_3OH in EtOAc) revealed the presence of isoquinolones **15a** and **15b**. In particular, preparative TLC (silica gel eluted with 10% CH_3OH in EtOAc) gave as a major product (R_f 0.30) 400 mg (34%) of a froth, mp 75–80 °C, whose TLC mobility and IR and NMR spectra were identical to isoquinolone **15a**. Conducting the reaction with the rigorous exclusion of O_2 resulted in a mixture of as yet unidentified products with no evidence of isoquinolone formation by IR.

4-[*p*-Bis(2-chloroethyl)amino]phenyl-2-(2-chloroethyl)-1-isoquinolone (16). To 300 mg (0.82 mmol) of **15a** in 70 mL of dry (stored over 4-Å molecular sieves) CH_3CN was added 0.125 mL (1.72 mmol) of $SOCl_2$ at room temperature. An immediate precipitate was observed but dissolved in the course of 1 h. After stirring overnight at room temperature, excess CH_3CN was stripped off and the residue was taken up in 40 mL of $CHCl_3$ and vigorously shaken with 1.0 g of $KHCO_3$ in 40 mL of H_2O. Drying (Na_2SO_4), filtration, and evaporation of the $CHCl_3$ solution yielded 424 mg of a brown froth. Purification by preparative TLC (silica gel eluted with $CHCl_3$–Et_2O–hexane, 2:1:1) afforded as a main product 170 mg (49%) of mustard **16** (R_f 0.50), positive Epstein and Beilstein tests: mp 171–173 °C; NMR ($CDCl_3$) δ 8.50 (m, 1, 8 H), 7.70–6.60 (m, 8), 4.35 (t, 2, J = 5 Hz, $CONCH_2$–), 4.10–3.50 (m, 10); IR ($CHCl_3$) 3000, 1650 (lactam C=O), 1620, 1520 cm^{-1}; UV λ_{max} (EtOH) 210 (log ϵ 4.65), 224 (4.43), 266 (4.43) nm; MS *m/e* (rel intensity) 422 (68) M^+, 424 (63) $M^+ + 2$, 426 (21) $M^+ + 4$, 373 (100) $M^+ - CH_2Cl$, 375 (79) $M^+ + 2 - CH_2Cl$, 377 (14) $M^+ + 4 - CH_2Cl$.

Anal. Calcd for $C_{21}H_{21}N_2Cl_3O$: C, 59.52; H, 5.00; N, 6.61; Cl, 25.10. Found: C, 59.38; H, 5.05; N, 6.50; Cl, 25.02.

2,3-Dihydro-10b*H*-oxazolo[2,3-*a*]isoquinoline (19). A solution

of 1.0 g (7.70 mmol) of isoquinoline and 12 mL (240 mmol) of ethylene oxide in 50 mL of glacial HOAc was allowed to sit at room temperature overnight. The solution (clear and colorless) was then cooled to 0 °C, basified with 20% aqueous NaOH, and extracted with $CHCl_3$. Drying (Na_2SO_4), filtration, and evaporation yielded 1.39 g of a yellow oil 18 that gradually turned deep red: NMR ($CDCl_3$) δ 7.20 (m, 4), 6.15 (d, 1, J = 7 Hz), 5.65 (d, 1, J = 7 Hz), 5.60 (s, 1), 3.50 (s, 4); IR ($CHCl_3$) 3000, 2940, 2875, 1625, 1560, 1490, 1460, 1430 cm^{-1}. After sitting overnight, the now red viscous oil was purified by preparative TLC (silica gel eluted with $CHCl_3$–Et_2O–hexane, 1:1:1) to yield 465 mg (35%) of oxazolidine **19** (R_f 0.50) as a viscous yellow oil. With exposure to air the oil turned violet: for ^1H and ^{13}C NMR ($CDCl_3$), see Table I; IR ($CHCl_3$) 3050, 3000, 2910, 1620, 1600, 1560, 1480, 1175 (OCN),[11a] 1120 (OCN),[11a] 1060 (OCN),[11a] 830 (OCN)[11b] cm^{-1}; UV λ_{max} (EtOH) 208 nm (log ε 3.97), 231 (3.67), 246 (3.45); For high-resolution MS data, see Table II.

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Registry No.—**6,** 31309-65-6; **7,** 64345-81-9; **8,** 64345-80-8; **9,** 64345-79-5; **10a,** 64345-78-4; **10b,** 64345-76-2; **15a,** 64345-77-3; **15b,** 64345-75-1; **16,** 64345-74-0; **19,** 64345-73-0; ethylene oxide, 75-21-8; $CHCl_3$, 67-66-3; isoquinoline, 119-65-3.

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Ozonation of Nucleophiles. 7.[1] Dibenzyl Sulfides

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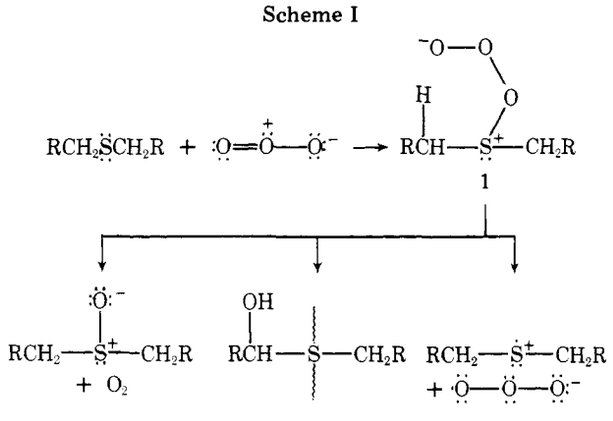
Ozonation of dibenzyl sulfide and two unsymmetrical benzyl sulfides afforded both sulfur and alkyl side-chain oxidation products. Sulfur oxidation was predominant in protic solvents and side-chain oxidation in hydrocarbon solvents. Ozonation of thianthrene produced the monoxide as the major product and the cation radical as a minor product. Mechanistic pathways are discussed.

Earlier papers in this series[1-5] elucidated the mechanistic pathways involved in the reactions of ozone with various types of aliphatic amines. After the initial reaction between the electrophilic ozone and the nucleophilic amine, four fates of the resulting adduct were proposed. Reactions analogous to the initial attack and three of the adduct fates should also be possible with suitable organic sulfides, as illustrated in Scheme I. These include sulfoxide formation (the only reaction previously shown to occur),[6-12] intramolecular side-chain oxidation, and cation-radical formation. It was the purpose of the present research to test this premise.

Scheme I



The ozonation of organic sulfides has been studied previously by several workers.[6-12] In all cases the only products isolated were the corresponding sulfoxides and/or sulfones, usually in high yields, although Barnard[11] reported the odor of butyraldehyde and butyric acid on the crude sulfone obtained from dibutyl sulfide. Maggiolo and Blair[9] and Horner et al.[10] found 1:1 and 1:2 sulfide–ozone stoichiometry in the conversions to sulfoxide and sulfone, respectively. For this and other reasons they[9,10] proposed electrophilic ozone attack, followed by loss of molecular oxygen from the adduct, as shown in Scheme I, followed by a similar attack on the sulfoxide. On the other hand, Barnard,[11] Boer and Kooyman,[8] and Thompson[12] stated that less than 1 mol of ozone per mole of sulfide was required. Thompson[12] found that close to three oxygen atoms (of ozone) per atom of sulfur participated in the oxidation.

In the earlier work just outlined,[6-12] protic solvents such as chloroform or water were used. Our studies were conducted with four different sulfides in both protic and nonprotic solvents and at two different temperatures. Table I displays the results obtained from ozonations of dibenzyl sulfide and of

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