1a was added to the homogenate with the expectation that any naturally occurring 1a would mix with this and be reisolated. Careful purification of 1a after reisolation demonstrated *no* activity to be present. This work was presented at the Montana Academy of Sciences, Dillon, Mont., 1973.

(4) See L. N. Ferguson in "Highlights of Alicyclic Chemistry," Franklin Publishing Corp., Palisade, N. J., 1973, for a well-documented review on cyclopropane chemistry.
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Facile Addition of Bromine to a Reissert Compound

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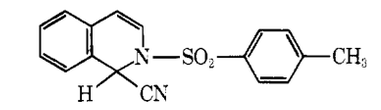
The chemistry of Reissert compounds has been reviewed in detail.[1] Dihydro Reissert compounds have been described by Shamma, *et al.*;[2] their nmr data have been studied by Bramley and Johnson.[3] This note describes the facile addition of bromine to Reissert compound **1** and the tentative stereochemistry of the vicinal dibromide **2** and its derivatives.

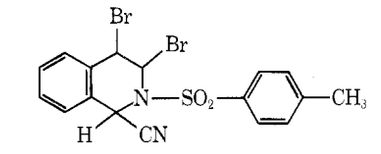
The bromination of isoquinoline is reported to give 4-bromoisoquinoline under drastic conditions.[4] A mechanism involving the addition of bromine followed by the elimination of hydrogen bromide has been postulated.[5] The dibromide has eluded isolation and characterisation. 1-Cyano-2-*p*-toluenesulfonyl-1,2-dihydroisoquinoline (**1**) was prepared according to the method described by Wefer, *et al.*[6] The bromination of **1** took place readily to give 1-cyano-3,4-*cis*-dibromo-2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (**2**), which could be isolated and characterized. The analytical values and the spectral data were in agreement with structure **2**. Refluxing **2** with ethanol and 2-propanol gave **5** and **6**, respectively. Treatment of **2** with aqueous sodium bicarbonate gave 4-bromo-1-cyano-3-hydroxy-1,2,3,4-tetrahydroisoquinoline (**7**). The above α-amino alcohol **7** would be expected to exist in equilibrium with the open-chain structure **8** in solution. However, poor solubility of the compound in solvents such as $CHCl_3$ and CCl_4 precluded such a study. The ir spectrum of **7** in Nujol showed bands at 3350 and 1700 cm^{-1}, showing evidence for the δ-amino aldehyde structure **8**. In the nmr spectrum of the compound in CD_3SOCD_3 the signal corresponding to the aldehydic proton was not discernible, showing the absence of any significant amount of **8** in solution.

That the addition of bromine to **1** may take place in the cis fashion is shown by the magnitude of the coupling constant of C_3 and C_4 protons in **2** (J = 2.5 Hz). The above coupling constant is consistent also with a configuration in which the bromine atoms are trans and diaxial. However, it is highly unlikely that the bromine atoms would be axial. The magnitude of the coupling constants of C_3 and C_4 protons in **5**, **6**, and **7** remains of the same order as in **2**, indicating a cis orientation of the hydrogen atoms. The facile formation of the above compounds can be visualised as the addition of elements of ethanol, 2-propanol, or water to the iminium species **3** or the enamine **4**.

Treating **2** with 1 mol of morpholine in dioxane gave 4-bromo-1-cyano-2-*p*-toluenesulfonyl-1,2-dihydroisoquinoline (**4**), in which the C_1 proton occurs as a doublet (J = 0.5 Hz). This is in agreement with the observations of Chhabra, *et al.*,[7] on the long-range spin coupling in isoquinoline Reissert compounds. In the presence of morpholine, a facile trans-diaxial elimination of the elements of hydrogen bromide can be postulated for the formation of **4** from **2**. However, the pathway involving the formation of iminium species **3** and loss of proton to give **4** cannot be ruled out under the above conditions. Confirmation of the product as **4** was obtained by establishing its identity with the product obtained by Reissert reaction on 4-bromoisoquinoline. Refluxing **2** with 3 mol of morpholine in dioxane caused elimination of *p*-toluenesulfonic acid along with hydrogen bromide to give 4-bromoisoquinaldonitrile (**9**). The latter compound has also been obtained by Wefer, *et al.*,[6] by use of sodium hydride in xylene.



1



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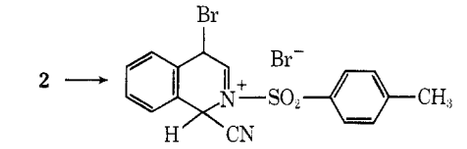

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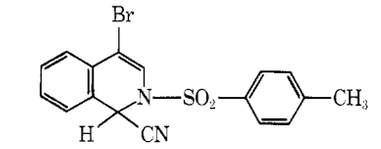
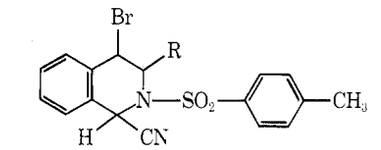
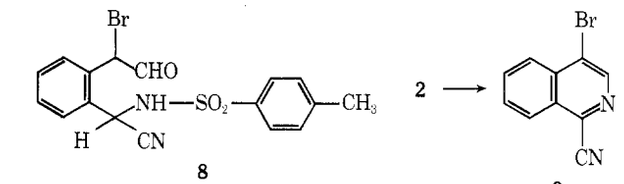


4



5, R = OC_2H_5
6, R = $OCH(CH_3)_2$
7, R = OH



8 **9**

Experimental Section

Melting points are uncorrected. The ir spectra were examined as Nujol mulls on a Perkin-Elmer Model 421 spectrophotometer. The uv spectra in 95% ethanol were recorded on a Beckman Model DK-2A spectrophotometer and the nmr spectra were recorded on a Varian Associates A-60 spectrometer with TMS as internal standard.

1-Cyano-2-*p*-toluenesulfonyl-1,2-dihydroisoquinoline (1). The above compound was prepared in 52% yield according to the procedure of Wefer, *et al.*:[6] mp 101°: ir 1620 and 1170 cm^{-1}; uv max 227 nm (log ϵ 4.26) and 285 (3.93); nmr ($CDCl_3$) δ 2.31 (s, 3 H, ArCH_3), 6.11 (d, 1 H, J = 6 Hz, C_4 H), 6.18 (d, 1 H, J = 0.6 Hz, C_1 H), 6.80 (d, 1 H, J = 6 Hz, C_3 H), 6.95–7.90 (m, 8 H, aromatic).

3,4-*cis*-Dibromo-1-cyano-2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (2). To a solution of 12.41 g (0.04 mol) of **1** in 150 ml of chloroform was added gradually 7.04 g (0.044 mol) of bromine in 40 ml of chloroform at room temperature and the solution was stirred for 4 hr. Evaporation of the solvent gave a residue, which crystallized on trituration with ether. It was recrystallized

from methylene chloride–ether to give 6.5 g (34.5%) of yellow crystals: mp 118–118.5°; ir 1595 cm^{-1}; uv 228 nm (log ϵ 4.29); nmr δ 2.42 (s, 3 H, $ArCH_3$), 5.62 (d, 1 H, J = 2.5 Hz, C_4 H), 6.11 (s, 1 H, C_1 H), 6.88 (d, 1 H, J = 2.5 Hz, C_3 H), 7.3–7.55 (m, 6 H, aromatic), 7.9–8.05 (m, 2 H, aromatic). *Anal.* Calcd for $C_{17}H_{14}Br_2N_2O_2S$: C, 43.43; H, 3.00; Br, 34.00. Found: C, 43.72; H, 3.29; Br, 34.32.

4-Bromo-1-cyano-3-ethoxy-2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (5). A mixture of 2.0 g of **2** and 20 ml of absolute ethanol was stirred under reflux for 4 hr. The clear solution obtained was evaporated to dryness. Addition of ether and filtration yielded 1.1 g (59.4%) of colorless crystals of **5**: mp 163°, raised to 169° by recrystallisation from methylene chloride–hexane; ir 1600 cm^{-1}; uv 230 nm (log ϵ 4.32); nmr ($CDCl_3$) δ 1.20 (t, 3 H, CCH_3), 2.38 (s, 3 H, $ArCH_3$), 3.80 (q, 2 H, OCH_2), 5.28 (d, 1 H, J = 2.5 Hz, C_4 H), 5.70 (s, 1 H, C_1 H), 5.82 (d, 1 H, J = 2.5 Hz, C_3 H), 7.22–7.40 (m, 6 H, aromatic H), and 7.88–8.05 (m, 2 H, aromatic H).

Anal. Calcd for $C_{19}H_{19}BrN_2O_3S$: C, 52.42; H, 4.39; N, 6.44. Found: C, 52.20; H, 4.49; N, 6.72.

4-Bromo-1-cyano-3-isopropoxy-2-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (6). A mixture of 3 g of **2** and 20 ml of 2-propanol was stirred under reflux for 4 hr. The clear solution was worked up under conditions described for **5** to give 2.2 g (76.8%) of colorless crystals of **6**: mp 162°, raised to 166° by recrystallisation from 2-propanol; ir and uv were similar to those of **5**; nmr ($CDCl_3$) δ 1.22 (t, 3 H, CCH_3), 2.40 (s, 3 H, $ArCH_3$), 4.12 (m, 1 H, OCH) 5.21 (d, 1 H, J = 2.5 Hz, C_4 H) 5.72 (s, 1 H, C_1 H) 5.90 (d, 11 H, J = 2.5 Hz, C_3 H), 7.22–7.40 (m, 6 H, aromatic H), and 7.88–8.05 (m, 2 H, aromatic H).

Anal. Calcd for $C_{20}H_{21}BrN_2O_3S$: C, 53.46; H, 4.71; N, 6.24. Found: C, 53.29; H, 4.91; N, 6.03.

4-Bromo-1-cyano-3-hydroxy-2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (7). To a solution of 2 g of **2** dissolved in 50 ml of chloroform was added 10 ml of a saturated aqueous solution of sodium bicarbonate and the solution was stirred overnight at room temperature. The chloroform layer was separated, dried over Na_2SO_4, and evaporated. After trituration with methylene chloride–ether the colorless crystals obtained were filtered to give 0.2 g (11.5%) of **7**: mp 177–178° (recrystallization from 2-propanol raised the melting point to 184°); ir (Nujol) 3350 and 1700 cm^{-1}; uv λ_{infl} 226 nm (log ϵ 4.32); nmr ($CDCl_3$, CD_3SOCD_3)[8] δ 2.35 (s, 3 H, $ArCH_3$), 5.25 (d, 1 H, J = 2.5 Hz, C_4 H), 5.85 (s, 1 H, C_1 H), 6.08 (d, 1 H, J = 2.5 Hz, C_3 H), 7.22–7.40 (m, 6 H, aromatic H), 7.75–8.00 (m, 2 H, aromatic H). *Anal.* Calcd for $C_{17}H_{15}BrN_2O_3S$: C, 50.14; H, 3.71; N, 6.88. Found: C, 50.14; H, 3.69; N, 7.15.

4-Bromo-1-cyano-2-*p*-toluenesulfonyl-1,2-dihydroisoquinoline (4). A. By Base Treatment of 2. A solution of 2.35 g (0.005 mol) of **2** in 30 ml of dioxane containing 0.44 g (0.005 mol) of morpholine was stirred for 6 hr at room temperature. The solution was evaporated to dryness under reduced pressure. Dilution with water and filtration gave 1.12 g (57.5%) of **4**: mp 161° (recrystallization from methylene chloride–ether raised the melting point to 164°); ir 1598 cm^{-1}; uv 232 nm (log ϵ 4.31) and 298 (3.99); nmr ($CDCl_3$) δ 2.35 (s, 3 H, $ArCH_3$), 6.15 (d, 1 H, J = 0.5 Hz, C_1 H), 7.15 (d, 1 H, J = 0.5 Hz, C_3 H), 7.22–7.45 (m, 6 H, aromatic H), 7.65–7.85 (m, 2 H, aromatic H). *Anal.* Calcd for $C_{17}H_{13}BrN_2O_2S$: C, 52.46; H, 3.37; N, 7.20. Found: C, 52.72; H, 3.70, N, 7.03.

B. By Reissert Reaction. To a suspension of 20.8 g (0.1 mol) of 4-bromoisoquinoline in methylene chloride (60 ml) containing 19.5 g (0.3 mol) of potassium cyanide in 48 ml of water was added gradually under vigorous stirring 57.0 g (0.3 mol) of *p*-toluenesulfonyl chloride in 40 ml of methylene chloride and stirring was continued for 6 hr. The methylene chloride layer was separated and washed with 10% aqueous hydrochloric acid, 5% aqueous sodium hydroxide, and finally water. It was dried over Na_2SO_4 and evaporated. On trituration of the residue with ether 22.5 g (57.85%) of **4** was obtained which was identical in all respects with the product obtained by procedure A.

1-Cyano-4-bromoisoquinoline (9). A solution of 2.35 g (0.005 mol) of **2** in 70 ml of dioxane containing 1.29 g (0.015 mol) of morpholine was refluxed for 4 hr. The solution was evaporated to dryness under reduced pressure. The residue was treated with sodium bicarbonate solution followed by water. Trituration with 2-propanol gave 0.92 g (78.9%) of **9**, mp 123°. Recrystallization from hexane afforded pure crystals of **9**: mp 125° (lit.[6] mp 122–123°); ir 1605 and 1550 cm^{-1}; uv 233 nm (log ϵ 4.62) and 339 (3.92). *Anal.* Calcd for $C_{10}H_5BrN_2$: C, 51.53; H, 2.16; N, 12.02. Found: C, 51.74; H, 2.27; N, 12.19.

Registry No.—**1**, 3340-68-9; **2**, 51270-04-3; **4**, 51270-05-4; **7**, 51270-06-5; **9**, 27224-09-5; bromine, 7726-95-6; 4-bromoisoquinoline, 1532-97-4; *p*-toluenesulfonyl chloride, 98-59-9; morpholine, 110-91-8.

References and Notes

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(2) M. Shamma and C. D. Jones, *J. Org. Chem.*, **35**, 3119 (1970).
(3) R. Bramley and M. D. Johnson, *J. Chem. Soc.*, 1372 (1965).
(4) E. E. Garcia, C. V. Greco, and I. M. Hunsberger, *J. Amer. Chem. Soc.*, **82**, 4430 (1960).
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(6) J. M. Wefer, A. Catala, and F. D. Popp, *J. Org. Chem.*, **30**, 3075 (1965).
(7) S. R. Chhabra, J. R. Kershaw, and B. C. Uff, *Tetrahedron Lett.*, 3199 (1967).
(8) Drops of CD_3SOCD_3 were added to the compound suspended in $CDCl_3$ until a homogenous solution was formed.

Medium-Ring Systems.[1] IV. Synthesis of Spiro[2.*n*]alkan-5-ones. Neighboring Hydroxyl in a Hofmann Elimination

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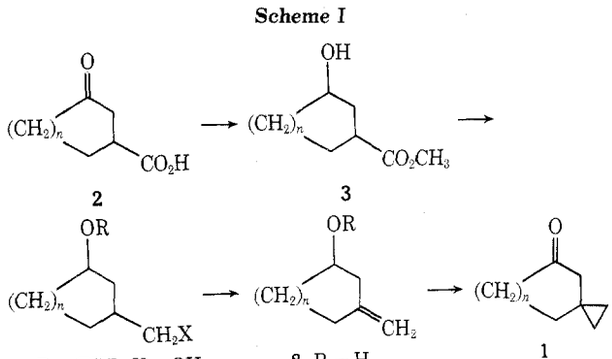
As a part of a study of the properties of medium-ring systems,[1] we have prepared spiro[2.7]decan-5-one (**1a**) and spiro[2.9]dodecan-5-one (**1b**) by the general route indicated in Scheme I. The appropriate 3-carboxycycloalkanones[1a] (**2**) were converted to the corresponding methyl 3-hydroxycycloalkanecarboxylates (**3**) by a reported procedure.[1b] The alcohol group was protected as the tetrahydropyranyl ether,[3] and the ester functionality was reduced to the alcohol level (**4**) with equimolar amounts of lithium aluminum hydride.[4] Attempts to directly dehydrate these alcohols using phosphorus oxychloride[5] or thionyl chloride[6] led to recovery of unreacted starting material.

Work[7] with cyclohexylmethanol and cyclooctylmethanol suggested that bromination with phosphorus tribromide in pyridine and benzene[8] followed by dehydrobromination with potassium *tert*-butoxide in dimethyl sulfoxide[9] might be the method of choice, but the bromination reaction

Scheme I



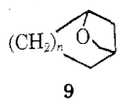
2 **3**

4, R = THP; X = OH
5, R = THP; X = OTs
6, R = H; X = $N(CH_3)_2$
7, R = H; X = $N^+(CH_3)_3{}^-OH$
11, R = CH_3; X = $N(CH_3)_2$

8, R = H
10, R = CH_3

1

a, $n = 4$
b, $n = 6$



9

a, $n = 4$
b, $n = 6$