

Attempted Hofmann Degradation of 32.—To a mixture of sodium hydroxide (14.0 g, 0.35 mol) and **32** (6.45 g, 0.05 mol) in an ice-water mixture (50 g) was added bromine (16.0 g, 0.1 mol) dropwise over 30 min. After heating the reaction mixture on a steam bath until it was clear, hydrochloric acid was added and the mixture was extracted three times with ether. Removal of ether gave a negligible residue as did continuous extraction of the aqueous layer.

Registry No.—**3**, 31420-47-0; **4**, 31443-73-9; **5**, 4606-09-1; **6**, 31420-49-2; **7**, 31420-50-5; **8**, 31420-51-6; **9**, 31392-62-8; **12**, 31420-52-7; **13**, 31420-53-8; **14**, 31420-54-9; **15**, 7687-28-7; **16**, 31420-56-1; **17**,

31420-57-2; **18**, 31420-58-3; **19**, 31392-63-9; **20**, 7371-67-7; **21**, 31420-60-7; **22**, 31443-74-0; **23**, 31420-61-8; **24**, 31420-62-9; **25**, 31420-63-0; **26**, 31420-64-1; **27**, 31420-65-2; **29**, 31420-66-3; **30**, 17868-78-9; **31**, 31420-68-5; **32**, 15982-33-9; *cis*-1,2-di(hydroxymethyl)-cyclopropane, 2345-68-8; *cis*-1,2-cyclopropane dihydrazide, 2374-08-5.

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The Synthesis of 2,5- and 2,6-Bis(bromomethyl)-1,4-diphenylpiperazines and Their Conversion into 2,5-Diphenyl-2,5-diazabicyclo[2.2.2]octane¹

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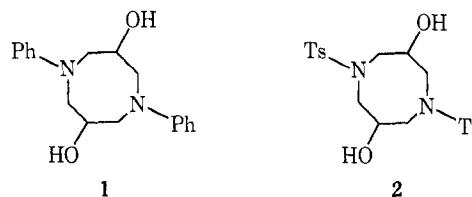
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Treatment of *cis*-1,5-diphenyl-3,7-dihydroxyoctahydro-1,5-diazocine (**1**) with phosphorus tribromide yielded a mixture of *cis*-2,6-bis(bromomethyl)-1,4-diphenylpiperazine (**4**) and *cis*-2,5-bis(bromomethyl)-1,4-diphenylpiperazine (**5**). The structures of **4** and **5** were confirmed by conversion to the corresponding dimethyl-1,4-diphenylpiperazines (**6** and **7**) by lithium aluminum hydride. Compounds **6** and **7** were synthesized from *cis*-2,5- and *cis*-2,6-dimethylpiperazines. Both **4** and **5** on treatment with magnesium in tetrahydrofuran were converted to 2,5-diphenyl-2,5-diazabicyclo[2.2.2]octane (**8**). The interconversion of **4** and **5** is discussed.

As part of a study of the chemistry of 3,7-disubstituted 1,5-diphenyloctahydro-1,5-diazocines, we have investigated the reaction of 1,5-diphenyl-3,7-dihydroxyoctahydro-1,5-diazocine (**1**) with phosphorus tribromide. The synthesis of **1** was first reported by Gaertner,² but the question of the stereochemistry of the hydroxyl groups was not settled. Thin layer chromatography on silica gel of **1** as it crystallized from the reaction mixture shows it to be essentially homogeneous, with only a trace of a second, faster moving component. Recrystallization from ethyl acetate-methanol gives a product homogeneous to thin layer chromatography under a variety of conditions. Paudler and coworkers³ have presented arguments for distinguishing the *cis* and *trans* isomers of 1,5-bis(*p*-toluenesulfonyl)-3,7-dihydroxyoctahydro-1,5-diazocine (**2**) by the separation of the nmr resonances of the ring methylene hydrogens. Thus, with their systems, it would appear that the ring methylene hydrogens are more nearly magnetically equivalent in the *trans* isomer than in the *cis* isomer, and with both isomers in hand, they assign the stereochemistry on this basis. Although the methylene signals of **1** show a comparable separation with *cis*-**2**, 0.89 vs. 0.80 ppm, an examination of both Dreiding and CPK space filling models show that the *N*-phenyl groups of **1** can cause a similar degree of magnetic nonequivalence of the ring methylene hydrogens in a variety of conformations of both *cis* and *trans* isomers. Without isolation of a second isomer, we hesitate to assign stereochemistry on the basis of Paudler's criteria

alone. However, the separation of the methylene resonances together with the stereochemistry of the dibromo derivative discussed below lead us to the conclusion that we are dealing with the *cis* isomer of **1**.



Treatment of **1** with phosphorus tribromide at 115° yields, after hydrolysis with water, a compound, C₁₈H₂₁Br₃N₂ (**3**), which, from its infrared spectrum, was deduced to be a hydrobromide salt. The nmr spectrum of **3** was not that to be expected from a dibromodiazocine, but clearly indicated its structure to be a bis(bromomethyl)-1,4-diphenylpiperazine monohydrobromide. The most significant signal in the spectrum of **3** was a doublet at δ 2.4 (4 H) which was assigned to the methylene hydrogens of the bromomethyl groups, split by the tertiary hydrogen (H_X). The signal from the tertiary hydrogens appeared as a broad multiplet at δ 4.5 (2 H). Irradiation of the signal at δ 4.5 collapsed the signal at δ 2.4 to a singlet. The remaining signals of the ring methylenes appeared as the AM part of an AMX system from δ 3 to 4.

Neutralization of **3** with ammonium hydroxide yielded a solid which upon recrystallization gave a compound C₁₈H₂₀N₂Br₂, mp 132–134°. Concentration of the mother liquor from the recrystallization gave an isomeric compound **5**, mp 117–119°.

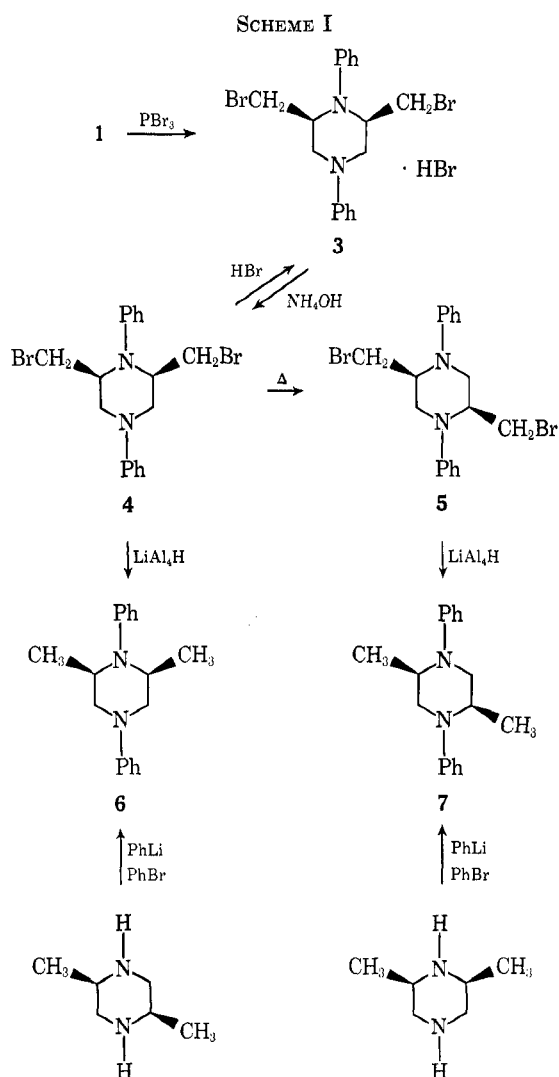
Compounds **4** and **5** were characterized as bromomethylpiperazines by their identical mass spectra, which showed a peak for the loss of a CH₂Br fragment from the molecular ion, and by their reduction to the

(1) (a) This research was supported, in part, by Public Health Service Grant GM-13117. (b) Presented in part at the First International Conference on Heterocyclic Chemistry, Albuquerque, N. M., June 1967. (c) Abstracted in part from the Ph.D. thesis of J. J. W., University of Wyoming, Aug 1968.

(2) V. R. Gaertner, *Tetrahedron Lett.*, 141 (1964).

(3) (a) W. W. Paudler, G. R. Gapski, and J. M. Barton, *J. Org. Chem.*, **31**, 277 (1966); (b) W. W. Paudler, A. G. Zeiler, and G. R. Gapski, *ibid.*, **34**, 1001 (1969).

corresponding dimethylpiperazines with lithium aluminum hydride.⁴ The major product from the reduction of **4** was identical in its nmr and mass spectrum, and vpc retention time, with *cis*-2,6-dimethyl-1,4-diphenylpiperazine (**6**). The lithium aluminum hydride reduction product of **5** was likewise shown to be *cis*-2,5-dimethyl-1,4-diphenylpiperazine (**7**). Compounds **6** and **7** were prepared by the diphenylation of the corresponding dimethylpiperazines. When an ether solution of **4** was treated with gaseous hydrogen bromide, **3** was formed. These reactions are summarized in Scheme I.

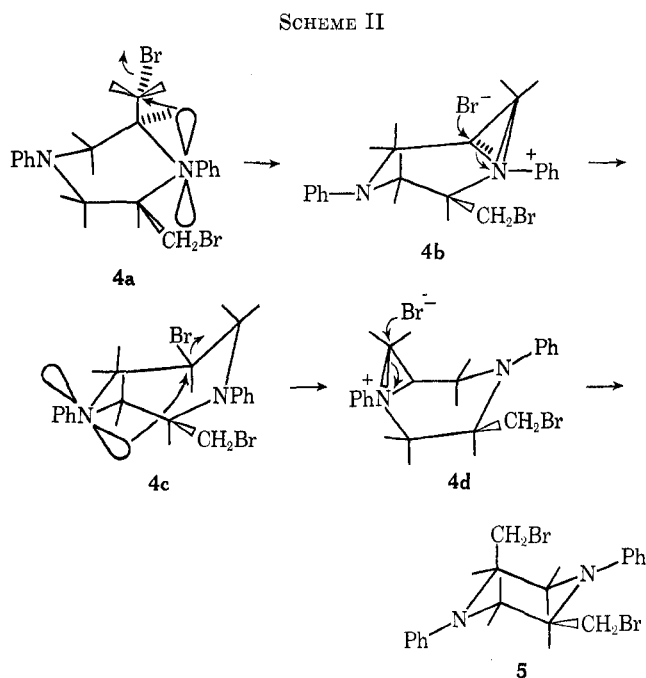


Thus, **3** must be the monohydrobromide salt of *cis*-2,6-bis(bromomethyl)-1,4-diphenylpiperazine (**4**). When **4** was recrystallized from ethyl acetate-methanol, **5** was found in the mother liquors. Also, when **4** was placed in a sublimator and heated to 170°, **5** formed in the melt. Since only one hydrobromide salt was isolated from the reaction of **1** with PBr_3 , the conclusion is that **4** is the major product of the reaction and that **5** results from the thermal rearrangement of **4** to **5**. Using arguments analogous to Paudler's,^{3b} **4** would re-

(4) We originally reported **4** and **5** as dibromodiazocines and proposed the ring contraction upon the reduction with lithium aluminum hydride: D. A. Nelson and J. J. Worman, 153rd National Meeting of the American Chemical Society, Miami Beach, Fla., April 1967, Abstract 85. A subsequent report by Paudler,^{3b} together with the results presented here, show that the ring contraction must occur on treatment of **1** with PBr_3 .

sult from the ring contraction of **1** by way of intermediate aziridinium ions. Assuming a similar mechanism, the *cis* stereochemistry of the bromomethyl groups in **4** should result from a *cis* configuration of the hydroxy groups in **1**.

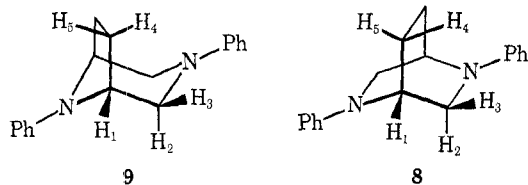
A reasonable mechanism for the rearrangement of **4** to **5** also involving aziridinium ions is shown in Scheme II. An analysis of the reaction pathway using Dreiding



models shows that, if **4** assumes a twist-boat conformation, **4a**, then the electron pair on nitrogen is most favorably located for back-sided displacement of a bromine atom from a pseudoaxial bromomethyl group. A reasonable population of this conformation would be expected because of the considerable nonbonded interactions between the *cis*-diequatorial bromomethyl groups and the 1-*N*-phenyl ring in the chair conformation. Displacement in this conformation leads to formation of the *cis*-aziridinium ion **4b**, which opens to the *cis*-diazepine **4c**. Ring contraction of this structure would be expected to proceed in a stereospecific manner through the aziridinium ion **4d** to give **5**.^{3b}

As part of an investigation of the chemistry of **4** and **5**, an attempt was made to prepare their corresponding Grignard reagents by treatment with magnesium in tetrahydrofuran. In an experiment designed to determine if any rearrangements had taken place, the Grignard solution from **4** was hydrolyzed with aqueous ethanol, and the major product (about 80%) was isolated by trapping from the gas chromatograph. The isolated product contained no bromine but was not the dimethylpiperazine **6**, since it had a mass spectrometric molecular weight of 264. The mass spectrum also showed no $M - 15$ peak, and the ultraviolet spectrum showed no unsaturation. These observations, coupled with the nmr spectrum which showed, in addition to the signals from aromatic hydrogens, three symmetrical multiplets centered at δ 4.34 (2 H), 3.26 (4 H), and 2.00 (4 H), led to the conclusion that the product was either 3,8-diphenyl-3,8-diazabicyclo[3.2.1]octane (**9**) or 2,5-diphenyl-2,5-diazabicyclo[2.2.2]octane (**8**).

An analysis of the nmr spectrum led to the conclusion that the product has structure **8**. The signal at δ 4.34 is assigned to the resonance from H_1 . This



hydrogen is most deshielded since it lies in the plane of the aromatic ring. The signal at δ 3.26 is assigned to H_2 and H_3 , and that at δ 2.00 to H_4 and H_5 . An examination of Dreiding models of **8** and **9** shows that in **8** H_1 has dihedral angles with H_2 , H_3 , H_4 , and H_5 all equal to 60° . Thus values of J_{12} , J_{13} , J_{14} , and J_{15} would all be expected to be very close. At 100-Hz sweep width, the signal at δ 4.34 appears as a broadened quintet, $J = 2.3$ Hz, which would be expected for H_1 split by four equivalent couplings. The broadening is attributed to the nitrogen atom and possible long-range couplings. Irradiation of the signal at δ 3.26 collapsed the signal at δ 4.34 to a triplet, $J = 2.3$ Hz. Upon irradiation of the signal at δ 4.34, the signal at δ 3.26 (H_2 , H_3) collapsed to an AB quartet, $J_{23} = 11$ Hz. In the [3.2.1] structure **9** with the six-membered ring in the boat conformation, $J_{H_{12}} \neq J_{H_{14}}$ and $J_{H_{13}} \neq J_{H_{15}}$. With the six-membered ring in the chair conformation, $J_{H_{12}} = J_{H_{13}}$, but $J_{H_{14}} \neq J_{H_{15}}$. In neither case would the H_1 and H_2 , H_3 resonances be expected to have the observed patterns. As confirmation of these conclusions, the nmr spectra of 3,8-dibenzyl-3,8-diazabicyclo[3.2.1]octane (**12**)⁵ and 2,5-diazabicyclo[2.2.2]octane dihydrochloride (**13**)⁶ were recorded. The H_{23} portion of the spectrum of **10** showed $J_{H_{12}} = 1.8$, $J_{H_{13}} = 2.5$ Hz. The H_{23} portion of the spectrum of **11** showed a pattern very similar to that of **8**, with $J_{12} = J_{13} = 2.3$ Hz.

When **5** was treated with magnesium in tetrahydrofuran, **8** was also formed as the major product. This observation serves to confirm the structure of **8**, and since this can be considered as an internal Grignard coupling reaction it also confirms the structure **5** as the *cis*-2,5-bis(bromomethyl)piperazine. The formation of **8** from **4** must also involve a rearrangement of **4** to **5**, followed by coupling. In refluxing tetrahydrofuran, the solvent of the reaction of **4** with magnesium, **4** was not converted to **5**. Therefore, the organometallic reagent must play some role in the isomerization. Compound **8** was also observed as a minor product in the reduction of both **4** and **5** with lithium aluminum hydride, and as the major product when a tetrahydrofuran solution of **4** was treated with methyllithium. A possible pathway for the conversion of **4** to **8** may involve anionic intermediates. A detailed study of this mechanism is now in progress.

Experimental Section

Infrared spectra were recorded on a Beckman IR-10 as Nujol mulls, KBr pellets, or neat samples on KBr plates. The Perkin-

(5) Kindly supplied by Professor G. G. Gallo, Lepetit Spa, Milano, Italy.

(6) Kindly supplied by Merck Sharp and Dohme Co., through arrangements with Dr. Norman Brink.

Elmer 621 was used to record the infrared spectrum of 2,5-diphenyl-2,5-diazabicyclo[2.2.2]octane (**8**) as a neat sample on KBr plates. Ultraviolet spectra for the diazocines were recorded on a Beckman DB spectrophotometer using 1-cm cells. The mass spectra were obtained from a CEC-21-103-C mass spectrometer or a Varian Mat CH-5 mass spectrometer. Nuclear magnetic resonance spectra were recorded on a Varian HA-100 instrument. The δ values are reported with respect to internal TMS. Gas chromatographic analyses were performed on an Aerograph 1520 using a thermal conductivity detector and helium as the carrier gas. The injector temperature was maintained at 290° and the detector was maintained at 300° . The oven temperature ranged from 185 to 255° depending on the number and types of components involved. Analyses were carried out on $1/8$ -in. columns and preparative work was done using $3/8$ -in. columns.

	Dimensions	Solid support	Liquid
Column A	$1/8$ in. by 5 ft stainless steel	Gas-Chrom P or ABS Anakrom	10% SE-30
Column B	$3/8$ in. by 5 ft aluminum	ABS Anakrom	10% SE-30

Boiling points are uncorrected (prevailing atmospheric pressure approximately 585 mm). The melting points were obtained using a Thiele tube containing paraffin oil and are uncorrected. Elemental analyses were performed by Huffman Laboratories, Wheat Ridge, Colo., and by Schwartzkopf Laboratories, New York, N. Y.

1,5-Diphenyl-3,7-dihydroxyoctahydro-1,5-diazocine (1).—The procedure described here represents a modification of the ones described by Gaertner.⁷ To 8.00 g (0.039 mol) of *N,N*-bis(2,3-epoxypropyl)aniline⁸ in 50 ml of methanol was added 3.72 g (0.039 mol) of aniline. The reaction was stoppered and allowed to stand at room temperature. After 5 days a white solid appeared, and after 11 days this was filtered and dried. After the mother liquor from the above sample was allowed to stand at room temperature for an additional 12 hr, a large mass of white crystals formed: mp 208 – 214° after two recrystallizations from methanol (lit.² mp 208 – 213°); yield 2.30 g (19.8%); uv max ($CH_3C \equiv N$) 250 nm (ϵ 27,000); ir (KBr) 3360, 2990, 1620, 1581, 1520, 1490, 1445, 1390, 1370, 1330, 1279, 1262, 1225, 1167, 1099, 1060, 1034, 1000, 905, 882, 860, 740, 690, 665 cm^{-1} ; nmr (acetone- d_6) δ 7.1 (m, 4), 6.5 (m, 6), 4.3–2.8 (m, 12); mass spectrum (70 eV) m/e (rel intensity) 298 (40), 280 (22), 253 (48), 174 (35), 148 (20), 132 (28), 120 (100).

Reaction of 1 with Phosphorus Tribromide (PBr_3). Preparation of *cis*-2,6-bis(bromomethyl)-1,4-diphenylpiperazine (**4**).—To 1.0 g (3.4×10^{-3} mol) of **1** was added 4.6 g (0.016 mol) of PBr_3 . The solution was stirred magnetically while being heated gently by means of an oil bath. When the temperature of the bath approached 100° , the dihydroxy compound was completely dissolved in the PBr_3 . At 115° a very obvious exothermic reaction took place with the formation of an orange solid. The oil bath was removed and the reaction mixture was allowed to cool to room temperature. The excess PBr_3 was hydrolyzed cautiously with water. Excess water was added and the reaction was stirred at room temperature for 1 hr. The orange solid was collected by filtration and then added slowly, with stirring, to a solution of concentrated ammonium hydroxide. After complete reaction, a light brown solid formed. Recrystallization from ethyl acetate-methanol gave 2.4 g (35%) of a white, cubic solid: mp 132 – 134° ; uv max (95% EtOH) 252 nm (ϵ 27,000) and 246 (23,000); ir (Nujol) 1600, 1280, 1215, 950, 745, 685, 650, 510 cm^{-1} (w); nmr ($CDCl_3$) δ 7.2 (m, 4), 6.8 (m, 6), 4.1–3.8 (m, 10); mass spectrum (70 eV) m/e (rel intensity) 422 (19), 343 (M - Br) (94), 329 (M - CH_2Br) (4), 250 (33), 158 (50), 145 (100), 132 (74), 104 (70), 91 (28), 77 (57).

Anal. Calcd for $C_{18}H_{20}N_2Br_2$: C, 50.97; H, 4.75. Found: C, 50.89; H, 4.97.

Isolation of *cis*-2,5-bis(bromomethyl)-1,4-diphenylpiperazine (5).—The ethyl acetate-methanol mother liquor from the recrystallization of **4** in the previous preparation was evaporated. This gave a white powder, which after repeated recrystallizations from ethyl acetate-methanol yielded white, needle-like crystals:

(7) V. R. Gaertner, private communication.

(8) J. B. McKelvey, B. C. Webre, and R. R. Benerito, *J. Org. Chem.*, **25**, 1424 (1960).

mp 117–119°; ir (Nujol) 1600, 1280, 1245, 1215, 945, 745, 685, 655, 520 cm^{-1} (m); nmr (CDCl_3) δ 7.3 (m, 4), 6.9 (m, 6) 4.2–2.8 (m, 10). The mass spectrum and the ultraviolet spectrum were identical with those of 4. Through many attempts, the maximum yield obtainable for this isomer was 12%.

Anal. Calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{Br}_2$: C, 50.97; H, 4.75. Found: C, 51.12; H, 4.78.

Preparation of *cis*-2,6-Bis(bromomethyl)-1,4-diphenylpiperazine Monohydrobromide (3).—This procedure was similar to that for the preparation of 4. After reaction of 1 with PBr_3 and prior to neutralization with concentrated ammonium hydroxide, the orange solid was recrystallized from ethyl acetate-methanol. Several recrystallizations yielded a white, crystalline compound: mp 217–220° dec; ir (Nujol) 2290, 2200, 1600, 1260, 1225, 950, 745, 700, 685, 645 cm^{-1} ; nmr (CF_3COOH) δ 7.9 (m, 10), 5.4 (m, 2), 4.2–4.3 (m, 4), 2.4 (d, 4). This material was only slightly soluble in water, but gave a positive test for ionic halogen using silver nitrate reagent.

Anal. Calcd for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{Br}_3$: C, 42.80; H, 4.19. Found: C, 43.15; H, 4.22.

Reaction of 4 with Anhydrous Hydrogen Bromide.—To 100 ml of ether-cyclohexane (8:2) was added 1 g of 4 and the solution was heated gently to dissolve all the material. Through this solution was passed a stream of anhydrous hydrogen bromide and after 5 min the solution became cloudy. The gas was passed through the solution for an additional 10 min. The solution was evaporated *in vacuo* and yielded a white solid, mp 160–180°. This solid was extracted with two 20-ml portions of chloroform, and most of the material was dissolved. The remaining insoluble material, 0.2 g, had mp 219–220°. The infrared spectrum of the solid melting at 219–220° was identical with that of 3.

Reaction of 4 with Lithium Aluminum Hydride (LiAlH_4) to 6.—To 1.5 g (0.0035 mol) of 4 in 10 ml of dry tetrahydrofuran (THF) was added a solution of 1 g of LiAlH_4 in 20 ml of dry THF, and the solution was stirred at room temperature for 5.5 hr. Excess LiAlH_4 was hydrolyzed with ethyl acetate, and, after the reaction ceased, 15 ml of water was added. After the reaction mixture was stirred overnight, a white solid appeared. To this was added excess water, and the solution was filtered. The lithium salts were washed well with water and ether. The ether layer was separated, dried over magnesium sulfate, filtered, and evaporated *in vacuo* to a volume of 3 ml. Vpc analysis of the residue showed the presence of four species, and the major product appeared to be present to the extent of 90%. This was trapped from column B, using a column temperature of 200° and a flow rate of helium of 120 ml/min: ir (Nujol) 3020, 2950, 2780, 1600, 1500, 1450, 1370, 1340, 1300, 1240, 1150, 1100, 1030, 1000, 930, 890, 810, 770, 745, 690 cm^{-1} ; mass spectrum (70 eV) m/e (rel intensity) 266 (42), 251 (27), 146 (63), 132 (18), 119 (47), 105 (100), 104 (67); nmr (CDCl_3) δ 7.2 (m, 10), 3.5 (q, 2), 3.3 (m, 2), 2.7 (q, 2), 0.86 (d, 6).

Reaction of 5 with LiAlH_4 to 7.—A 1-g sample of 5 was dissolved in 10 ml of THF and the solution was added to a solution of 0.5 g of LiAlH_4 in 15 ml of THF. The remainder of the procedure was identical with that described for the reaction of 4 with LiAlH_4 . The major product was isolated by vpc trapping techniques from column B, using a column temperature of 200° and a flow rate of 120 ml/min. The mass spectra showed a molecular ion at m/e 266 and was essentially identical with that of product isolated from the reaction of 4 with LiAlH_4 : ir (Nujol) 3070, 3020, 2980, 2830, 1600, 1500, 1450, 1380, 1250, 1160, 1060, 1030, 990, 910, 865, 840, 785, 745, 685, 550, 510 cm^{-1} ; nmr (CDCl_3) δ 7.2 (m, 4), 6.8 (m, 6), 3.5 (m, 2), 3.5 (q, 2), 2.9 (q, 2), 1.13 (d, 6).

Isolation of 2,5-Diphenyl-2,5-diazabicyclo[2.2.2]octane (8).—The last peaks observable on the gas chromatograms of the two foregoing reactions were trapped. The mass spectrum gave a molecular ion at m/e 264 and no $M - 15$ fragment; uv max (95% EtOH) 252 nm (ϵ 27,000); ir (Nujol) 3060, 3040, 3030, 2960, 2900, 2840, 1600, 1500, 1455, 1370, 1340, 1320, 1300, 1245, 1220, 1190, 1160, 1125, 1080, 1055, 1030, 990, 950, 905, 870, 795, 750, 690, 540, 520, 490 cm^{-1} ; nmr (CDCl_3) δ 7.2 (m, 4), 6.8 (m, 6), 4.34 (m, 2) 3.26 (m, 4), 2.00 (m, 4).

Reaction of 4 with Lithium Aluminum Deuteride.—The procedure used here was identical with the one described for the reaction of 4 with LiAlH_4 except that reduction was carried out with LiAlD_4 . Analysis and isolation of the products was carried out by vpc using column B, a column temperature of 200°, and a flow rate of 120 ml/min. The mass spectrum of the major product gave a molecular ion at m/e 268 with a major fragment

at $M - 16$ ($-\text{CH}_2\text{D}$); nmr (CDCl_3) δ 7.4–6.8 (m, 10), 3.5 (q, 2), 3.25 (m, 2), 2.75 (q, 2), 0.88 (t, 2), 0.82 (t, 2).

Preparation of *cis*-2,6-Dimethyl-1,4-diphenylpiperazine (6).—The procedure used was a modification of the one used by Starker⁹ for the preparation of monophenylpiperazines. A solution containing 12 g (0.10 mol) of *cis*-2,6-dimethylpiperazine (Aldrich) in 24 ml (0.20 mol) of bromobenzene and 65 ml of THF was added to a solution of 100 ml (0.20 mol) of phenyllithium in ether (Alpha Inorganics). The addition was carried out with stirring and at such a rate that the temperature did not exceed 70°. After total addition (3 hr), the reaction was allowed to come to room temperature. The excess phenyllithium was hydrolyzed with water (caution—the hydrolysis reaction had a latent period). The organic layer was separated and was evaporated under reduced pressure. Vpc analysis, using column A, a temperature of 185°, and a flow rate of 60 ml/min, gave a peak identical in retention time with the product isolated from the reaction of 4 with LiAlH_4 . Many peaks appeared on the chromatogram, and the desired product was estimated to be present to the extent of about 2%. This dark brown, oily residue (10 ml) was extracted with 30 ml of 6 *N* hydrochloric acid, and the aqueous solution was extracted with ether repeatedly until no more biphenyl was observed in the ether extract (by vpc analysis). The acidic aqueous solution was neutralized with approximately 29% aqueous ammonium hydroxide until the solution became basic to litmus. The resulting free base was extracted with ether, and the ether layer was separated, dried over magnesium sulfate, and evaporated *in vacuo* to give a dark brown oil. The desired compound was trapped by techniques using column B at a column temperature of 215° and a flow rate of 180 ml/min. The nmr spectrum in CDCl_3 was identical with that of the product of the reaction of 4 with LiAlH_4 .

Preparation of *cis*-2,5-Dimethyl-1,4-diphenylpiperazine (7).—The quantities and conditions were similar to those described for the preparation of 6 except that after addition of the starting materials to the phenyllithium, the reaction was heated and stirred at 41° overnight and then hydrolyzed with water. The yield of the compound did not appear to increase under these conditions (2% by glc analysis). The infrared and nmr spectra were identical with those of the product of the reaction of 5 with LiAlH_4 .

Reaction of 4 with Magnesium.—In 5 ml of dry THF was placed 0.5 g of magnesium turnings and a small crystal of iodine to initiate the reaction. To this was added 5 ml of a solution containing 1 g of 4 in 25 ml of THF. No apparent reaction took place. A small amount of *n*-butyl bromide was added and the reaction was brought to reflux. The remainder of the solution of 4 was then added, and the reaction mixture seemed to darken. After the system was maintained at reflux for 5 hr the solution was black. The reaction was allowed to cool to room temperature and 5 ml of ethanol was added to decompose the Grignard reagent. After the ethanol reaction had ceased, 10 ml of water was added and the reaction mixture was stirred overnight. More water was added to give a two-phase system with ether, and the reaction mixture was extracted with two 40-ml portions of ether. The extracts were combined, dried over magnesium sulfate, and evaporated *in vacuo*. Vpc analysis using column B, a column temperature of 215°, and a flow rate of 180 ml/min gave a peak of retention time 39 min. This peak was trapped and showed identical vpc retention time and infrared and nmr spectra with those of the sample of 8, which was isolated from the reaction of 4 with LiAlH_4 . As estimated by vpc, the product was obtained in 80% yield.

Reaction of 4 with Methylolithium.—To a solution of 4.0 ml of 2.6 *M* methylolithium (Alpha Inorganics) in 25 ml of ether was added a solution containing 1.0 g (0.0024 mol) of 4 in 25 ml of THF. The reaction was brought to reflux and was maintained at these conditions for 20 hr. The reaction mixture gave a yellow solution and a white precipitate. When water was added to hydrolyze the excess methylolithium, the white precipitate dissolved, giving a two-layer system. The ether layer was separated and the aqueous layer was extracted repeatedly with ether. The ether layers were combined, dried over magnesium sulfate, and evaporated *in vacuo*. Vpc analysis, using column B, a column temperature of 255°, and a flow rate of 180 ml/min, showed one major product and five smaller peaks. The major product was trapped and proved to be identical in all spectral properties with the sample of 8 which was isolated from the re-

(9) L. N. Starker, J. K. Paul, and L. Goldman, U. S. Patent 3,173,917 (Cl. 260-268); *cf. Chem. Abstr.*, **62**, 13160d (1965).

action of **4** with LiAlH_4 . It was estimated by vpc to be present to the extent of 50% of the reaction mixture.

The Nmr Spectrum of 2,5-Diazabicyclo[2.2.2]octane (13).—2,5-Diazabicyclo[2.2.2]octane dihydrochloride was obtained from Merck.⁶ This sample was dissolved in D_2O and the nmr spectrum showed the following signals: δ 2.20 (4 H, m, 80-Hz width), 3.69 (4 H, octet), and 4.05 (2 H, m). To this sample was added concentrated ammonium hydroxide such that the solution was just basic to litmus. The nmr spectrum of this sample had the following signals: δ 2.25 (4 H, m, 80 Hz width) and 3.53 (6 H, m). In the dihydrochloride salt the signal at δ 3.69 represented an AB portion of an ABX system where $J_{\text{AX}} = 2.3$, J_{BX} and $J_{\text{AB}} = 11$ Hz.

The Nmr Spectrum of 3,8-Dibenzyl-3,8-diazabicyclo[3.2.1]-octane (12).—The sample used here was supplied by Gallo,⁵ who prepared the sample by a procedure described by Blackman.¹⁰ The nmr of this sample had the following signals: δ 7.25 (10 H, m), 3.45 (4 H, d), 3.0 (2 H, m), 2.35 (4 H, octet), 1.85 (4 H,

m). The signal at δ 2.35 represented the AB portion of an ABX pattern in which $J_{\text{AX}} = 3$, $J_{\text{BX}} = 2$, and $J_{\text{AB}} = 10$ Hz.

Conversion of 4 to 5.—A 1-g sample of **4** was placed in a vacuum sublimator and was heated gradually from 50 to 170° over a 3-hr period at 4 mm. No visual sublimation occurred. The resulting material appeared as a slightly darkened melt. This was taken up in methanol-ethyl acetate. A minimum amount was used such that only the dark impurities dissolved. The remaining white, crystalline solid was recrystallized from ethanol-ethyl acetate to give a solid, mp 117–119°, whose infrared and nmr spectra were identical with those of a sample of **5**. The above conversion also occurred on recrystallization. A 1-g sample of **4** was recrystallized from ethanol-ethyl acetate to give 0.80 g of pure material. Evaporation of the mother liquor gave 0.15 g of a material whose melting point and nmr spectrum were identical with those of a sample of **5**.

Registry No.—**1**, 30715-42-5; **3**, 30715-43-6; **4**, 30788-18-2; **5**, 30715-44-7; **6**, 30715-45-8; **7**, 24425-88-5; **8**, 30715-47-0; **12**, 17740-42-0; **13**, 658-24-2.

(10) S. W. Blackman and R. Blatzly, *J. Org. Chem.*, **26**, 2750 (1961).

1,1-Dimethyl-1-sila-2,3:6,7-dibenzocycloheptatriene. A Dibenzosilepin

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The first example of the dibenzosilepin ring system has been synthesized. 1,1-Dimethyl-1-sila-2,3:6,7-dibenzocycloheptatriene (**6**) was prepared through cyclization of *o,o'*-dilithiobibenzyl and dichlorodimethylsilane followed by free-radical (NBS) dibromination and finally debromination with metallic zinc. The nonplanarity of **6** could not be established through low-temperature nmr studies. The uv spectrum of **6** revealed no evidence of ($\pi \rightarrow d$) π bonding.

When the vast research effort which has been exerted toward the synthesis and study of heterocycloheptatrienes [*e.g.*, oxepines (**1a**), azepines (**1b**), thiepins (**1c**), and diazepines]² is considered, it is rather surprising to note that only one proven³ and two possible^{4,5} examples of a silicon-containing cycloheptatriene (silacycloheptatriene or silepin, **1d**) have been reported. This dearth

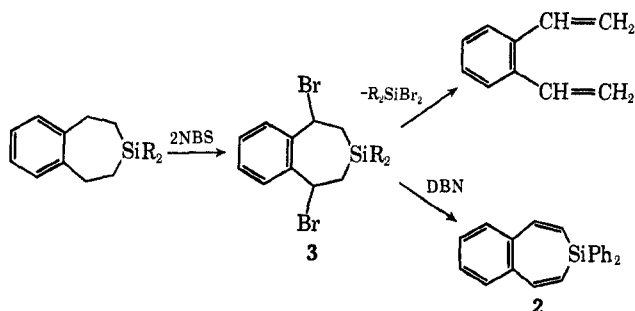


- 1a**, X = O
b, X = NR
c, X = S
d, X = SiR₂

of information in the chemical body of knowledge is particularly glaring in view of the unique situation for the possible observation of ($\pi \rightarrow d$) π bonding⁶ in the silepin ring system. It could be hoped that the aromatic character derived from cyclic delocalization of the six

π electrons would put this type of valence expansion to a stern test.

A search of the literature revealed a single unambiguous example of an intentional silepin synthesis, the benzosilepin **2**, which originally failed⁷ due to the extreme lability of the synthetic intermediate, 1,5-dibromo-3,3-dimethyl-1,2,4,5-tetrahydro-3H-3-benzosilepin (**3**), which was due to operation of that persistent



stumbling block of organosilicon chemistry, the β effect.⁵ Birkofer⁸ was finally able to prepare **2**, in low yield, through the use of 1,5-diazabicyclo[4.3.0]nonene (DBN) as a dehydrobromination agent. Examination of the carbon-carbon double bond stretching frequencies in the infrared spectrum of **2** led Birkofer to conclude that there was interaction between the π electrons of the olefinic system and the vacant d orbitals of silicon. However, it should be noted that these ir bands (1592 and 1550 cm^{-1}) were not significantly different from the double-bond stretches of other vinylsilanes (*e.g.*,

(1) National Science Foundation Undergraduate Research Participant, summers of 1969 and 1970.

(2) For an excellent review of the syntheses and chemistry of azepines, oxepines, and thiepins, see L. A. Paquette in "Nonbenzenoid Aromatics," Vol. 1, J. P. Snyder, Ed., Academic Press, New York, N. Y., 1970, pp 249–310.

(3) L. Birkofer and H. Haddad, *Chem. Ber.*, **102**, 432 (1969).

(4) H. Gilman, S. G. Cottis, and W. H. Atwell, *J. Amer. Chem. Soc.*, **86**, 5584 (1964).

(5) K. A. Andrianov, L. M. Vokova, N. V. Delazari, and N. A. Chumayevskii, *Akad. Nauk Latv. SSR*, 435 (1967), report that dimethylmethoxychlorosilane and *o*-dichlorobenzene react with sodium to afford 1,1-dimethyltrienosilepin in <0.02% yield.

(6) For a summary of the evidence relating to ($p \rightarrow d$) π and ($\pi \rightarrow d$) π bonding to silicon, see E. A. V. Ebsworth in "Organometallic Compounds of the Group IV Elements," Vol. 1, A. G. MacDiarmid, Ed., Marcel Dekker, New York, N. Y., 1968, part 1, Chapter 1.

(7) L. Birkofer and E. Kramer, *Chem. Ber.*, **102**, 427 (1969).

(8) C. Eaborn, "Organosilicon Compounds," Butterworths, London, 1960.