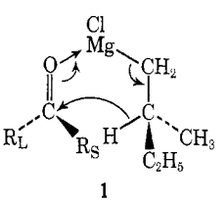
TABLE I
ASYMMETRIC REDUCTION OF KETONES BY (+)-TRIS[(S)-2-METHYLBUTYL]ALUMINUM ETHERATE IN BENZENE SOLUTION

Ketone	Product	Isolated yield, %	$[\alpha]^{25}D$	Configuration	Optical purity, %
Acetophenone	Methylphenylcarbinol	83	−3.38[a]	S[b]	8[c]
Isobutyrophenone	Isopropylphenylcarbinol	93	−14.10[d]	S[e]	30[f]
n-Butyrophenone	*n*-Propylphenylcarbinol	97	−3.39[g]	S[e]	7[h]
3,3-Dimethyl-2-butanone	*tert*-Butylmethylcarbinol	*i*	−0.64[i]	R[k]	13[l]

[a] Determined for the neat liquid. [b] K. Mislow, *J. Amer. Chem. Soc.*, **73**, 3954 (1951). [c] R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **99**, 45 (1911). [d] Determined in ether solution, *c* 23.76. [e] R. MacLeod, F. J. Welch and H. S. Mosher, *J. Amer. Chem. Soc.*, **82**, 876 (1960). [f] P. A. Levene and L. A. Mikeska, *J. Biol. Chem.*, **70**, 355 (1926). [g] Determined in benzene solution, *c* 11.34. [h] J. Kenyon and S. M. Partridge, *J. Chem. Soc.*, 128 (1936). [i] Product isolated by preparative gas chromatography on a 15 ft × 0.25 in. column packed with 10% silicone QF-1 on Chromosorb P; purity >99% by gas chromatography. [j] Determined in absolute ethanol, *c* 7.11. [k] J. Jacobus, Z. Majerski, K. Mislow, and P. v. R. Schleyer, *J. Amer. Chem. Soc.*, **91**, 1998 (1969). [l] R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, **105**, 1115 (1914).

tones, positions the larger carbonyl substituent, R_L, opposite the methyl group of the Grignard reagent while the smaller carbonyl substituent, R_S, is opposite the ethyl group.[2] A similar transition state, **2**, would



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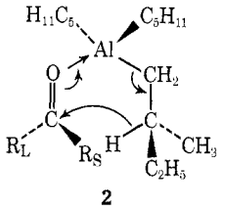

2

be anticipated to control the product stereochemistry in the asymmetric reduction of ketones with (+)-tris-[(*S*)-2-methylbutyl]aluminum etherate.[3a] This model does, in fact, correctly predict the absolute configuration of the predominant enantiomer resulting from reduction of each alkyl phenyl ketone examined. Surprisingly, however, it fails to predict the absolute configuration of the principal enantiomer resulting from reduction of 3,3-dimethyl-2-butanone. Since only one of the three alkyl groups of a trialkylaluminum reagent is utilized in the reduction of ketones,[3b] it appears that the asymmetry of the two alkyl groups not participating in hydride transfer is capable of exerting a controlling influence on the stereochemistry of this reduction.

Experimental Section[5]

(+)-Tris[(*S*)-2-methylbutyl]aluminum Etherate.—Conversion of 34.006 g (0.319 mol) of (+)-(*S*)-1-chloro-2-methylbutane, $[\alpha]^{25}D$ +1.58° (neat), 95% optical purity,[6] to the Grignard reagent followed by reaction with 9.883 g (0.074 mol) of anhydrous aluminum chloride according to the procedure of Pino, *et al.*,[7] afforded 13.882 g (60%) of (+)-tris[(*S*)-2-methylbutyl]-aluminum etherate: bp 111.0–115.0° (3 mm) [lit.[7] bp 87–89° (0.6 mm)]; $[\alpha]^{25}D$ +22.04° (*c* 16.78, hexane).

Reduction of Acetophenone.—The following preparation is representative of the general procedure. Under an atmosphere of dry nitrogen, 1.191 g (10 mmol) of acetophenone was added by syringe to a solution of 3.192 g (10 mmol) of (+)-tris[(*S*)-2-methylbutyl]aluminum etherate in 30 ml of benzene. An immediate orange coloration developed which faded within 30 sec. The solution was heated at reflux under nitrogen for 2 hr. After cooling to room temperature, the resulting mixture was decomposed with 25 ml of 3 *M* HCl and diluted with an additional 30 ml of benzene. The benzene layer was separated, washed with 25 ml of water, and dried over anhydrous $MgSO_4$. Removal of solvent *in vacuo* followed by distillation afforded 1.008 g (83%) of methylphenylcarbinol: bp 77.0–78.0° (4.5 mm); $[\alpha]^{25}D$ −3.38° (neat); >99% pure by gas chromatography on a 15 ft × 0.25 in. column packed with 10% silicone QF-1 on Chromosorb P.

(5) Optical rotations were measured with an O. C. Rudolph and Sons, Inc., Model 200 photoelectric polarimeter equipped with a Model 340 oscillating polarizer.

(6) F. C. Whitmore and J. H. Olewine, *J. Amer. Chem. Soc.*, **60**, 2570 (1938).

(7) P. Pino, L. Lardicci, and G. P. Lorenzi, *Ann. Chim. (Rome)*, **48**, 1426 (1958).

Registry No.—(+)-Tris[(*S*)-2-methylbutyl]aluminum etherate, 18902-57-3; acetophenone, 98-86-2; isobutylophenone, 611-70-1; *n*-butyrophenone, 495-40-9; 3,3-dimethyl-2-butanone, 75-97-8; methylphenylcarbinol, 1445-91-6.

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Ring Expansion of 1-Azirines to Azepines *via* Cycloaddition

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The chemistry of heterotropilidenes has received considerable impetus in recent years due in large part to the elegant synthetic contributions of Paquette and coworkers.[1] In the course of our work on the chemistry of 1-azirines,[2-5] we examined some symmetry-allowed thermal [$\pi^4 + \pi^2$] cycloadditions of the rigid C=N double bond with dienes. We discovered, as reported briefly earlier,[6] that cyclopentadienones reacted readily with 1-azirines (**1**) to furnish in good yields azatropilidenes.

When 2-phenyl-1-azirine (**1a**) was treated with 2,5-dimethyl-3,4-diphenylcyclopentadienone in benzene at reflux temperatures for 4 days, a relatively stable, pale yellow, crystalline compound was isolated in 65% yield. Mass spectral data and elemental analysis were consistent with the molecular formula $C_{26}H_{23}N$. The in-

(1) L. A. Paquette in "Nonbenzenoid Aromatics," Vol. I, J. P. Snyder, Ed., Academic Press, New York, N. Y., 1969.

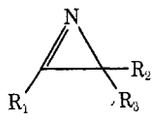
(2) V. Nair, *J. Org. Chem.*, **33**, 2121 (1968).

(3) G. Smolinsky and C. A. Pryde, *ibid.*, **33**, 2411 (1968).

(4) N. J. Leonard and B. Zwanenburg, *J. Amer. Chem. Soc.*, **89**, 4456 (1967).

(5) A. Hassner and F. W. Folwler, *ibid.*, **90**, 2869 (1968).

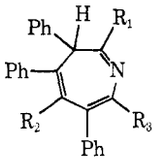
(6) A preliminary report of our results was announced in the 15th Annual Report of the Petroleum Research Fund, 1970. After this manuscript was submitted for publication, a communication on the cycloaddition of azirines to cyclopentadieones by D. J. Anderson and A. Hassner appeared in *J. Amer. Chem. Soc.*, **93**, 4339 (1971).



1a, R_1 = Ph; R_2 = H; R_3 = H
b, R_1 = Ph; R_2 = CH_3; R_3 = H
c, R_1 = Ph; R_2 = Ph; R_3 = H

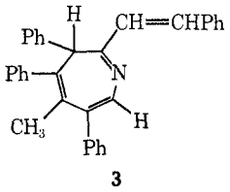
frared spectrum showed no carbonyl or NH absorption. The ultraviolet spectrum in CH_2Cl_2 exhibited absorption maxima at 302 nm (log ϵ 4.03), 270 (4.21), and 235 (4.58). The nmr spectrum ($CDCl_3$) at room temperature showed singlets at δ 1.77 (3 H) and 2.27 (3 H), 5.28 (1 H) and 6.94 (1 H), and a complex multiplet between 7.05 and 7.36 (15 H). The singlet at δ 2.27 disappeared within 20 min at 80° on D_2O exchange.[7] It could not be hydrogenated easily.[8] Attempted cycloadditions with tetracyanoethylene and 1,3-diphenylisobenzofuran were unsuccessful.

The data presented above together with the mechanistic rationalization suggested below led to the 3*H*-azepine (**2a**) as a plausible structure.



2a, R_1 = R_2 = CH_3; R_3 = H
b, R_1 = R_2 = Ph; R_3 = H
c, R_1 = R_2 = R_3 = CH_3
d, R_1 = R_2 = Ph; R_3 = CH_3
e, R_1 = R_2 = CH_3; R_3 = Ph
f, R_1 = R_2 = R_3 = Ph

The protons responsible for the rapid deuterium exchange are those of the 2-methyl group. Thus, when the compound was heated with benzaldehyde in the presence of pyrrolidine, a smooth condensation to the 2-styryl derivative (**3**) occurred.



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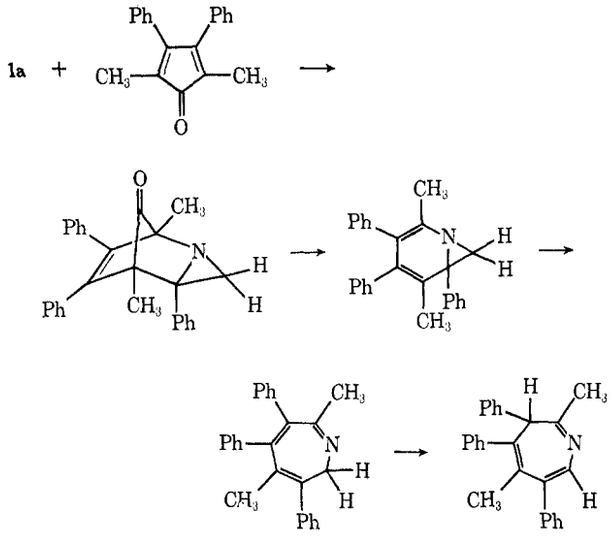
The generality of this transformation was established by preparation of compounds **2c** and **2e** from azirines **1b** and **1c** and 2,5-dimethyl-3,4-diphenylcyclopentadienone, and **2b**, **2d**, and **2f** from 2,3,4,5-tetraphenylcyclopentadienone and azirines **1a**, **1b**, and **1c**.

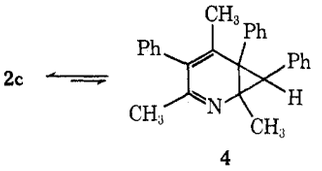
A possible mechanism for the formation of the azepine (Scheme I) assumes a normal Diels–Alder cycloaddition to furnish a strained adduct which undergoes a cheletropic fragmentation[9,10] to give an azanorcaradiene. The symmetry-allowed electrocyclic rearrangement of the azanorcaradiene to its valence tautomer, the azacycloheptatriene (or 2*H*-azepine)[11] is followed by a 1,5-suprafacial sigmatropic shift of the 2 hydrogen to give apparently the thermodynamically more stable 3*H*-azepine.

SCHEME I



Several interesting aspects of the chemistry of these azepines need explanation. Their inability to react with dienophiles or as dienophiles in the Diels–Alder fashion is the result of considerable steric crowding from the spatially large phenyl and methyl substituents. The ultraviolet and nmr spectra reflect not only differences arising from substituents but also any changes in preferred geometry resulting from the crowding.

Of particular interest in our informative D_2O exchange experiments was the observation that the azepine **2c** underwent deuterium exchange not only at the 2-methyl group (20 min at 80°) but also at the 7-methyl group, although the latter exchange was very slow (24 hr at 80°). In contrast, azepine **2d** did not show any tendency to exhibit this behavior at the 7-methyl group. One possible explanation for this is that **2c** undergoes this exchange *via* its valence tautomer **4**, which may be present in very small amounts in equilibrium with the azacycloheptatriene **2c**. This valence tautomerism may not be possible in **2d** because of steric crowding.



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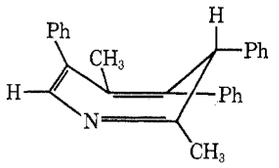
Initial variable-temperature nmr studies (−100 to 130°) suggest that these azepines (**2a–f**) exist predominantly in one conformation at room temperature and that the energy of activation for the flipping process is high.[12] Of the two conformations **5** and **6** (for **2a**), it would be reasonable to suggest that the preferred

(7) (a) L. A. Paquette, *J. Org. Chem.*, **28**, 3590 (1963); (b) T. J. van Bergen and R. M. Kellog, *ibid.*, **36**, 978 (1971).
(8) Prolonged hydrogenation in the presence of Pt gave a very complex mixture of products which could not be easily handled.
(9) R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).
(10) M. A. Battiste, *Chem. Ind. (London)*, 550 (1961).
(11) G. Maier, *Angew. Chem., Int. Ed. Engl.*, **6**, 402 (1967).
(12) A. Mannschreck, G. Rissmann, F. Vögtle, and D. Wild, *Chem. Ber.*, **100**, 335 (1967).

conformation would be **5**, where the bulky phenyl group at C-3 occupies the equatorial position.



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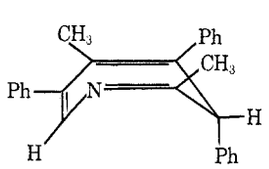

6

Experimental Section

2,5-Dimethyl-3,4,6-triphenyl-3*H*-azepine (**2a**).—A solution of 468 mg (4 mmol) of 2-phenyl-1-azirine (**1a**)[6] in 10 ml of benzene was treated with a solution of 520 mg (2 mmol) of 2,5-dimethyl-3,4-diphenylcyclopentadienone[13] in 10 ml of benzene.[14] The reaction mixture was heated under reflux for 4 days and then separated by preparative layer chromatography using silica gel PF_{254} with 50% benzene–pentane as the developing solvent. The azepine **2a** crystallized slowly from pentane to give 458 mg of pale yellow plates (65% yield based on the cyclopentadienone): mp 133–134°; uv $\lambda_{max}^{CH_2Cl_2}$ 235 nm (log ϵ 4.58), 270 (4.21), and 302 sh (4.03); nmr $\delta_{TMS}^{CDCl_3}$ 1.77 (s, 3 H), 2.27 (s, 3 H), 5.28 (s, 1 H), 6.94 (s, 1 H), 7.05–7.36 (m, 15 H).

Anal. Calcd for $C_{26}H_{23}N$: C, 88.59; H, 7.43; N, 3.97. Found: C, 88.21; H, 7.05; N, 3.93.

5-Methyl-3,4,6-triphenyl-2-styryl-3*H*-azepine (**3**) was formed when a solution of the azepine **2c** (100 mg) in benzene (10 ml) was heated under reflux for 4 days with an excess of a mixture of benzaldehyde and pyrrolidine. The solvent and excess reagents were removed under reduced pressure and the residue was chromatographed on preparative plates using silica gel PF_{254}. The styryl derivative **3** crystallized slowly from pentane to give 44 mg of bright yellow rods (36%): mp 161–163°; uv $\lambda_{max}^{CH_2Cl_2}$ end absorption, 283 nm (log ϵ 4.51), 315 (4.26), and 375 (4.16); nmr $\delta_{TMS}^{CDCl_3}$ 1.77 (s, 3 H), 5.81 (s, 1 H), 6.93 (d, 1 H), 7.17–7.38 (m, 22 H).

Anal. Calcd for $C_{33}H_{27}N$: C, 90.57; H, 6.22; N, 3.20. Found: C, 90.74; H, 5.92; N, 3.35.

2,3,4,5,6-Pentaphenyl-3*H*-azepine (**2b**) was prepared by reaction of 2-phenyl-1-azirine (**1a**) and tetraphenylcyclopentadienone in refluxing mesitylene. The azepine **2b** crystallized from benzene–hexane as yellow plates (90%): mp 217–218°; uv $\lambda_{max}^{CH_2Cl_2}$ 235 nm (log ϵ 4.46), 270 (4.52), and 325 (3.99); nmr $\delta_{TMS}^{CDCl_3}$ 6.45 (s, 1 H), 6.79–7.83 (m, 26 H).

Anal. Calcd for $C_{36}H_{27}N$: C, 91.30; H, 5.74; N, 2.96. Found: C, 90.23; H, 5.21; N, 3.00.

2,5,7-Trimethyl-3,4,6-triphenyl-3*H*-azepine (**2c**) was prepared from 3-methyl-2-phenyl-1-azirine (**1b**)[2] and 2,5-dimethyl-3,4-diphenylcyclopentadienone. The azepine **2c** crystallized from benzene–pentane as pale yellow plates (69%): mp 182–183°; uv $\lambda_{max}^{CH_2Cl_2}$ 233 nm (log ϵ 4.24), 270 (4.18), and 305 sh (4.03); nmr $\delta_{TMS}^{CDCl_3}$ 1.51 (s, 3 H), 1.57 (s, 3 H), 2.18 (s, 3 H), 5.16 (s, 1 H), 6.74–7.39 (m, 15 H).

Anal. Calcd for $C_{27}H_{25}N$: C, 89.21; H, 6.93; N, 3.85. Found: C, 88.90; H, 6.96; N, 3.79.

7-Methyl-2,3,4,5,6-pentaphenyl-3*H*-azepine (**2d**) was prepared from 3-methyl-2-phenyl-1-azirine (**1b**) and tetraphenylcyclopentadienone in 84% yield as pale yellow rods: mp 208°; uv $\lambda_{max}^{CH_2Cl_2}$ 235 nm (log ϵ 4.48), 270 (4.54), 350 (3.89); nmr $\delta_{TMS}^{CDCl_3}$ 1.80 (s, 3 H), 6.28 (s, 1 H), 6.83–7.83 (m, 25 H).

Anal. Calcd for $C_{37}H_{29}N$: C, 91.14; H, 6.00; N, 2.86. Found: C, 91.85; H, 6.47; N, 2.45.

A minor product of this reaction (<5% yield) was a very pale yellow crystalline compound, mp 198–201°, which had the molecular formula $C_{37}H_{29}N$ (microchemical analysis and mass spectrometry) and the following spectral characteristics: uv $\lambda_{max}^{CH_2Cl_2}$ 232 nm (log ϵ 4.49), 270 sh (4.33), 292 (4.38), and 325 (4.23); nmr $\delta_{TMS}^{CDCl_3}$ 2.20 (s, 3 H), 5.61 (s, 1 H), 6.68–7.33 (m, 25 H).[15]

Anal. Calcd for $C_{37}H_{29}N$: C, 91.14; H, 6.00; N, 2.86. Found: C, 91.14; H, 5.79; N, 2.94.

2,5-Dimethyl-3,4,6,7-tetraphenyl-3*H*-azepine (**2e**) was prepared from 2,3-diphenyl-1-azirine (**1c**)[5] and 2,5-dimethyl-3,4-diphenylcyclopentadienone in 58% yield as pale yellow plates: mp 186–188°; uv $\lambda_{max}^{CH_2Cl_2}$ 242 nm (log ϵ 4.16), 270 (4.22), and 312 (4.11); nmr $\delta_{TMS}^{CDCl_3}$ 1.63 (s, 3 H), 2.26 (s, 3 H), 5.27 (s, 1 H), 6.40–7.38 (m, 20 H).

Anal. Calcd for $C_{32}H_{27}N$: C, 90.31; H, 6.40; N, 3.29. Found: C, 90.16; H, 6.90; N, 3.15.

2,3,4,5,6,7-Hexaphenyl-3*H*-azepine (**2f**) was prepared from 2,3-diphenyl-1-azirine (**1c**) and tetraphenylcyclopentadienone in 91% yield as pale yellow plates: mp 227°; uv $\lambda_{max}^{CH_2Cl_2}$ 243 nm (log ϵ 4.42), 270 (4.53), and 350 (4.12); nmr $\delta_{TMS}^{CDCl_3}$ 6.40 (s, 1 H), 6.74–7.86 (m, 30 H).

Anal. Calcd for $C_{42}H_{31}N$: C, 91.76; H, 5.68; N, 2.56. Found: C, 91.78; H, 5.65; N, 2.82.

Registry No.—**2a**, 33070-60-9; **2b**, 33070-61-0; **2c**, 33070-62-1; **2d**, 33070-63-2; **2d**, 4*H*-azepine isomer, 33070-64-3; **2e**, 33070-65-4; **2f**, 33070-66-5; **3**, 33070-67-6.

Acknowledgment.—Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society (Grant No. 1871-G1), for partial support of this research.

(13) (a) F. W. Graw, *J. Chem. Soc.*, **95**, 2131 (1909); (b) C. F. H. Allen and J. A. Van Allan, *J. Amer. Chem. Soc.*, **64**, 1260 (1942).

(14) A twofold excess of the azirine was used in all runs because of the instability of the azirines at elevated temperatures.

(15) This compound is tentatively assigned the 4*H*-azepine isomer of **2d** on analytical and spectral evidence. Further support for this structure came from D_2O exchange studies, which indicated rapid exchange of the methyl group.