The original mother liquor consisted mainly of ethyl acetoacetate and some IX according to gas chromatography.

**Reaction of Diketene with Acetic Acid.**—DABCO (1.0 g) was added to glacial acetic acid (60 g, 1.0 mole). Diketene (84 g, 1.0 mole) was added slowly at 25–50° over a period of 1 hr. After the addition the mixture was kept at 45–50° until carbon dioxide stopped evolving. The mixture was cooled to 0° and filtered to give 8.6 g of IX, mp 102–105° (mixture melting point with a pure sample of IX showed no depression). The filtrate was then fractionally distilled. The first fraction of the distillate was identified by infrared spectroscopy as acetone, while the later fractions were a mixture of unchanged acetic acid and acetic anhydride. On filtering the residue, 14.4 g of a solid identified as III was obtained, mp 128–132°. Gas chromatographic analyses indicated that the filtrate also contained about 7 g of II.

**Reaction of Diketene with Hydrogen Sulfide.**—DABCO (0.5 g) was dissolved in benzene (200 ml) containing about 2 g of hydrogen sulfide. Diketene (84 g, 1.0 mole) was added over a period of 2 hr at 18–20° while hydrogen sulfide (17 g) was also bubbled through. After the addition the mixture was kept at 20° for 2 hr and then at 40° for a few hours longer until gas ceased to evolve. The gas was identified by mass spectroscopy as carbonyl sulfide. Gas chromatographic analyses indicated that the reaction mixture contained mainly IX, and small amounts of II and III. The combined yield of II and III was approximately 10%.

# Synthesis of *cis*- and *trans*-7-Azabicyclo[4.2.0]octanes[1-3]

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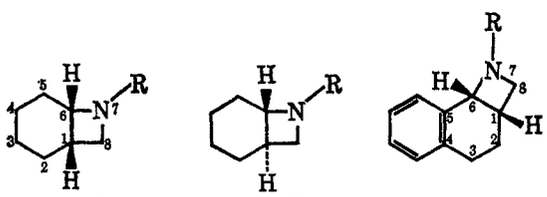
Base treatment of N,O-ditosyl-*trans*-2-aminomethylcyclohexanol (**8**) and N,O-ditosyl-*cis*-2-aminocyclohexanemethanol (**12**) led to the identical fused-ring azacyclobutane derivative, 7-tosyl-*cis*-7-azabicyclo[4.2.0]octane (**1a**). Similar treatment of N,O-ditosyl-*trans*-2-aminocyclohexanemethanol (**16**) converted it to 7-tosyl-*trans*-7-azabicyclo[4.2.0]octane (**2a**). Reductive detosylation of **1a** and **2a** with sodium in isoamyl alcohol led, respectively, to the previously unreported parent heterocycles, *cis*- (**1b**) and *trans*-7-azabicyclo[4.2.0]octane (**2b**). The adduct, 7-chlorosulfonyl-8-ketobenzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (**17**), prepared by chlorosulfonyl isocyanate addition to 1,2-dihydronaphthalene, was reduced with lithium aluminum hydride to benzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (**3a**). Unstable **1b**, **2b**, and **3a** were converted to their equally unstable N-methyl derivatives *via* the Eschweiler–Clarke procedure.

We have applied an interest in both strained bicyclic compounds[4] and ring-fused azacyclobutanes[5] to the successful synthesis of the previously unreported parent heterocycles, *cis*- (**1b**) and *trans*-7-azabicyclo[4.2.0]-octane (**2b**),[7,8] and benzo[*d*]-*cis*-7-azabicyclo[4.2.0]-octane (**3a**).



**1a**, R = Ts; **b**, R = H; **c**, R = $CH_3$



**2a**, R = Ts; **b**, R = H; **c**, R = $CH_3$



**3a**, R = H; **b**, R = $CH_3$

In the reaction sequence summarized in Chart I, the key compound required was the N,O-ditosylate (**8**) of the known *trans*-2-aminomethylcyclohexanol (**7**).[10] The less stable conformer of **8** would have the two *trans*-axial tosyl-substituted groups most favorably situated for ring closure to a *cis*-fused azacyclobutane.

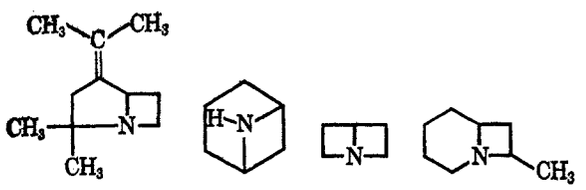
(1) This research was supported by the Directorate of Chemical Sciences, Air Force Office of Scientific Research under Grant AF-AFOSR-488-64.

(2) Taken entirely from the Ph.D. Thesis of P. H. M., Fordham University, 1966.

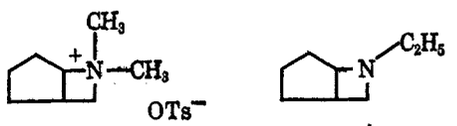
(3) Presented, in part, at the 4th Annual Metropolitan Regional Meeting of the American Chemical Society, Hoboken, N. J., Feb 1, 1965, and before the Organic Division at the 150th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 14, 1965; Abstracts, p 18S.

(4) See J. Meinwald, J. T. Tufariello, and J. J. Hurst, *J. Org. Chem.*, **29**, 2914 (1964), for leading references and a discussion of highly strained *trans*-fused bicyclic compounds.

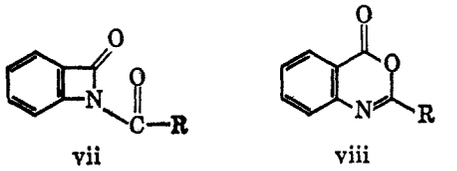
(5) Aside from the penicillins which contain a fused β-lactam system, authentic examples of fused azacyclobutanes include: 2,2-dimethyl-4-isopropylidene-1-azabicyclo[3.2.0]heptane (i),[6a] 6-azabicyclo[3.1.1]heptane (ii),[6b] 1-azabicyclo[2.2.0]hexane (iii),[6c] two diastereoisomers of 8-methyl-1-azabicyclo[4.2.0]octanes (iv),[6d] N,N-dimethyl-6-azabicyclo[3.2.0]heptane tosylate (v),[6e] and 6-azabicyclo[3.2.0]heptane (vi).[6f] The so-called acylanthranils (vii)[6g] have been shown to have the isomeric benzoxazine structure (viii).[6h]



i ii iii iv



v vi



vii viii

(6) (a) A. I. Meyers and W. Y. Libano, *ibid.*, **26**, 1682 (1961); (b) J. V. Braun, W. Haensel, and F. Zobel, *Ann.*, **462**, 283 (1928); (c) C. A. Grob, *Helv. Chim. Acta*, **47**, 2145 (1964); (d) K. Loffler, *Ber.*, **37**, 1879 (1904); K. Loffler and A. Grosse, *ibid.*, **40**, 1325 (1907); K. Loffler and H. Remmler, *ibid.*, **43**, 2048 (1910); (e) C. A. Grob, *Bull. Soc. Chim. France*, 1360 (1960); (f) P. G. Gassman and D. C. Heckert, *Tetrahedron*, **21**, 2725 (1965); (g) P. R. Levy and H. Stephen, *J. Chem. Soc.*, 1588 (1938); (h) D. T. Zentmyer and E. C. Wagner, *J. Org. Chem.*, **14**, 967 (1949).

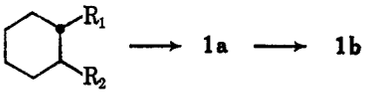
(7) J. A. Moore ["Heterocyclic Compounds with Three- and Four-Membered Rings," Vol. XIX, Part 2, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, p 914] has noted "no authentic members have been recorded" containing the 7-azabicyclo[4.2.0]octane framework.

(8) Oxygen and sulfur analogs of **1b** and/or **2b** recently reported include *cis*- and *trans*-7-oxabicyclo[4.2.0]octanes[9a] and 7-thiabicyclo[4.2.0]octane[9b] of unspecified stereochemistry.

(9) (a) Ö. Kovács, Z. Tuba, I. Weisz, and Gy. Schneider, *Chem. Ind.* (London), 1222 (1961); A. Rosowsky and D. S. Tarbell, *J. Org. Chem.*, **26**, 2255 (1961); (b) D. C. Dittmer and F. A. Davis, *ibid.*, **29**, 3131 (1964); D. C. Dittmer and F. A. Davis, *J. Am. Chem. Soc.*, **87**, 2064 (1965).

(10) M. Mousseron, J. Jullien, and F. Winternitz, *Bull Soc. Chim. France*, **15**, 878 (1948).

CHART I




4, $R_1$ = OH; $R_2$ = Cl
5, $R_1$ = OH; $R_2$ = CN
6, $R_1$ = OH; $R_2$ = $CO_2H$
7, $R_1$ = OH; $R_2$ = $CH_2NH_2$
8, $R_1$ = OTs; $R_2$ = $CH_2NHTs$

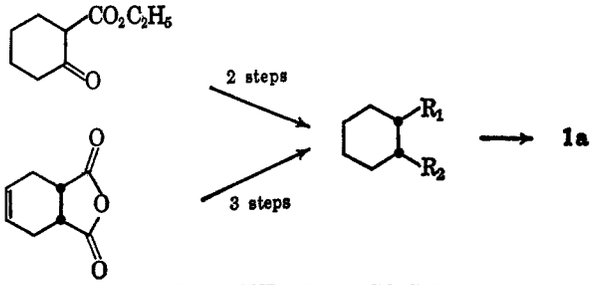
Thus base removal of the amide proton could be accompanied by a *trans* displacement of the *p*-toluenesulfonate anion to lead to 7-tosyl-*cis*-7-azabicyclo[4.2.0]octane (**1a**) in which the stereochemistry of the bridgehead hydrogen at the displacement site has been inverted. Experimentally, ring closure of **8** → **1a** was effected in a refluxing aqueous sodium hydroxide–ethanol solution (22% yield). Reduction of **1a** with sodium in refluxing isoamyl alcohol gave **1b** stored as the picrate in an over-all yield of 3% from *trans*-2-chlorocyclohexanol (**4**). The secondary amine **1b** was regenerated from its picrate by passage through a column packed with strongly basic Amberlite ion-exchange resin. Compound **1b** was an unstable colorless liquid which decomposed on standing even under nitrogen; it had a pronounced amine-like odor and gave a positive secondary amine test.[11] Retosylation of **1b** converted it to **1a** indicating the intact nature of the fused azetidine ring during the reductive detosylation step. Eschweiler–Clarke methylation of **1b** led to the colorless 7-methyl-*cis*-7-azabicyclo[4.2.0]octane (**1c**), analyzed as the picrate.

Although the stereochemistry of **4**[12] was firmly established by its easy conversion (73%) with base to cyclohexene oxide[13] the evidence for the *trans* geometry of **5** was less certain.[14] Mousseron, Jullien, and Winternitz[10] had reported that saponification of **5** led ultimately to the known *trans*-hexahydrosalicylic acid (**6**). In our hands, the hydrolysis of **5** → **6** (12%) with 3.3 *N* potassium hydroxide solution required 30–40 hr before ammonia evolution ceased. Since it is also known that *cis*-hexahydrosalicylic acid can be epimerized to the thermodynamically more stable isomer **6** in 65% yield on refluxing in 7.5 *N* potassium hydroxide solution for 35 hr,[15] the utility of alkaline hydrolysis as a proof of the stereochemistry of **5** becomes moot.[16]

We have however prepared **1a** by an alternate, unambiguous route (Chart II) substantiating the stereochemical conclusion that **5** must be the *trans* isomer.

Ethyl *cis*-2-amino-1-cyclohexanecarboxylate (**9**) was prepared in 16% over-all yield from ethyl 2-cyclohexanonecarboxylate[17,18] and in 59% yield from 4-cyclohexene-*cis*-1,2-dicarboxylic anhydride.[19] The *cis* geometry of **9** was decisively established by its acid

CHART II

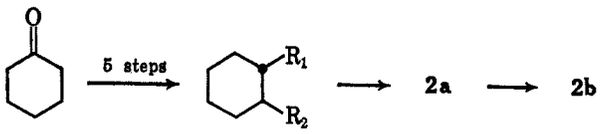



9, $R_1$ = $NH_2$; $R_2$ = $CO_2C_2H_5$
10, $R_1$ = $NH_2$; $R_2$ = $CO_2H$
11, $R_1$ = $NH_2$; $R_2$ = $CH_2OH$
12, $R_1$ = NHTs; $R_2$ = $CH_2OTs$

hydrolysis to the known *cis*-2-aminocyclohexanecarboxylic acid (10).[18] Reduction of **9** with lithium aluminum hydride led to *cis*-2-aminocyclohexanemethanol (**11**); treatment of **11** with excess *p*-toluenesulfonyl chloride and triethylamine produced N,O-ditosyl-*cis*-2-aminocyclohexanemethanol (**12**). In **12**, the tosyl-substituted groups have an axial-equatorial orientation. Its passage through an IRA-400 Amberlite ion-exchange resin (hydroxide form) quantitatively converted it to the *cis*-fused **1a**, identical by all the usual criteria with that obtained from **8**. The over-all yield of **1a** from 4-cyclohexene-*cis*-1,2-dicarboxylic anhydride was 35%.

Ethyl *trans*-2-aminocyclohexanecarboxylate (**13**) (Chart III) was prepared by the following reaction

CHART III




13, $R_1$ = $NH_2$; $R_2$ = $CO_2C_2H_5$
14, $R_1$ = $NH_2$; $R_2$ = $CO_2H$
15, $R_1$ = $NH_2$; $R_2$ = $CH_2OH$
16, $R_1$ = NHTs; $R_2$ = $CH_2OTs$

sequence: cyclohexanone → cyclohexanone cyanohydrin[20,21] → 1-cyclohexene-1-carbonitrile[20,22–24] → 1-cyclohexene-1-carboxylic acid[25] → *trans*-2-aminocyclohexanecarboxylic acid (**14**) → **13**. Acid hydrolysis of **13** to the known *trans*-2-aminocyclohexanecarboxylic acid (**14**)[18,26] established the *trans* geometry of **13**. Reduction of **13** to *trans*-2-aminocyclohexanemethanol (**15**)[27] followed by tosylation to N,O-ditosyl-*trans*-2-aminocyclohexanemethanol (**16**) was effected in the same manner as **9** → **11** → **12**. The proximate equatorial:equatorial reacting centers in **16** ring closed nicely to 7-tosyl-*trans*-7-azabicyclo[4.2.0]octane (**2a**) on refluxing 24 hr with sodium methoxide in absolute methanol. Reductive detosylation of **2a** with sodium

(11) With $NiCl_2$, $CS_2$, and $NH_4OH$ (R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "Systematic Identification of Organic Compounds," 4th ed, John Wiley and Sons, Inc., New York, N. Y., 1958, p 124).

(12) G. H. Coleman and H. F. Johnston, "Organic Syntheses," Coll. Vol. I, 2nd ed, H. Gilman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, p 158.

(13) A. E. Osterberg, ref 12, p 185.

(14) Mechanistically, the conversion of **4** (*trans*) to **5** (*trans*) would necessitate a precedented double inversion with net retention involving anchimeric assistance of the hydroxyl group *via* an epoxy intermediate.

(15) J. Pascual, J. Sistaré, and A. Regás, *J. Chem. Soc.*, 1943 (1949).

(16) Compound **5** could be *cis*/*trans*, or a mixture of both; all would lead predominantly to **6** under saponification conditions.

(17) W. Dieckmann, *Ann.*, **317**, 100 (1901).

(18) S. Hünig and H. Kahonek, *Ber.*, **86**, 518 (1953).

(19) H. Plieninger and N. Schneider, *ibid.*, **92**, 1594 (1959).

(20) S. M. McElvain and R. E. Starns, Jr., *J. Am. Chem. Soc.*, **77**, 4571 (1955).

(21) R. F. B. Cox and R. T. Stormont, "Organic Syntheses," Coll. Vol. II, A. H. Blatt, Ed., John Wiley and Sons, Inc., New York, N. Y., 1943, p 7.

(22) D. L. MacPeek, P. S. Starcher, and B. Phillips, *J. Am. Chem. Soc.*, **81**, 680 (1959).

(23) A. S. Dreiding and J. A. Hartman, *ibid.*, **75**, 939 (1953).

(24) R. Franck and H. O. House, unpublished information.

(25) E. J. Boorman and R. P. Linstead, *J. Chem. Soc.*, 261 (1935).

(26) A. Einhorn and A. Meyenberg, *Ber.*, **27**, 2466 (1894).

(27) The boiling point of **11** and **15** are virtually indistinguishable, 82–85° (1.5 mm), 83–85° (1 mm), respectively; however, the mixture melting point of their hydrochlorides was markedly depressed.

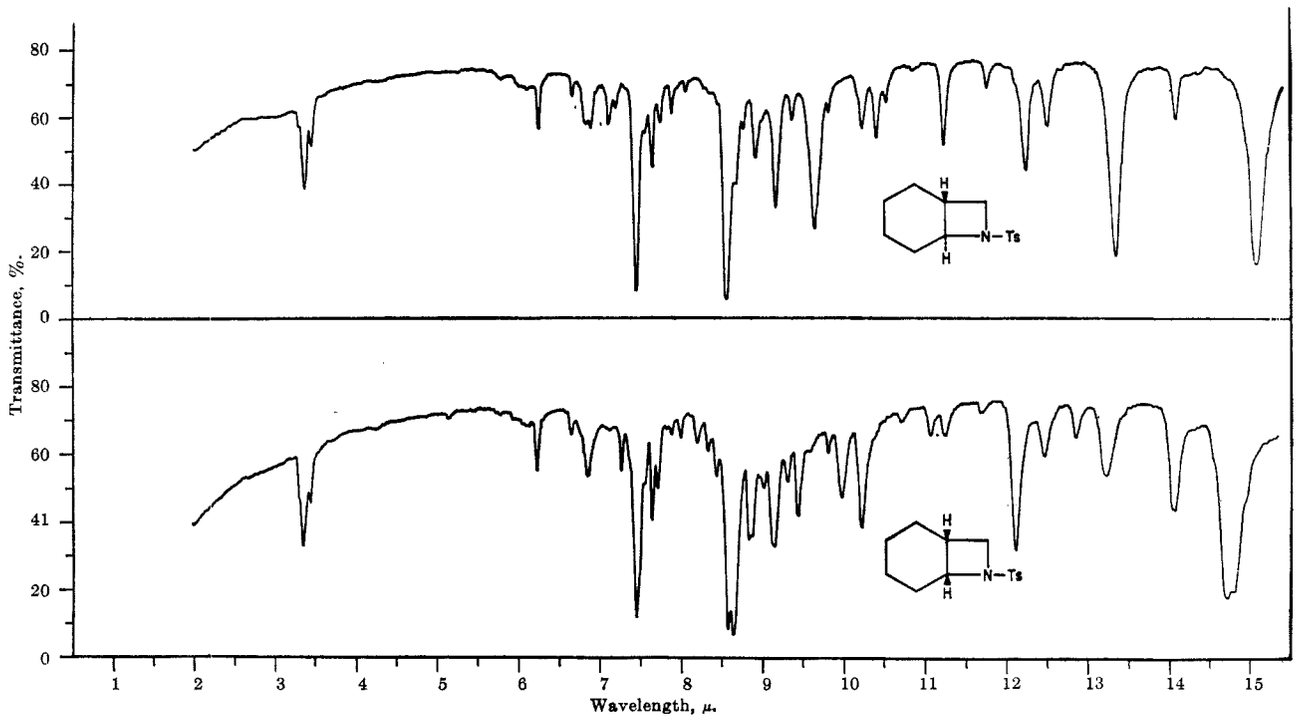



Figure 1.—Infrared spectra of 7-tosyl-*cis*- (**1a**) and 7-tosyl-*trans*-7-azabicyclo[4.2.0]octane (**2a**).

in isoamyl alcohol led finally to the parent heterocycle, *trans*-7-azabicyclo[4.2.0]octane (**2b**) in 1% over-all yield from cyclohexanone.

The infrared spectra of isomers **8**, **12**, and **16** in carbon tetrachloride showed expected absorptions at 3.05–3.06 $\mu$ (NH), 6.25–6.26 $\mu$ (aromatic), and strong, sharp, split band patterns for $SO_2$ stretching modes in the 7.36–7.52- and 8.36–8.68-$\mu$ regions. The infrared spectra of ring closed **1a** and **2a** (Figure 1) display neither NH nor OH bands from 2.5–3.2 $\mu$; in the area 2.5–8.7 $\mu$, the spectra are all but indistinguishable except for minor differences in CH absorption and in the position of weak bands; the phenyl absorption is weak at *ca.* 7.5 $\mu$, while the sulfone bands are strong and sharp at *ca.* 7.5 and 8.6 $\mu$.

The nmr spectra of **1a** and **2a** (Figure 2) display strong similarities: respectively, $\delta$ = 7.51 and 7.53 (phenyl ring protons), multiplets centered *ca.* $\delta$ = 3.40 and 3.30 ($H_a$, $H_b$, $H_c$), methyl singlets at $\delta$ = 2.44, and multiplet patterns centered at $\delta$ = 1.64 and 1.60 ($H_d$ and cyclohexyl protons), both with identical area ratios of 4:3:3:9. The only real but expected difference in the nmr spectrum of **1a** and **2a** lies in the shape of the methylene (plus $H_d$) envelope and in the splitting pattern of the resonances in the area $\delta$ = 2.8–3.8. The unresolved complexity of the multiplet attributed to the three protons $\alpha$ to nitrogen is also not unexpected since, in the simplest case, the spectrum in this area should consist of an ABX pattern (eight lines from $H_a$ and $H_b$ coupled with each other and with $H_d$) and a multiplet (from $H_c$).

Cenco–Peterson models suggest that **1b** should be more stable than **2b**. In both cases, the cyclohexane ring is deformed into a twisted chair. In **1b**, however, flexibility of the cyclohexane ring permits two interchangeable chairs obtained by changing the bonds comprising the fused azetidine ring from e–a to a–e. There seem to be no strong nonbonded axial proton interactions. In **2b**, the cyclohexane ring is rigid and there are severe interactions between the bridgehead and axial protons. This effect is even more severe than normal axial:axial nonbonded interactions, since one consequence of *trans*-ring fusion is that the bridgehead protons are forced inward toward the ring and thus closer to other axial protons.

The addition of chlorosulfonyl isocyanate (CSI)[28] to 1,2-dihydronaphthalene in ether deposited in 76% yield a white crystalline adduct assigned the structure 7-chlorosulfonyl-8-ketobenzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (**17**) (Chart IV). Compound **17** was stable in anhydrous methylene chloride and ether but decomposed rapidly in protonic solvents even under nitrogen. Its infrared spectrum displayed a carbonyl band at 5.49 $\mu$ reflecting the combined effects of a strained $\beta$-lactam containing a strong electron-withdrawing substituent ($SO_2Cl$) on the amide nitrogen. Aqueous hydrolysis of **17** led to 3,4-dihydro-2-naphthamide (**19**), which could be quantitatively oxidized with 2,3-dichloro-5,6-dicyanobenzoquinone to the known 2-naphthamide (**20**). Barring unprecedented bond migration, the formation of **20** indicates that the lactam carbonyl is attached to C-2 of the tetralin moiety in **17**. The *cis* geometry in **17** is suggested by Graf's[28a,b] pioneering work on the reaction of CSI with simple olefins. Removal of the chlorosulfonyl group in **17** was accomplished either by inverse addition of lithium aluminum hydride (19% yield) or with benzenethiol in pyridine[28b] (46% yield) to give 8-ketobenzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (**18**). The infrared spectrum is again clearly indicative of the $\beta$-lactam structure: NH and C=O absorptions, *e.g.*, appear at 2.92 and 5.62 $\mu$, respectively. The nmr spectrum of **18** is also consistent with the assigned structure: resonances centered at $\delta$ = 7.30 (aromatic multiplet, 4 H), $\delta$ = *ca.* 6.6 (broad band, amide H, 1 H), $\delta$ = *ca.*

(28) (a) R. Graf, *Ber.*, **89**, 1071 (1956); (b) *Ann.*, **661**, 111 (1963); (c) The use of this reagent was first suggested to us by Dr. E. E. Gilbert, General Chemical Division, Allied Chemical Corp.

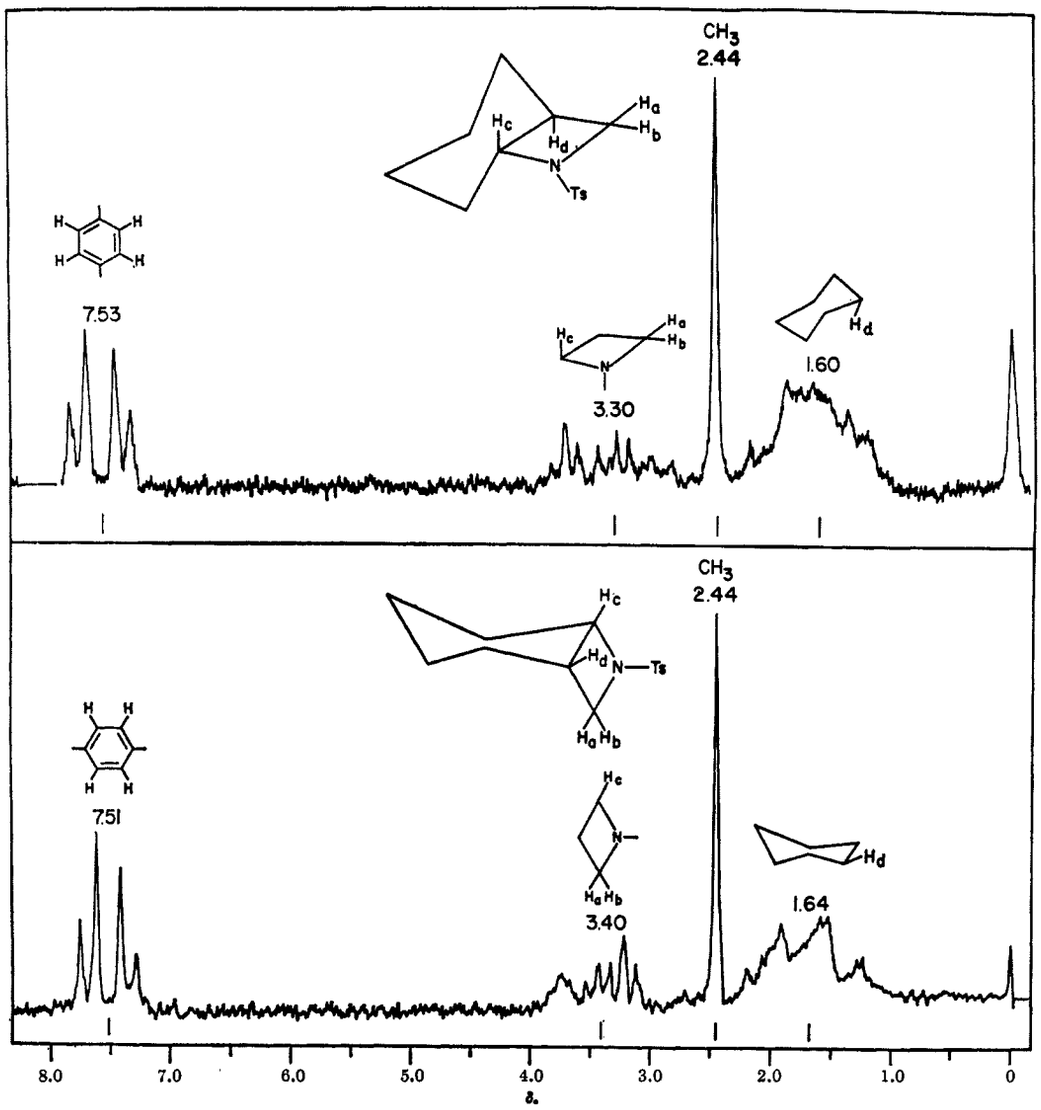
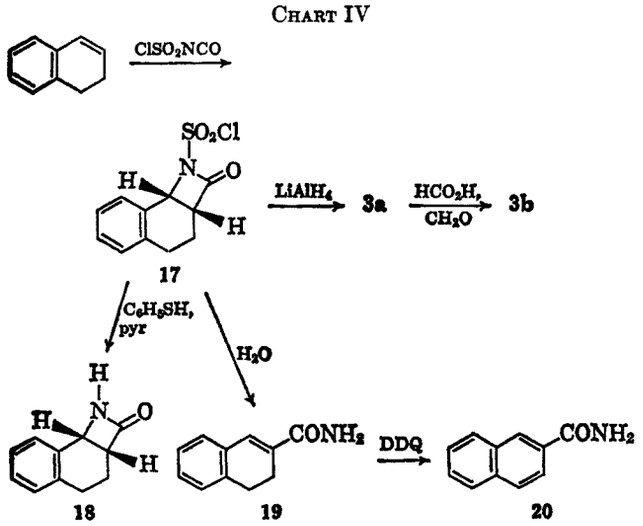



Figure 2.—Nmr spectra of 7-tosyl-*cis*- (**1a**) and 7-tosyl-*trans*-7-azabicyclo[4.2.0]octane (**2a**).

CHART IV




2.3 (multiplet $H_{c-f}$, 4 H); in addition, the doublet *ca.* $\delta$ = 4.69 is assigned to $H_a$ coupled with $H_b$ ($J_{ab}$ = 5 cps) while the three-peak pattern at $\delta$ = 3.69 is assigned to $H_b$. Normally $H_b$ would couple with $H_a$, $H_c$, and $H_d$. Models indicate the dihedral angle between the planes defined by $H_b$–$C_1$–$C_2$–$H_c$ to be approximately 90°, and consequently $J_{bc} \cong 0$.[29,30] The pattern then degenerates to the X portion of an ABX pattern[30b] where $J_{ab} = J_{db}$ and thus appears as three peaks. The nmr spectrum of **17** (Figure 3) is quite similar, with the obvious absence of the NH signal and with all other resonances shifted downfield. Reduction of **17** with excess lithium aluminum hydride in ether gave the unstable parent heterocycle, benzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (**3a**) in 45% over-all yield from 1,2-dihydronaphthalene. Compound **3a** decomposed overnight to a viscous gum, but could be stored and analyzed as stable thiourea and chloroplatinate derivatives. It too gave a positive nickel dithiocarbamate test for secondary amines.[11] Eschweiler–Clarke methylation of **3a** led to the N-methyl derivative (**3b**) which formed a stable 2-nitro-1,3-indandione salt.[31]

The oxidation of **3a**, **3b**, and **17**, **18**, respectively, to naphth[*a*]azetines and naphth[*a*]azetidinones with such

(29) "Applications of NMR Spectroscopy in Organic Chemistry," N. S. Bhacca, and D. H. Williams, Ed., Holden-Day, Inc., San Francisco, Calif., 1946, p 50.

(30) "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," L. M. Jackman, Pergamon Press Ltd., New York, N. Y., 1959: (a) p 87; (b) p 91.

(31) B. E. Cristensen, C. H. Wang, I. W. Davies, and D. Harris, *Anal. Chem.*, **21**, 1573 (1949).

reagents as 2,3-dichloro-5,6-dicyanobenzoquinone was unsuccessful.[32]

## Experimental Section[33]

*trans*-**2-Aminomethylcyclohexanol** (**7**).—The reduction of *trans*-2-cyanocyclohexanol (**5**) [prepared from *trans*-2-chlorocyclohexanol (**4**)[10,12]] in 68% yield with sodium and ethanol has been reported.[10] The use of lithium aluminum hydride raised the yield to 90%. For the reduction of larger quantities (100–200 g) of **5**, however, catalytic reduction was preferred: 100 g (0.80 mole) of **5** in 200 ml of absolute ethanol saturated with ammonia was hydrogenated under 80 atm of hydrogen at 125–145° in the presence of W-7 Raney nickel for 2 hr. The catalyst was filtered through a Filter-Cel mat and the solvent was evaporated (Rinco). Distillation gave 69.6 g (67%) of **7**: bp 79–81° (1.5 mm), $n^{25}D$ 1.4879; lit.[10] bp 133° (17 mm), $n^{25}D$ 1.4910. An elemental analysis of **7** has not been previously reported.

*Anal.* Calcd for $C_7H_{15}NO$: C, 65.12; H, 11.63. Found: C, 65.06; H, 11.73.

The hydrochloride of **7** had a mp 150–151°, lit.[10] mp 150–151°.

**N-Tosyl-***trans*-**2-aminomethylcyclohexanol** was quantitatively obtained from **7** as a white solid, mp 109–110°, from ether–petroleum ether (bp 30–60°).

*Anal.* Calcd for $C_{14}H_{21}NO_3S$: C, 59.33; H, 7.42; N, 4.95. Found: C, 59.00; H, 7.30; N, 4.85.

The infrared spectrum of the monotosylate showed absorptions at 2.87 (OH), 3.15 (NH), 7.58, 7.69, and 8.62 $\mu$ ($SO_2$). The ultraviolet spectrum had a maximum at 227 m$\mu$ ($\epsilon$ 9500).

**Alkaline Hydrolysis of 5 to** *trans*-**Hexahydrosalicylic Acid** (**6**).—Ten grams (0.08 mole) of **5** in a solution of 15 g of potassium hydroxide in 80 ml of water was refluxed until the evolution of ammonia ceased (30–40 hr). The mixture was washed with ether; the aqueous layer was acidified with concentrated hydrochloric acid and extracted with ether. The ether extracts were dried, filtered, and evaporated. The residue was recrystallized three times from ethyl acetate to give 1.34 g (12%) of impure **6**: mp 107–111°; lit. mp 108°,[10] 111°.[15]

**N,O-Ditosyl-***trans*-**2-aminomethylcyclohexanol** (**8**).—Compound **8** was prepared in 31% yield from the monotosylate, or directly from **7**. A solution of 15.0 g (0.079 mole) of *p*-toluenesulfonyl chloride in 35 ml of chloroform was added to a solution of 8.5 g (0.066 mole) of **7** in 35 ml of triethylamine and 35 ml of chloroform cooled in an ice–salt bath. After standing for 24 hr at 0°, another 15 g of *p*-toluenesulfonyl chloride in 35 ml of chloroform was added. After an additional 48 hr at 0°, the solution was poured into 200 ml of an ice–water mixture. The organic layer was separated, washed with two 100-ml portions of water, and solvent removed *in vacuo*. The residual oil was dissolved in benzene, washed with two 100-ml portions of water, dried, filtered, and evaporated. The brown oil was dissolved in a minimal amount of ethyl acetate, deposited on a 1 × 15 in. column of silicic acid (deactivated with 3% by weight water), and eluted with 9:1 benzene–hexane. The column developed as a dark brown band at the top from which moved a yellow band. The yellow eluate was collected as one fraction. Hexane was added to this eluate to the cloud point, the mixture warmed until cloudiness was dispelled and the mixture refrigerated overnight. The precipitate was filtered, washed with 50 ml of of 1:18 benzene–hexane and dried, giving 17.6 g (0.04 mole, 61%) of crude **8**. Two recrystallizations of this material from methylene chloride–hexane produced white, chunky crystals, mp 95.5–97.5°.

*Anal.* Calcd for $C_{21}H_{27}NO_5S_2$: C, 57.67; H, 6.18; N, 3.20. Found: C, 57.27; H, 6.04; N, 3.39.

The infrared spectrum showed strong sharp absorptions at 3.00 (NH), 6.25 (phenyl), and doublets at 7.36, 7.49, and 8.54, 8.57 $\mu$ ($SO_2$).

**7-Tosyl-***cis*-**7-azabicyclo[4.2.0]octane** (**1a**).—A solution containing 8.0 g of sodium hydroxide in 20 ml of water was added to a solution of 28.0 g (0.064 mole) of **8** in 200 ml of 95% ethanol. The mixture was refluxed for 2 hr. The ethanol was removed by distillation at atmospheric pressure and 50 ml of water added to the residue. The mixture was extracted with three 50-ml portions of benzene; the extracts were dried, filtered, and evaporated. The residual oil was column chromatographed (1 × 10 in.; neutral alumina) with hexane as the eluent. The first fraction of 300 ml of hexane gave crude **1a** on evaporation. Recrystallization from carbon tetrachloride–petroleum ether (bp 30–60°) gave 3.99 g (22%) of white crystals, mp 89–90°.

*Anal.* Calcd for $C_{14}H_{19}NO_2S$: C, 63.37; H, 7.22; N, 5.28; mol wt, 265. Found: C, 63.18; H, 7.38; N, 5.13; mol wt, 273.

The infrared and nmr spectra of **1a** and **2a** are shown, respectively, in Figures 1 and 2.

*cis*-**7-Azabicyclo[4.2.0]octane** (**1b**).—A solution containing 8.71 g (0.0304 mole) of **1a** in 100 ml of isoamyl alcohol was heated to boiling. The heat source was removed and 7.2 g (0.0314 g-atom) of sodium was added at a rate such that the solution remained at reflux. On completion of the addition, 50 ml of water was added and the mixture was steam distilled until the distillate was neutral to litmus. The alcoholic layer of the distillate was separated and washed with two 25-ml portions of 1 *N* $H_2SO_4$. The acid washings were combined with the aqueous layer and the whole washed with two 50-ml portions of ether. The aqueous solution was saturated with potassium hydroxide and extracted with ether. The ether extracts were dried, filtered, and evaporated. A saturated ethanolic solution of picric acid was added to the residue; the solution was heated on a steam bath several minutes and cooled to yield 3.99 g (36%) of the picrate of **1b** as yellow crystals, mp 131–133°, after one recrystallization from ethanol.

*Anal.* Calcd for $C_7H_{13}N \cdot C_6H_3N_3O_7$: C, 45.99; H, 4.71; N, 16.47. Found: C, 45.99; H, 4.42; N, 16.30.

To obtain the free base, the picrate was deposited on a column of IRA-400 Amberlite ion, exchange resin (hydroxide form) and eluted with methanol. The basic eluate fractions were collected and distilled to yield **1b**, bp 140–150° (atm). Pure **1b** decomposed on standing, even under nitrogen; its picrate, however, could be stored indefinitely.

Reduction of **1a** with lithium aluminum hydride or sodium in ammonia was unsuccessful.

**Tosylation of 1b.**—A solution containing 200 mg (1.1 mmoles) of *p*-toluenesulfonyl chloride in 2 ml of chloroform was added to a solution of 100 mg (0.9 mmole) of **1b** in 2 ml of chloroform and 400 mg of triethylamine cooled in an ice–salt bath. The mixture was allowed to stand at 0° for 48 hr and then poured into 10 ml of water. The organic layer was separated, washed with two 10-ml portions of water, dried, filtered, and deposited on a 2.5 × 25 cm column of neutral alumina. Elution with 50 ml of carbon tetrachloride gave no product on evaporation, but similar treatment of a second fraction eluted with methylene chloride gave 56 mg (23%) of **1a**, mp 89–90° [from carbon tetrachloride–petroleum ether (bp 30–60°)] identical by all the usual criteria with **1a** prepared from **8**.

**7-Methyl-***cis*-**7-azabicyclo[4.2.0]octane** (**1c**).—A solution containing 2.2 g (0.021 mole) of **1b**, 3.2 g (0.063 mole) of a 90% solution of formic acid, and 10 ml of 37% formaldehyde was refluxed on a steam bath for 10 hr. The mixture was cooled in an ice–bath and saturated with potassium hydroxide. The mixture was then extracted with three 20-ml portions of ether, the extract dried, filtered, and evaporated. Distillation of the residue gave 1.8 g (70%) of **1c**, bp 120–125° (atm). Treatment of **1c** with a saturated solution of picric acid gave the picrate, mp 191–193°, after two recrystallizations from ethanol.

*Anal.* Calcd for $C_8H_{15}N \cdot C_6H_3N_3O_7$: C, 47.47; H, 5.12; N, 15.82. Found: C, 47.76; H, 5.19; N, 15.97.

*cis*-**2-Aminocyclohexanemethanol** (**11**).—A solution containing 36 g (0.21 mole) of ethyl cis-2-aminocyclohexanecarboxylate (**9**)[17–19,35] [bp 73–75° (1.2 mm), 88–90° (5.0 mm), $n^{21}D$ 1.4653,

(32) *Cf.* the recent attempts to prepare such fused aromatic derivatives of azetine and azetidinone [J. C. Sheehan and G. B. Daves, Jr., *J. Org. Chem.*, **30**, 3247 (1965)].

(33) Melting points and boiling points are corrected. The infrared spectra were obtained on a Perkin-Elmer 337 spectrophotometer using KBr wafers unless otherwise stated. The microanalyses were determined by Schwarzkopf Microanalytical Laboratory. The ultraviolet spectra were recorded in ethanol solution on a Cary 15 spectrophotometer. The nmr spectra were obtained on a Varian A-60 spectrometer[34] using dilute deuteriochloroform solutions; chemical shifts are given in parts per million downfield from tetramethylsilane.

(34) We acknowledge with pleasure the assistance of a National Science Foundation Grant GP 1482 to the Department of Chemistry toward the purchase of this instrument.

(35) In adapting the Plieninger and Schneider procedure to the preparation of **9**,[19] the *cis*-2-aminocyclohexanecarboxylic acid (**10**) precursor was not isolated but esterified directly in absolute ethanol saturated with gaseous hydrogen chloride.

$\lambda_{C=O}^{neat}$ 5.78 $\mu$; lit.[17] bp 103–104° (11 mm)] in 100 ml of ether was added dropwise to a stirred solution of 16.5 g (0.43 mole) of lithium aluminum hydride in 500 ml of ether. The mixture was refluxed for 48 hr, decomposed with a saturated aqueous potassium carbonate solution, and the whole refluxed with stirring for 30 min. Filtration gave a solid which was washed with two 50-ml portions of 1:1 ethanol–ether. The filtrate and the washings were dried, filtered, and evaporated; the residual oil was distilled to give 21.7 g (80%) of **11**, bp 82–85° (1.5 mm), $n^{21}D$ 1.4980. The hydrochloride of **11** had a mp 133–135°.

**N-Tosyl-*cis*-2-aminomethylcyclohexanol** was obtained from **11** in 56% yield as a white solid, mp 126–128°, from methylene chloride–hexane.

*Anal.* Calcd for $C_{14}H_{21}NO_3S$: C, 59.33; H, 7.47; N, 4.95. Found: C, 59.41; H, 7.63; N, 4.83.

The infrared spectrum of the monotosylate showed sharp bands at 2.82 (OH), 3.05 (NH), 7.49, 7.61, 8.57, 8.62 $\mu$ ($SO_2$).

**N,O-Ditosyl-*cis*-2-aminocyclohexanemethanol (12).**—A solution containing 28 g (0.15 mole) of *p*-toluenesulfonyl chloride in 72 ml of chloroform was added to a solution of 7.50 g (0.058 mole) of **11** in 35 ml of chloroform and 36 g of triethylamine cooled in an ice–salt bath. The mixture was refrigerated for 48 hr and then poured into 150 ml of water. The organic layer was washed with two 100-ml portions of water and then evaporated (Rinco) to a gummy residue. This material was dissolved in 100 ml of benzene and again washed with two 100-ml portions of water. The benzene solution was dried, filtered, and the solvent evaporated. The residual oil was dissolved in *ca.* 50 ml of methylene chloride, and hexane added to incipient cloud point. This solution was chromatographed on a 2.5 × 40 cm silicic acid column (containing 3% by weight water) using 600 ml of 1:9 benzene–hexane as eluent. The solvent was permitted to evaporate at ambient temperature, and the partially crystalline product was twice recrystallized from carbon tetrachloride hexane to yield 19.2 g (75%) of **12**, mp 116–117°.

*Anal.* Calcd for $C_{21}H_{27}NO_5S_2$: C, 57.67; H, 6.18; N, 3.20. Found: C, 57.74; H, 6.35; N, 3.09.

The infrared spectrum showed strong sharp absorptions at 3.07 (NH), 6.26 (phenyl), and bands at 7.36, 7.52, 8.38, 8.48 and 8.61 $\mu$ ($SO_2$).

**7-Tosyl-*cis*-7-azabicyclo[4.2.0]octane (1a).**—A solution of 2.0 g (0.0045 moles) of **12** in 250 ml of methanol was passed through a column packed with 40 g of IRA-400 Amberlite ion exchange resin (hydroxide form). The column was eluted with 250 ml of methanol and the combined eluates evaporated to yield 1.16 g (quantitative) of **1a**, identical by the usual criteria with the sample of **1a** prepared from **8**.

**Ethyl *trans*-2-Aminocyclohexanecarboxylate (13).**—Cyclohexanone cyanohydrin [bp 117–119° (10 mm), lit.[20] bp 109–113° (9 mm)] was prepared in 92% yield from cyclohexanone and *in situ* generated hydrogen cyanide using the procedure of Cox and Stormont.[21] Its dehydration to **1-cyclohexene-1-carbonitrile** has been accomplished with acetic anhydride–sulfuric acid[22] and with thionyl chloride–pyridine.[20,23] We preferred an unpublished procedure[24] successfully utilized for the dehydration of cyclopentanone cyanohydrin: the dehydrating reagent [432 g (2.82 moles) of phosphorus oxychloride and 258 ml of pyridine] was added to a cooled (0°) solution containing 125 g (1.0 mole) of cyclohexanone cyanohydrin in 130 ml of benzene and 258 ml of pyridine.

The mixture was stirred at 10–20° for 5 hr and allowed to stand at room temperature overnight. The reaction mixture was decomposed by the careful addition of ice and extracted with three 250-ml portions of ether. The extracts were washed consecutively with two 250-ml portions of 10% hydrochloric acid, two 250-ml portions of water, and 250 ml of saturated sodium chloride solution. The extract was then dried, filtered, and distilled through a 25-cm Vigreux column to yield 84.9 g (80%) of 1-cyclohexene-1-carbonitrile: bp 73–78° (11 mm), $n^{21}D$ 1.4813; lit.[20] bp 74–76° (12 mm), $n^{21}D$ 1.4796. This nitrile was saponified (48-hr reflux) in 87% yield to **1-cyclohexene-1-carboxylic acid**, bp 97–99° (1 mm), lit.[25] bp 107° (3 mm).

A mixture of 1-cyclohexene-1-carboxylic acid (50 g, 0.397 mole) in 300 ml of concentrated aqueous ammonium hydroxide was heated in a bomb at 140–160° for 48 hr. The solution was then treated with Norit, filtered, and water removed *in vacuo*. The residue was dissolved in 250 ml of ethanol, and gaseous hydrogen chloride bubbled through the solution for 1 hr. The solution was evaporated (Rinco) and 150 ml of water added to the residue. The acidic solution was extracted with three 50-ml portions of ether. The ether extracts were dried, filtered, and evaporated. Vacuum distillation of the remaining liquid gave 21.4 g of ethyl 1-cyclohexene-1-carboxylate, bp 67–69° (2 mm), $n^{21}D$ 1.4702.

The acidic, aqueous solution was saturated with potassium carbonate and extracted with three 50-ml portions of ether. The extracts were dried, filtered, and evaporated. Vacuum distillation gave 21 g (48% based on unreacted 1-cyclohexene-1-carboxylic acid recovered as its ethyl ester) of ethyl *trans*-2-aminocyclohexanecarboxylate (**13**), bp 74–76° (1.5 mm), $n^{21}D$ 1.4643.

**Acid Hydrolysis of Ethyl *cis*- (9) and *trans*-2-Aminocyclohexanecarboxylate (13).**—Hydrolysis of 4.0 g (0.023 mole) of **13** was accomplished by refluxing in 20 ml of 2 *N* hydrochloric acid for 2 hr. The acidic solution was made basic by the addition of 25 ml of 2 *N* ammonium hydroxide solution and placed on a column packed with 80 g of Dowex 50. The column was washed with 500 ml of distilled water followed by 1200 ml of 0.1 *N* aqueous ammonia. Evaporation of the eluate gave 2.4 g (72%) of ***trans*-2-aminocyclohexanecarboxylic acid (14)**, mp 269–271° after one recrystallization from water–acetone, lit. mp 273°,[18] 274°.[26] Similar hydrolysis of **9** gave ***cis*-2-aminocyclohexanecarboxylic acid (10)**, mp 236–236°, lit.[18] mp 235°, in 78% yield.

***trans*-2-Aminocyclohexanemethanol (15)** was prepared in 84% yield from **13** by the same procedure used for the preparation of **11** from **9**. Compound **15** was obtained as a colorless oil, bp 83–85° (1 mm), which crystallized on standing.

*Anal.* Calcd for $C_7H_{15}NO$: C, 65.12; H, 11.63. Found: C, 65.10: H, 11.73.

The hydrochloride of **15** had a mp 140–142°. The mixture melting point of **11** and **15** showed a marked depression.

**N,O-Ditosyl-*trans*-2-aminocyclohexanemethanol (16)** was prepared in 46% yield from **15** by the same procedure used for the preparation of **12** from **11**. After four recrystallizations from methanol, **16** had a mp 119–122°. The mixture melting points of **12** and **16** was depressed to 100–110°.

*Anal.* Calcd for $C_{21}H_{27}NO_5S_2$: C, 57.67; H, 6.18; N, 3.20. Found: C, 57.65; H, 6.43; N, 2.90.

The infrared spectrum showed strong, sharp bands at 3.05 (NH), 6.25 (phenyl), and 7.41, 7.52, 8.36, 8.48, 8.62, and 8.68 $\mu$ ($SO_2$).

**7-Tosyl-*trans*-7-azabicyclo[4.2.0]octane (2a).**—A solution containing 7.0 g (0.016 mole) of **16** and 0.80 g (0.018 mole) of sodium methoxide in 20 ml of absolute methanol was refluxed under anhydrous conditions for 24 hr. The pH of the solution at this point had dropped to 6.0. After standing overnight, the sodium *p*-toluenesulfonate crystals were removed by filtration, and the solvent evaporated. Water (20 ml) was added to the residue and the cloudy, white suspension extracted with four 15-ml portions of benzene. The combined extracts were dried, filtered, and evaporated to *ca.* 15 ml. The residual solution was deposited on a 2.5 × 25 cm alumina column (Woelm neutral, activity grade I) and eluted successively with 300 ml of 1:9 methylene chloride–hexane, 200 ml of 1:1 methylene chloride–hexane, and 300 ml of methylene chloride. Evaporation of the first two fractions afforded 2.3 g (55%) of crude **2a**. Two recrystallizations from methylene chloride–hexane gave pure **2a**, mp 104.5–106°. A mixture melting point of **1a** and **2a** was depressed to 74–85°. Tlc of **1a** and **2a** (silica gel G, 0.5 mm, benzene eluent) showed the two compounds also to have slightly different $R_f$ values.

*Anal.* Calcd for $C_{14}H_{19}NO_2S$: C, 63.37; H, 7.22; N, 5.28; mol wt, 265. Found: C, 63.11; H, 7.33; N, 5.21; mol wt, 271.

***trans*-7-Azabicyclo[4.2.0]octane (2b).**—A solution containing 1.0 g (0.0037 mole) of **2a** in 30 ml of isoamyl alcohol was heated to boiling. The heat source was removed and 1.5 g (0.065 g-atom) of sodium was added at a rate such that the solution remained at reflux temperature. The work-up procedure which was identical with that for **1b** gave 272 mg (21%) of the picrate of **2b**, mp 128–130°, after three recrystallizations from ethanol. A mixture melting point of the picrates of **1b** and **2b** was depressed to 116–125°.

*Anal.* Calcd for $C_7H_{13}N \cdot C_6H_3N_3O_7$: C, 45.88; H, 4.71; N, 16.47. Found: C, 45.93; H, 4.68; N, 16.33.

**Chlorosulfonyl Isocyanate (CSI).**—The preparation of CSI was carried out according to the directions of Graf[28a,b] with the exception that Sulfan (Allied Chemical Co. stabilized sulfur trioxide) was used instead of sulfur trioxide distilled from 30% fuming sulfuric acid. Thus, 403 g (5 moles) of Sulfan was added

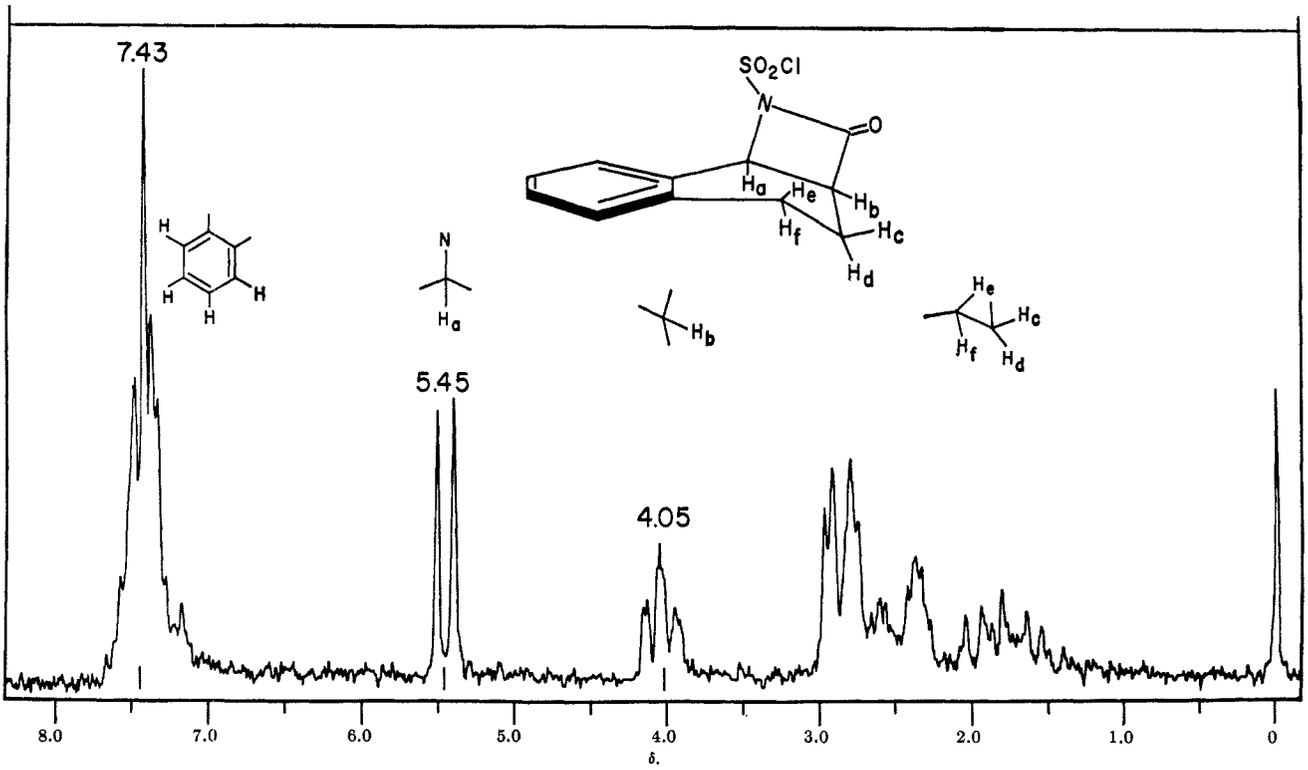



Figure 3.—Nmr spectrum of 7-chlorosulfonyl-8-ketobenzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (17).

to 171 g (2.80 moles) of cyanogen chloride[36] cooled in a Dry Ice–acetone bath (−5°), at such a rate that the temperature did not rise above 0°. After addition was complete, the apparatus was set up for distillation as described.[28a] The reaction mixture was heated in an oil bath to 125°, and 145 g (2.54 moles) of cyanogen chloride slowly bubbled through the mixture. CSI, bp 110°, distilled from the reaction mixture as it was formed. The reaction gave 417 g (57%) of CSI as a colorless liquid which reacted violently with water.

**7-Chlorosulfonyl-8-ketobenzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (17).**—A solution of 40.0 g (0.28 mole) of CSI in 50 ml of ether was added to a solution of 25 g (0.19 mole) of 1,2-dihydronaphthalene (Aldrich) in ether. After an induction period of several minutes, the solution began to reflux. The solution was stirred for 1 hr, 100 ml of hexane added, and the whole cooled in a freezer. Filtration gave 29.6 g (76%) of a white solid which was crystallized from ethyl ether–hexane to yield **17**, mp 76–78° dec. Decomposition of **17** to gums commences almost immediately after solvent removal, even under an inert atmosphere. Decomposition is slower in aprotic solvents.

The infrared spectrum showed strong bands at 5.49 (C=O), 5.99 (phenyl), 7.19, 8.16, and 8.55 μ ($SO_2$). The nmr spectrum (Figure 3) consisted of absorptions at *ca.* δ = 7.43 (aromatic multiplet, 4 H), 5.45 (doublet, $J$ = 7 cps, $H_a$), 4.05 (triplet, $H_b$), and *ca.* 2.2 (multiplet, $H_{c-f}$, 4 H).

**3,4-Dihydro-2-naphthamide (19).**—A 10-g sample of **17** in 150 ml of ether was allowed to stand exposed to the atmosphere for 3 days. The ether was decanted from the amorphous solid; the solid was dissolved in acetone, treated with charcoal (Norit), and filtered. Water was added to the solution until it became cloudy, then acetone was added until the solution cleared and the mixture was cooled. The tan solid was filtered and recrystallized from ethyl acetate to give 1.3 g (21%) of 3,4-dihydro-2-naphthamide (**19**) as colorless needles, mp 158–161°.

*Anal.* Calcd for $C_{11}H_{11}NO$: C, 76.30; H, 6.36. Found: C, 76.18; H, 6.62.

The infrared spectrum of **19** showed $NH_2$ absorptions at 3.00 and 3.17 μ, and amide C=O bands at 6.01 and 6.21 μ. The ultraviolet spectrum had maxima at 225 mμ (ε 20,000) and 287 mμ (ε 15,000).

**Oxidation of 19 to 2-Naphthamide (20).**—A mixture of 2.26 g (0.01 mole) of 2,3-dichloro-5,6-dicyanobenzoquinone and 1.73 g (0.01 mole) of **19** in 15 ml of *o*-xylene was heated at reflux for 4 hr. The hot mixture was filtered and the solid washed with 15 ml of boiling *o*-xylene. The combined filtrates were cooled, precipitating crude 2-naphthamide (**20**) which was filtered. Four recrystallizations from ethanol (Norit) gave 1.43 g (83%) of pure **20**, mp 197–198°, identical by the usual criteria with authentic 2-naphthamide.

**Reduction of 17 to 8-Ketobenzo[*d*]-*cis*-7-azabicyclo[4.2.0]-octane (18). With Benzenethiol.**—To a solution of 20.0 g of benzenethiol in 110 ml of acetone cooled to −25° in a Dry Ice–ethanol–water bath was added 22.0 g (0.081 mole) of **17**. A solution containing 9.0 g of pyridine in 40 ml of acetone was then added dropwise over a 30-min period; the solution was stirred for an additional 2 hr at −25° at which time 100 ml of water was added. The precipitated solid was filtered, and the filtrate was extracted with three 50-ml portions of ether. The combined extracts were dried, filtered, and evaporated. The residual oil was taken up in 30 ml of carbon tetrachloride with sufficient methylene chloride added to give a clear solution. The solution was deposited on a 2.5 × 40 cm column packed with alumina (Woelm, neutral, activity grade I) and successively eluted with 200 ml of petroleum ether (bp 60–75°), 400 ml of 1:1 carbon tetrachloride–petroleum ether (bp 60–75°), 200 ml of carbon tetrachloride, and 200 ml of ethyl acetate. Evaporation of the first three fractions gave 6.45 g (46%) of **18**, mp 97–101°. Two recrystallizations from petroleum ether (bp 60–75°) raised the melting point to 100–102°. An analytical sample was prepared by sublimation at 90–100° (0.3 mm).

*Anal.* Calcd for $C_{11}H_{11}NO$: C, 76.27; H, 6.40; N, 8.08. Found: C, 76.38; H, 6.38; N, 8.25.

The infrared spectrum ($CCl_4$) showed weak bands at 2.92 (NH) and 3.40 (CH), and strong bands at 5.62 (C=O) and 6.45 μ (aromatic). The ultraviolet spectrum had maxima at 263 mμ (ε 300) and 271 mμ (ε 300).

**With Lithium Aluminum Hydride.**—A slurry of 2.28 g (0.06 moles) of lithium aluminum hydride in 250 ml of ether was added slowly to a stirred solution of 13.57 g (0.05 mole) of **17** in 300 ml of ether. The mixture was stirred at room temperature for 2 hr and then decomposed in the cold with 30% ammonium chloride solution. The solid was filtered and washed with 50 ml of 1:1 methanol–ether. The combined filtrates were dried, filtered, and evaporated. The residue was taken up in methylene chloride and chromatographed as before. The second, third, and fourth 100-ml fractions gave 1.62 g (19%) of **18** on evaporation.

**Benzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (3a).**—A solution containing 27.0 g (0.10 mole) of **17** in 300 ml of anhydrous ether

(36) A. A. Wolf, *J. Chem. Soc.*, 4121 (1953).

was added dropwise (30 min) to a stirred solution of 18.0 g (0.047 mole) of lithium aluminum hydride in 300 ml of ether. The mixture was heated at reflux for 3 hr and cooled. A saturated solution of ammonium chloride was added dropwise, with stirring, until further reaction was no longer evident and then 10 ml excess added. The mixture was stirred for an additional 15 min; the precipitated white solid was filtered and washed with 150 ml of 1:1 methanol–ether. The combined filtrates were washed with four 50-ml portions of 10% hydrochloric acid. The acid washings were saturated with solid potassium hydroxide under a layer of ether and extracted with four 50-ml portions of ether. The combined ether extracts were dried, filtered; solvent was removed *in vacuo*. The residual oil was distilled to give 9.4 g (59%) of **3a**, bp 138–142° (0.7 mm), $n^{25}D$ 1.5761. Its infrared spectrum ($CCl_4$) showed a broad band at 2.96 $\mu$ (NH) and at least four bands in the 3.20–3.50-$\mu$ region (CH). On standing in air, **3a** decomposed to a viscous gum within 48 hr.

Compound **3a** gave a strong positive test for secondary amines with nickel chloride–carbon disulfide–ammonium hydroxide.[11]

Compound **3a**, in hydrochloric acid was treated with a 30% solution of chloroplatinic acid. The amber solid that precipitated was filtered and recrystallized from ethanol–ether acidified with hydrochloric acid to yield the chloroplatinate of **3a** as amber chunks, mp 193–194° dec.

*Anal.* Calcd for $C_{22}H_{28}N_2 \cdot PtCl_6 \cdot H_2O$: C, 35.40; H, 4.05. Found: C, 35.59; H, 4.33.

The phenylthiourea derivative of **3a** was obtained in the usual manner as a white solid, mp 168.5–169° after two recrystallizations from ethanol–petroleum ether (bp 60–75°).

*Anal.* Calcd for $C_{18}H_{18}N_2S \cdot H_2O$: C, 69.23; H, 6.45; N, 9.03. Found: C, 69.44; H, 6.50; N, 9.03.

**7-Methylbenzo[*d*]-*cis*-7-azabicyclo[4.2.0]octane (3b).**—A solution of 9.40 g of **3a**, 25 g of 38% formaldehyde, and 25 g of 90% formic acid was heated on a steam bath for 2 hr. The mixture was saturated with solid sodium hydroxide and extracted with ether. The extracts were dried, filtered, and evaporated. The residue was distilled to give 9.24 g (90%) of **3b**, bp 107–109° (0.6 mm), $n^{25}D$ 1.5550.

The 2-nitro-1,3-indandione salt of **3b** was obtained in the usual manner,[31] mp 164–166° dec.

*Anal.* Calcd for $C_{21}H_{20}N_2O_4 \cdot 0.5H_2O$: C, 67.39; H, 5.67. Found: C, 67.39; H, 5.73.

# The Reaction of Cyclopropyl Ketones with Phosphorus Pentachloride[1]

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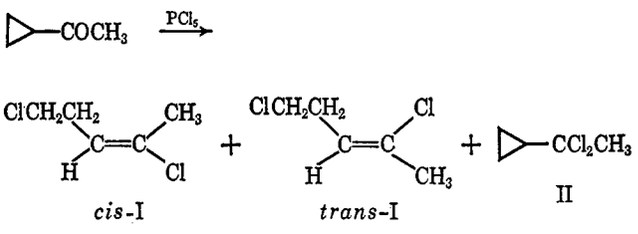
The reactions of a number of cyclopropyl ketones with phosphorus pentachloride have been studied. When run in carbon tetrachloride, the ketonic oxygen of phenyl 1-phenylcyclopropyl ketone is replaced by two chlorines. However, when run in methylene chloride, the cyclopropyl ring of all of the ketones studied is opened and 1,4-dichloro-1-butenes are formed. These facts are explained by nonionic mechanisms utilizing the observation that phosphorus pentachloride is dimeric in carbon tetrachloride and monomeric in methylene chloride.

In an earlier publication[3] the reactions of ketones with phosphorus pentachloride were explained in terms of a chlorocarbonium ion mechanism. The work described herein was undertaken to obtain more information about the reaction mechanism by studies on the reaction of phosphorus pentachloride with ketones containing a cyclopropyl group attached to the ketonic carbonyl group. The result of these studies makes it unlikely that a chlorocarbonium ion is involved for reasons stated below. This conclusion is in agreement with that reached in another study on the reactions of 4-phenyl-2-butanone and 5-phenyl-2-pentanone with phosphorus pentachloride.[4]

The reaction of methyl cyclopropyl ketone with phosphorus pentachloride has been reported to yield 2,5-dichloro-2-pentene[5] (I) and a mixture of I and 1,1-dichloroethyl cyclopropane (II).[6] No mention of the stereochemistry of the 2,5-dichloro-2-pentene produced was made.[5,6] We have found that in methylene chloride at 0° approximately an 80% yield of 70% *cis*- and 30% *trans*-2,5-dichloro-2-pentene is obtained. This ratio was remarkably constant over reaction periods of from 18 to 72 hr. When the reaction was carried out in refluxing carbon tetrachloride for 2 hr, a mixture of unreacted ketone (23%), *cis*-I (26%), *trans*-I (15%), and 36% of a compound believed to be 1,1-dichloroethylcyclopropane (II) (see Experimental Section) was obtained. On standing for 1 week at room temperature, any II had rearranged to a mixture of *cis*-I and *trans*-I. The ratio of *cis*-I to *trans*-I in this mixture was the same as that in reactions run in methylene chloride. The significance of the difference in




products obtained depending on whether methylene chloride or carbon tetrachloride was the solvent will be discussed later in this paper.

On reaction of cyclopropyl phenyl ketone with phosphorus pentachloride in methylene chloride at room temperature for 3 days, or in carbon tetrachloride at reflux for 1 day, there was obtained a mixture of the isomers of 1,4-dichloro-1-phenyl-1-butene (III) in 86 and 95% yield, respectively. *trans*-III (90–98%) was formed in preference to *cis*-III (10–2%) in different runs.

The reaction of cyclopropyl *m*-nitrophenyl ketone with phosphorus pentachloride in methylene chloride was much slower, as after 13 days at room temperature

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(2) Upjohn Fellow, 1960–1961; Lubrizol Fellow, 1962–1963.

(3) M. S. Newman and L. L. Wood, Jr., *J. Am. Chem. Soc.*, **81**, 4300 (1959).

(4) M. S. Newman, G. Fraenkel, and W. N. Kirn, *J. Org. Chem.*, **28**, 1851 (1963).

(5) I. A. Diyakonov, *Zh. Obshch. Khim.*, **10**, 414 (1940); *Chem. Abstr.*, **34**, 7861 (1940).

(6) Y. M. Slobodin and I. N. Shokhor [*Zh. Obshch. Khim.*, **22**, 195 (1952); *Chem. Abstr.*, **46**, 10122 (1952)] did not actually isolate II but assumed its presence because of the formation of cyclopropylacetylene on treatment of the reaction mixture with base.