146.25, 150.00, and 151.77; m/e 270 (M^+), 241 (base), and 226; M_r+ calcd 270.1232, found 270.1228. Anal. Calcd for $C_{15}H_{17}F_3O$: C, 66.66; H, 6.34. Found: C, 66.74; H, 6.35.

Preparation of (η^2-2-Acetyl-4-cyanophenyl)tetracarbonylmanganese (4g) by Reaction of 3-Acetylbenzonitrile with Benzylpentacarbonylmanganese. A solution containing 2.7 mmol of 3-acetylbenzonitrile and 0.85 g of benzylpentacarbonylmanganese in 50 mL of heptane was heated under reflux for 12 h. At the end of this time the reaction mixture was concentrated, and the residue was subjected to silica gel flash chromatography with hexane as the eluent to give as the only isolable product 88 mg (11%) of (2-acetyl-4-cyanophenyl)tetracarbonylmanganese (**4g**) as an orange solid: mp 109–110 °C (from hexanes); IR ($CHCl_3$) 2230, 2085, 2000, 1950, 1595, and 1310 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 2.69 (s, 3 H), 7.58 (d, J = 7.6 Hz, 1 H), 8.07 (s, 1 H), and 8.27 (d, J = 7.6 Hz, 1 H). Anal. Calcd for $C_{13}H_6MnNO_5$: C, 50.19; H, 1.94; N, 4.50. Found: C, 50.20; H, 2.02; N, 4.48.

Reaction of α-Tetralone with Benzylpentacarbonylmanganese. A solution containing 6.9 mmol of α-tetralone and 2.37 g of benzylpentacarbonylmanganese in 75 mL of heptane was heated under reflux for 3 h and 45 min. At the end of this time the mixture was concentrated, and the residue was subjected to flash chromatography with hexane as the eluent to give 1.98 g (92%) of [4a,8a-(5,6-dihydro-8(7*H*)-naphthalenone)]tetracarbonylmanganese (**10**) as orange-yellow crystals: mp 96–98 °C (from hexanes); IR ($CHCl_3$) 2080, 1990, 1940, 1592, 1570, 1545, 1423, and 1410 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 2.10 (tt, J = 6.4 and 6.1 Hz, 2 H), 2.71 (t, J = 6.4 Hz, 2 H), 2.90 (t, J = 6.1 Hz, 2 H), 6.93 (d, J = 7.4 Hz, 1 H), 7.34 (dd, J = 7.4 and 7.3 Hz, 1 H), and 7.91 (d, J = 7.3 Hz, 1 H); m/e 312 (M^+), 258, 228, 200, 146, 131, 118 (base), and 90; M_r+ calcd 311.9830, found 311.9835. Anal. Calcd for $C_{14}H_9MnO_5$: C, 53.87; H, 2.91. Found: C, 53.91; H, 2.95.

Attempted reaction of this material with trimethylamine *N*-oxide and 3-hexyne at room temperature in acetonitrile gave a complex mixture and no evidence of cyclized product.

Reaction of Benzosuberone with Benzylpentacarbonylmanganese. A solution containing 3.9 mmol of benzosuberone and 1.23 g of benzyl(pentacarbonyl)manganese in 75 mL of heptane was heated under reflux for 10 h. At the end of this time the mixture was concentrated, and the residue was subjected to flash chromatography with hexane as the eluent to give 81% of [4a,9a-(benzosuber-9-one)]tetracarbonylmanganese (**11**) as yellow crystals: mp 96–97 °C (from hexanes); IR ($CHCl_3$) 2080, 1990, 1935, 1572, and 1558 cm^{-1}; ^1H NMR ($CDCl_3$, 360 MHz) δ 1.73–1.85 (m, 2 H), 1.87–2.0 (m, 2 H), 2.89 (t, J = 6.0 Hz, 2 H), 2.96 (t, J = 6.0 Hz, 2 H), 6.95 (d, J = 7.3 Hz, 1 H), 7.30 (dd, J = 7.3 and 7.3 Hz, 1 H), and 7.93 (d, J = 7.5 Hz, 1 H). Anal. Calcd for $C_{15}H_{11}MnO_5$: C, 55.23; H, 3.40. Found: C, 55.22; H, 3.47.

The above complex was reacted with trimethylamine *N*-oxide and 3-hexyne to yield 65% of 1,2-diethyl-9a-hydroxy-6,7,8,9-tetrahydro-9a*H*-benz[*cd*]azulene (**12**) as a white crystalline solid: mp 103–104 °C (from hexanes); IR ($CHCl_3$) 3585, 2960, 2920, 2840, 1595, 1447, 1087, 1067, 1010, and 985 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.08–1.52 (m, 9 H), 1.9–2.12 (m, 2 H), 2.17–2.7 (m, 7 H), 3.20 (m, 1 H), 6.84 (d, J = 7.1 Hz, 1 H), 6.98 (d, J = 7.0 Hz, 1 H), and 7.11 (dd, J = 7.1 and 7.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 13.33, 14.95, 17.50, 18.54, 26.75, 28.89, 32.90, 34.46, 85.30, 116.16, 125.63, 127.99, 138.44, 139.57, 142.87, 146.69, and 148.76. Anal. Calcd for $C_{17}H_{22}O$: C, 84.25; H, 9.15. Found: C, 84.15; H, 9.17.

Acknowledgment. We thank Monsanto Company for support of this research.

Registry No. **1**, 50831-23-7; **2a**, 117583-04-7; **2b**, 5418-21-3; **2c**, 117583-05-8; **2d**, 117583-06-9; **2e**, 117583-07-0; **2f**, 117583-08-1; **2g**, 117583-09-2; **2h**, 117583-10-5; **2i**, 117583-11-6; **2j**, 117583-12-7; **2k**, 117583-13-8; **2l**, 117583-14-9; **2m**, 117583-15-0; **2n**, 117583-16-1; **2o**, 117583-17-2; **2p**, 117583-18-3; **2q**, 117583-19-4; **2r**, 117583-20-7; **3a**, 117583-32-1; **3b**, 117583-33-2; **3c**, 117583-34-3; **3e**, 55401-25-7; **4a**, 117583-35-4; **4b**, 117583-36-5; **4c**, 117583-37-6; **4d**, 55401-24-6; **4e**, 55401-27-9; **4f**, 117583-38-7; **4g**, 117583-39-8; **5**, 117583-30-9; **6**, 117583-26-3; **7**, 117583-28-5; **8**, 529-34-0; **9**, 826-73-3; **10**, 117583-40-1; **11**, 117583-41-2; **12**, 117583-31-0; **13**, 75421-59-9; **14**, 117583-21-8; **15**, 117583-24-1; **16**, 22303-81-7; **17**, 117583-27-4; **18**, 117583-29-6; **19**, 117583-25-2; **20**, 117583-23-0; EtC≡CEt, 928-49-4; PhC≡CPh, 501-65-5; C_4H_9C≡CH, 693-02-7; *c*-$C_6H_{11}C$≡CH, 931-48-6; PhC≡CH, 536-74-3; Me_3SiC≡CH, 1066-54-2; C_4H_9C≡$CSiMe_3$, 3844-94-8; EtO_2CC≡CMe, 4341-76-8; EtO_2CC≡CEt, 55314-57-3; *c*-$C_6H_{11}C$≡CCO_2Et, 33547-94-3; EtOC≡CH, 927-80-0; EtOC≡CEt, 14272-91-4; EtOC≡$CSiMe_3$, 1000-62-0; Me_3SiCH_2C≡CMe, 18825-29-1; EtC≡CCH_2SiMe_3, 40748-39-8; 3-FC_6H_4COMe, 455-36-7; 3-ClC_6H_4COMe, 99-02-5; 3-BrC_6H_4COMe, 2142-63-4; 3-MeC_6H_4COMe, 585-74-0; 3-$MeOC_6H_4COMe$, 586-37-8; 3-HOC_6H_4COMe, 121-71-1; 3-$F_3CC_6H_4COMe$, 349-76-8; 3-$O_2NC_6H_4COMe$, 121-89-1; 3-NCC_6H_4COMe, 6136-68-1; $PhCH_2Mn(CO)_5$, 14049-86-6; acetophenone, 98-86-2; trimethylamine *N*-oxide, 1184-78-7; 2-ethoxy-3-ethyl-1-methyl-1*H*-inden-1-ol, 117583-22-9; 1-hepten-4-yne, 19781-78-3.

Efficient Preparation of Cis Vicinal Tertiary Diamines from 2-Hydroxy Ketones in Two Steps†,[1]

Gideon Fraenkel,* Judith Gallucci, and Howard S. Rosenzweig

Department of Chemistry, The Ohio State University, Columbus, Ohio 43210

Received July 12, 1988

Cyclic (C_5 and C_6) cis vicinal tertiary diamines are efficiently prepared by catalytic hydrogenation, Pd(C), of the corresponding N-substituted amino enamines, e.g. **6**. The latter are obtained by *p*-toluenesulfonic acid catalyzed condensation of secondary amines with cyclic 2-hydroxy ketones in refluxing benzene under Dean–Stark conditions or from the N-substituted 2-amino ketones. For example *cis*-1,2-dipyrrolidinocyclohexane has been obtained from adipoin in 69% overall yield, isolated.

Cis vicinal tertiary diamines, a hitherto neglected functionality, are potentially important ligands for Pt^{2+}, Mg^{2+}, Zn^{2+}, and Li^+ as well as catalysts for the reactions of organolithium compounds.[2] However, due to the absence of efficient methods to make them, these interesting

† Dedicated to Professor E. J. Corey on the occasion of his 60th birthday.

(1) Abstracted from the Ph.D. Thesis of Howard Rosenzweig, The Ohio State University, 1987.

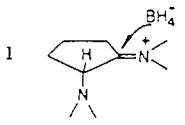
(2) Langer, A. W. *Trans. N. Y. Acad. Sci. Ser. II* **1965**, *27*, 741.

0022-3263/89/1954-0677$01.50/0

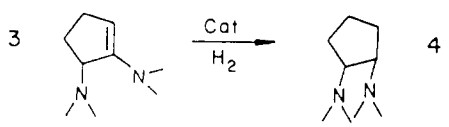
compounds[3-12] have not been readily available for extensive investigation. This situation has now been alleviated via a new two-step procedure, starting from 2-hydroxy ketones, the subject of this paper.

Results and Discussion

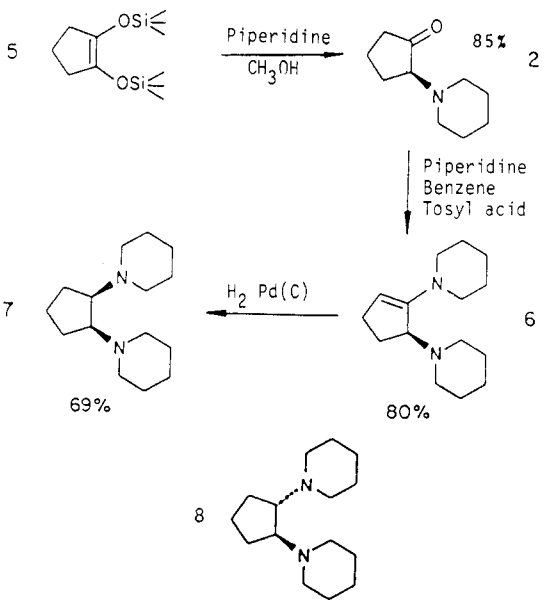
We have already reported that reductive amination of 2-(*N,N*-dimethylamino)cyclopentanone, using buffered dimethylamine with sodium borohydride, gives exclusively *cis*-bis(dimethylamino)cyclopentane, a result ascribed to attack of borohydride at the unhindered side of the intermediate imminium ion, see **1**. However, when the



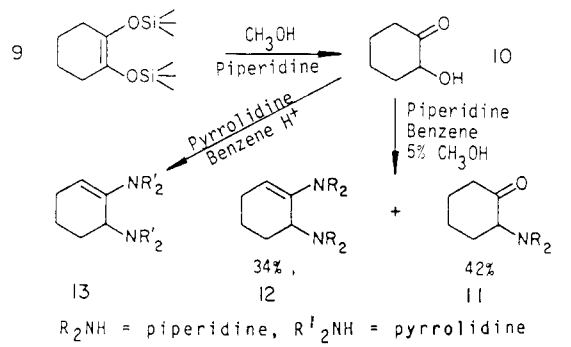
analogous reaction was attempted with 2-(1-piperidino)-cyclopentanone (**2**) and piperidine, only *cis*- and *trans*-2-(1-piperidino)cyclopentanol were obtained. It was then decided to prepare separately and purify cyclic amino enamines in the hope that such compounds would undergo catalytic hydrogenation from the unhindered side to render the desired *cis*-diamines. These transformations have now



been accomplished and form the basis of an unusually simple and economical synthesis of cyclic cis vicinal tertiary diamines. Thus piperidine reacted with silyl ether **5** in methanol at 25 °C over 20 h to give the expected α-amino ketone, **2**, in 83% yield. Reaction of **2** with piperidine in benzene with a few crystals of *p*-toluenesulfonic acid under Dean–Stark conditions yielded enediamine **6**. Hydrogenation of **6** over 5% Pd on carbon for 10 h gave exclusively *cis*-diamine **7** in 69% yield, isolated. Trans isomer **8** was not detected. The cis stereochemistry of **7** was confirmed via X-ray crystallography of its dipicrate, mp 188–190 °C; see below. It is noteworthy that catalytic hydrogenation of these cyclic amino enamines invariably results in cis stereochemistry.



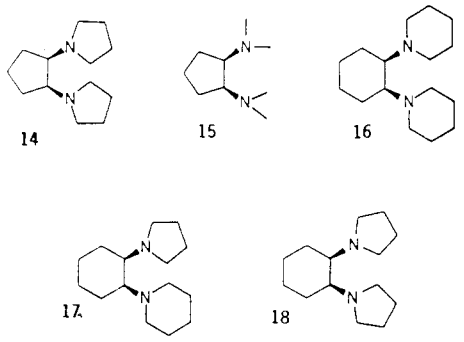
A serendipitous simplification of the above procedure emerged during experiments with 1,2-bis(trimethylsiloxy)cyclohexene, **9**. When **9** was reacted with piperidine in methanol, 25 °C, *adipoin*, **10**, was observed to be the sole product. Treatment of crude **10** (contaminated by 5% methanol) with piperidine in benzene (Dean–Stark conditions) gave rise to a mixture of amino ketone **11** (42%) and enediamine **12** (34%). Note that a similar reaction



of adipoin with pyrrolidine in benzene (no methanol) reported by Jerussi gave only 2-(1-pyrrolidino)cyclohexanone.[15] Thus it appeared that 2-hydroxy ketone would be an even more useful starting material to make *cis*-diamines than the 1,2-disiloxy enes. Thus refluxing adipoin and pyrrolidine in benzene with a few crystals of *p*-toluenesulfonic acid in a Dean–Stark apparatus for 50 h produced the required amino enamine **13**. Hydrogenation of the cannulated benzene solution over 5% Pt (Al_2O_3) gave *cis*-1,2-di-1-pyrrolidinocyclohexane, **18**, in 60% yield, isolated, based on adipoin. Compounds **14–18** are typical examples of cis vicinal tertiary diamines prepared by the above described exhaustive amination–reduction routes. These procedures are simple, inexpensive, and involve minimum workup.

From the present as well as previous studies[13] it appears that amination of 1,2-disiloxy enes only produces amino ketones when methanol is the solvent. However, the formation of 2-(*N,N*-dimethylamino)cyclopentanone from **5** and dimethylamine is always accompanied by 10% am-

(3) Fraenkel, G.; Pramanik, P. *J. Org. Chem.* **1984**, *49*, 1314.
(4) Confalone, P. N.; Pizzolato, G.; Uskokovic, M. R. *J. Org. Chem.* **1977**, *42*, 135–39. Baker, B. R.; Anerry, M. V.; Safir, S. R.; Bernstein, S. *J. Org. Chem.* **1946**, *12*, 138–54. Olsen, R. K.; Hennen, W. J.; Wardle, R. B. *J. Org. Chem.* **1982**, *47*, 4605–4611.
(5) (a) Parry, R. J.; Kunitani, M. G.; Vielle, O., III *J. Chem. Soc., Chem. Commun.* **1975**, 321. (b) Swift, G.; Swern, D. *J. Org. Chem.* **1967**, *32*, 511–517. (c) Confalone, P. N.; Pizzolato, G.; Baggiolini, E. G.; Lollar, D.; Uskokovic, M. R. *J. Am. Chem. Soc.* **1975**, *97*, 5936.
(6) Mercuriamination: Barluenga, J.; Alonso-Cives, L.; Ansenio, G. *Synthesis* **1979**, 962–964. Barluenga, J.; Aznar, F.; Liz, R. *J. Chem. Soc., Chem. Commun.* 1181–1182. (**1981**,) Aminopalladation: Backvall, J. *Tetrahedron Lett.* **1978**, 163–166.
(7) Chong, A. O.; Oshima, K.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 3420–3426.
(8) Sharpless, K. B.; Singer, S. P. *J. Org. Chem.* **1976**, *41*, 2504–2506.
(9) (a) Levy, N.; Scaife, W.; Wilder-Smith, A. E. *J. Chem. Soc.* **1948**, 52–60. (b) Marx, M.; Marti, F.; Reisdorff, J.; Sandmeier, R.; Clark, S. *J. Am. Chem. Soc.* **1977**, *99*, 6754.
(10) Broadbent, H. S.; Allred, E. L.; Pendleton, L.; Whittle, W. C. J. *J. Am. Chem. Soc.* **1960**, *82*, 189–93.
(11) Becker, P. N.; White, M. A.; Bergman, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 5676.
(12) Kohn, H.; Jung, S.-H. *J. Am. Chem. Soc.* **1983**, *105*, 4106. Jung, S.-H.; Kohn, H. *J. Am. Chem. Soc.* **1985**, *107*, 2931.
(13) Heine, H. G.; Fischler, H. M. *Chem. Ber.* **1972**, *105*, 975.
(14) All NMR and IR spectra are consistent with the assigned structures.
(15) Jerussi, R. A. *J. Org. Chem.* **1969**, *34*, 3648. Klemmensen, P.; Schroll, G.; Lawesson, S. *Ark. Kemi.* **1968**, *28*, 405.

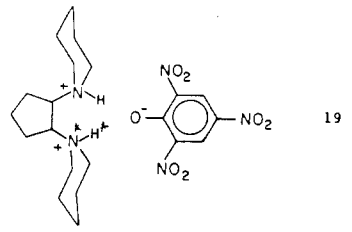


14 15 16

17 18

ino enamine, even with use of methanol as reaction medium.

The structure of diamine **7**, confirmed via X-ray crystallography[16-18] of its dipicrate (Figure 1), clearly shows cis nitrogens, both protonated. One phenoxy O^- is bridged between the two NH^+ protons. A second picrate lies on the far side of the dication. This triple ion arrangement is reminiscent of the structures of dimeric ion-paired carbanion salts observed spectroscopically[19] and others proposed from kinetic data.[20] Hydrogen bond distances, see **19**, H–O and H*–O, are respectively 1.99 and 1.63 Å,



19

shorter than those commonly seen for ammonium salts,[21] 2.57–3.22 Å. Other significant parameters are bond distances, N*–N 3.164 Å and N–H–O 2.856 Å, and angles, H*–O–H 75.7° and N*–C–C–N 50.6° (dihedral). The latter may be the result of N^+, N^{*+} repulsion mitigated by the hydrogen bonds. Note that the *N,N* distance in dimers of organolithium compounds bidentately complexed to TMEDA is 2.75 Å.[22]

In conclusion we have shown that exhaustive amination of a 2-hydroxy ketones or its bis(silyl enol ether) followed by catalytic hydrogenation of the resulting amino enamine is a simple inexpensive route to previously inaccessible cis vicinal tertiary diamines. Extensions of the chemistry described above are currently under investigation.

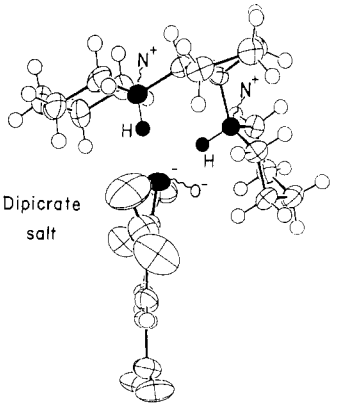


Figure 1. ORTEP diagram, triple ion portion, of the dipicrate of *cis*-1,2-di-*N*-piperidinocyclopentane.

Experimental Section

Gas chromatography was carried out with a Hewlett-Packard Model HP-5710A instrument equipped with a flame ionization detector and a 12-m glass capillary column of internal diameter 0.2 mm and coated with SP2100 liquid phase. Manipulations requiring an inert open atmosphere were carried out in a Vacuum Atmospheres Co. Model HE-43 dry box under argon. All melting and boiling points are uncorrected.

Reactions involving enamines as well as amines were carried out under an inert atmosphere due to the sensitivity of these compounds to oxygen and of the enamines to hydrolysis. All enamines and amines were stored under argon.

The purity of each title compound was shown to be >97% by GC, ^1H NMR, and/or ^{13}C NMR analyses, except where mixtures are specifically indicated.

1,2-Bis(trimethylsiloxy)cyclopentene (5). In a modification that improves upon Ruhlmann's method,[23] sodium (50.6 g, 2.2 g-atom) in 600 mL of dry toluene was reacted with trimethylchlorosilane (254 g, 2.33 mol) and dimethyl glutarate (80.5 g, 0.5 mol) under reflux conditions and agitation with a Vibra-Mixer for 5 h. Filtration of the reaction mixture (argon atmosphere) followed by evaporation of solvent yielded an oil, which on distillation, bp 40–47 °C (0.41 Torr), gave 67.8 g (56%) of the title compound. ^1H NMR (90 MHz, $CDCl_3$): δ 2.13 (t, J = 0.7 Hz, 4 H, allylic), 1.7 (quintet, J = 0.7 Hz, 2 H, methylene), 0.1 (s, 18 H, trimethylsiloxy). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 130.63 (vinyl), 30.25 (allylic), 16.96 (methylene), and 0.72 (trimethylsiloxy).

2-(1-Piperidino)cyclopentanone (2). Via the method of Heine and Fischler,[13] piperidine (6.1 g, 0.07 mol) and 1,2-bis(trimethylsiloxy)cyclopentene (16.5 g, 0.069 mol) were allowed to react in anhydrous methanol (17 mL) in a closed pressure bottle under an argon atmosphere with stirring over 27 h. Evaporation of solvent followed by vacuum distillation of the residue, bp 48–53 °C (0.33 Torr), gave 9.16 g of the title compound in 83% yield. This product must be stored under an inert atmosphere. ^1H NMR (90 MHz, $CDCl_3$): δ 3.0 (t, J = 0.9 Hz, 1 H, methinyl), 2.8–1.25 (mu, 16 H). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 219.59 (carbonyl), 71.93 (methinyl), 51.23, 39.50, 26.13, 24.34, 23.96, and 18.40. IR ($CDCl_3$): 2750 (s), 1750 cm^{-1} (s). MS: 167.1302 (d, parent ion) and 111.1031 (d, base peak).

1,5-Di-1-piperidinocyclopent-1-ene (6). In a flame-dried flask, fitted with a Dean–Stark assembly, was placed a magnetic stirring bar, ca. 2–3 mg of *p*-toluenesulfonic acid, 19 mL of benzene, amino ketone **2** (8.99 g, 0.05 mol), and piperidine (4.8 g, 0.05 mol). Benzene was introduced into the Dean–Stark trap, and the reaction solution was allowed to reflux (oil bath) with stirring for 48 h. By this time accumulation of water in the Dean–Stark trap had ceased. After removal of volatile components first by distillation through glass helices (12 cm), the residue was fractionated through a 10-cm Vigreux column, bp 100–106 °C (0.54 Torr), giving 9.46 g (80%) of **6**. ^1H NMR (90 MHz, $CDCl_3$ filtered through basic alumina): δ 4.25 (1 H, vinyl), 3.75 (hump, 1 H,

(16) Crystal data for **8**: space group $P\bar{1}$, a = 8.725 (2) Å, b = 12.574 (2) Å, c = 15.216 (2) Å, α = 90.04 (1)°, β = 109.03 (1)°, and δ = 98.97 (1)°. Data were measured by the $\theta - 2\theta$ scan out to 2θ = 45° with Mo Kα radiation. The structure was solved by a combination of MULTAN 80[17] and routine Fourier transform methods. Full-matrix least-squares refinement in SHELX-76[18] resulted in R = 0.079 and R_w = 0.056 for the 3097 intensities with $F_o^2 > 1\sigma(F_o^2)$. Hydrogens were included at calculated positions, with assumed bond lengths of 1 Å for NH and CH. One nitro group in coordinated picrate is disordered.

(17) Maia, P.; Fiske, S. J.; Hull, S. E.; Lessinger, L.; Germain, G.; Declereq, J.-P.; Woolfson, M. M. *MULTAN80, A System of Computer Programs for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*; Universities of York, England and Louvain, Belgium, 1980.

(18) Sheldrick, G. M. *SHELX-76. Program for Crystal Structure Determination*; University Chemical Laboratory, Cambridge, England, 1976.

(19) Fraenkel, G.; Hallden-Abberton, M. P. *J. Am. Chem. Soc.* **1981**, *103*, 5657.

(20) Ise, M.; Mirota, H.; Makino, J.; Takaya, K.; Kakayamo, M. *J. Phys. Chem.* **1970**, *74*, 606. Bhattacharyya, D. N.; Smid, J.; Szwarc, M. *J. Am. Chem. Soc.* **1964**, *86*, 5024.

(21) Stout, G. H.; Jensen, L. H. *X-ray Structure Determination - A Practical Guide*; Macmillan Publishing Co.: New York, 1968.

(22) Zerger, R. P.; Stucky, G. D. *J. Chem. Soc., Chem. Commun.* **1973**, 44. Thoennes, D.; Weiss, E. *Chem. Ber.* **1978**, *111*, 3157.

(23) Ruhlmann, K. *Synthesis* **1971**, 236.

methinyl), 3.25–2.05 (8 H, *N*-methylene), 2.0–1.69 (m), and 1.69–1.18 (12 H, methylene). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 151.08 (quaternary vinyl), 99.01 (vinyl), 68.22 (methinyl), 49.12, 28.87, 26.83, 25.87, 25.17, 24.72, and 22.23. IR (neat, NaCl plates): 3060 (w), 2925 (s), and 1628 cm^{-1} (m). MS: 234.2090 (d, parent ion), 149.1150 (d, base peak).

***cis*-1,2-Di-1-piperidinocyclopentane (7).** A 500-mL Parr bottle closed with a no. 6 bored-out neoprene stopper, with attached septum, was flamed-out under a stream of argon. After cooling, anhydrous ethyl acetate (100 mL) was syringed in, followed by endiamine **6** (7.54 g, 0.032 mol), and then the 5% Pd/C catalyst (0.754 g) was introduced. The bottle was re-stoppered and flushed again with argon once and with hydrogen four times and then charged with over 40 psi of hydrogen, and the system was allowed to rock overnight to insure completion of reduction. After completion, the Parr bottle was quickly stoppered as above and flushed with argon before gravity-filtering the reaction mixture (through two funnels with fluted filter paper in series). The bottle was then washed twice with ethyl acetate (50 mL × 2), and the washings were filtered. The ethyl acetate was evaporated, and the liquid residue was dissolved in 10 mL of anhydrous diethyl ether. Calcium hydride, 50 mg, was added to this solution, and the ether was removed by distillation at atmospheric pressure under argon. Vacuum distillation of the residue, bp 83–87 °C (0.17 Torr), gave 5.25 g (69%) of diamine **7** as a clear, colorless liquid. The picrate derivative was formed in a stirred, refluxing saturated ethanolic solution of picric acid. The crude picrate was recrystallized twice from methanol, mp 190 °C dec, in order to obtain crystals suitable for X-ray diffraction. The *cis*-diamine was stored under argon. ^1H NMR (90 MHz, $CDCl_3$): δ 2.8–2.2 (mu, 10 H, methylene-N), 1.9–1.2 (mu, 18 H, methylene). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 67.63 (methinyl), 52.70, 27.23, 26.73, 25.04, and 22.47. IR ($CDCl_3$): 2940 (s), 1446 (w), 1250 cm^{-1} (m). MS: 236.2270 (d, parent ion) and 124.1110 (d, base peak). Dipicrate crystals were obtained as yellow rectangular rods, of $P\bar{1}$ space group, a = 8.725 Å, b = 12.574 Å, c = 15.216 Å, β = 109.03°, and Z = 2.

2-(1-Pyrrolidino)cyclopentanone. This compound was prepared in similar fashion to amino ketone **2**. Thus from silyl ether **5** (12.5 g, 0.05 mol) and pyrrolidine (3.6 g, 0.05 mol) in 12.5 mL of methanol was obtained 5.2 g (68%) of the title compound, bp 35–43 °C (0.25 Torr). ^1H NMR (90 MHz, $CDCl_3$): δ 3.19–1.52 (mu). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 210.39 (carbonyl), 69.40 (methinyl), 51.54, 36.95, 27.93, 23.14 and 18.45. IR ($CDCl_3$): 2974 (s), 2886 (w), 2811 (m), and 1740 cm^{-1} (s). MS: 153.1162 (parent ion) and 97.0812 (base peak).

1,5-Di-1-pyrrolidinocyclopent-1-ene. From 2-*N*-pyrrolidinocyclopentanone (4.67 g, 0.031 mol) and pyrrolidine (2.46 g, 0.035 mol) in benzene (40 mL), via the procedure for 1,5-di-1-piperidinocyclopent-1-ene, was obtained after the usual workup 5.28 g (83%) of the title compound as a light yellow liquid, bp 55–65 °C (0.2 Torr). ^1H NMR (90 MHz, $CDCl_3$ filtered through basic alumina): δ 4.07 (1 H, vinyl), 3.87 (hump, 1 H, methinyl), 3.40–2.0 (12 H), 1.99–1.4 (8 H). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 149.11 (quaternary vinyl), 94.71 (vinyl), 64.31 (methinyl), 48.51, 48.02, 25.05, 24.67, 23.85, 23.52. IR ($CDCl_3$): 3035 (w), 2965 (s), 1630 cm^{-1} (s). MS: 206.1811 (d, parent ion) and 135.1050 (d, base peak).

***cis*-1,2-Di-1-pyrrolidinocyclopentane (14).** From 1,5-di-1-pyrrolidinocyclopent-1-ene (4.35 g, 0.021 mol) and 5% Pd/C (0.42 g) in ethyl acetate, 50 mL, via the procedure for diamine **7**, was obtained 2.40 g (58%) of the title compound, bp 63–72 °C (0.30 Torr). ^1H NMR (90 MHz, $CDCl_3$): δ 2.89–2.36 (mu, 10 H), 2.02–1.32 (14 H, methylene). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 69.12 (methinyl), 53.21, 28.33, 23.41, 20.90. IR ($CDCl_3$): 2970 (s), 2887 (w), 2791 (m), 1465 cm^{-1} (w). MS: 208.1946 (d, parent ion) and 110.0988 (d, base peak).

2-(*N*,*N*-Dimethylamino)cyclopentanone. Via the procedure to prepare amino ketone **2**, silyl ether **5** (19.7 g, 0.08 mol) and dimethylamine (8.8 g, 6.0 mL) in 19 mL of methanol, for 40 h, gave 9.7 g of a mixture, bp 32–37 °C (0.3 Torr), containing 76% of the title compound and 12% of 1,5-bis(*N*,*N*-dimethylamino)cyclopentene. ^1H NMR (90 MHz, $CDCl_3$): δ 3.0 (t, J = 0.9 Hz, 1 H, methinyl), 2.33 (s, 6 H, dimethylamino), 2.12–1.4 (>6 H, CH_2). Resonances clearly discernable from the amino enamine: δ 4.42 (1 H, vinyl), 2.63 (s, 6 H, dimethylamino), 2.18 (s, >6 H, dimethylamino), and from starting material δ 0.1 (s, 18 H, trimethylsilyl).

***cis*-1,2-Bis(*N*,*N*-dimethylamino)cyclopentane (15).** Into a Schlenk flask, equipped with a magnetic stirring bar and fitted with a glass stopcock with septum, was introduced cyclopentane (50 mL × 2), followed by the product mixture from the previous reaction, 2-(*N*-dimethylamino)cyclopentanone (2.67 g, 0.021 mol), methanol (0.53 g, 0.017 mol), and 1,5-bis(*N*,*N*-dimethylamino)-cyclopent-1-ene (0.71 g, 0.0046 mol). After the system was cooled with a dry ice/acetone bath, anhydrous dimethylamine (5.86 g, 8.6 mL, 0.13 mol) was very quickly introduced under argon by a precooled syringe.

A mixture of titanium tetrachloride (3.6 g, 2.1 mL, 0.019 mol in 9 mL of cyclopentane) was then syringed into the stirred reaction mixture over a period of 1 min. The mixture was stirred for 5 min at −78 °C and then for 13.5 h at room temperature. At this point gas chromatography revealed only the presence of 1,5-bis(*N*,*N*-dimethylamino)cyclopent-1-ene. The Schlenk-filtered reaction mixture was cannulated under argon into a 500-mL Parr jar and subjected to hydrogenation for 17 h using 0.39 g of a 5% Pd/C catalyst, as described above. The TiO_2 was removed by gravity filtration through a column of Celite (4.5 × 2.5 cm) using pentane to wash the precipitate. After evaporation of volatile components, vacuum distillation of the residue gave 1.1 g (28%) of **15**, bp 23–25 °C (0.027 Torr). This product had properties identical with those described by Fraenkel and Pramanik,[3] the result of a stereochemically unambiguous preparation. ^1H NMR (90 MHz, $CDCl_3$): δ 2.72–2.48 (mu, 2 H, CH_2), 2.29 (singlet, 12 H, CH_3), 2.03–1.43 (6 H, CH_2). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 68.90 (CH), 44.41, 26.09, 22.10. IR ($CDCl_3$): 2964 (s), 2865 (w), 2823 (m), 2776 (m), 1470 cm^{-1} (m). MS: 156.1666 (d, parent ion) and 84.0858 (d, base peak).

1,2-Bis(trimethylsiloxy)cyclohexene (9). This compound was prepared via the modified Ruhlmann method,[23] described above, from dimethyl adipate (44.6 g, 0.26 mol), trimethylchlorosilane (120 g, 1.1 mol), and sodium (26.03, 1.13 g-atom) in 800 mL of toluene, and 24.8 g (37%) of **9** was obtained, bp 60–68 °C (0.13 Torr). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 132.21 (vinyl), 29.76 (allylic), 23.41 (methylene), and 0.89 (trimethylsiloxy).

2-(1-Piperidino)cyclohexanone (11) and 1,6-Di-1-piperidinocyclohex-1-ene (12). Under an argon atmosphere, anhydrous methanol, 17 mL, piperidine (6.0 g, 0.07 mol), and compound **9** (17.69 g, 0.069 mol) were allowed to react in a stoppered gas bottle, with stirring overnight. Volatile constituents were removed under reduced pressure, leaving behind a moist amorphous solid, identified to be the dimer of adipoin, IR (cm^{-1}, $CHCl_3$ solution) 1715 (s) and 3495 (w). This crude product was reacted at reflux in a Dean–Stark apparatus with piperidine (6.0 g, 0.07 mol) in 35 mL of benzene for 3 days. After removal of piperidine and benzene, vacuum distillation gave 5.3 g (42%) of **11**, bp 55–62 °C (0.18 Torr), in 42% yield and 1,6-di-*N*-piperidinocyclohexene, bp 90–97 °C (0.15 Torr), in 34% yield, based on starting siloxene, with total conversion of bis(siloxene) **9** by amination being 76%. Compound **11**. ^1H NMR (90 MHz, $CDCl_3$): δ 3.1–1.2. ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 212.28 (carbonyl), 73.21 (methinyl), 50.86, 40.76, 30.10, 28.18, 26.26, 24.54, 22.62. IR ($CDCl_3$): 2946 (s) and 1714 cm^{-1} (s). MS: 181.1473 (d, parent ion) and 124.1144 (d, base peak). Compound **12**. ^1H NMR (90 MHz, $CDCl_3$): δ 4.7 (t, 0.4 Hz, 1 H, vinyl), 3.42–3.18 (hump, 1 H, methinyl), 3.15–1.2 (mu, 26 H, CH_2). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 148.23 (quat vinyl), 103.07 (vinyl), 59.66 (methinyl), 49.77, 49.66, 27.24, 26.58, 25.27, 25.11, 22.81, 21.88. IR ($CDCl_3$): 3050 (w), 2938 (s), 2957 (m), 2802 (m), 1635 cm^{-1} (m). MS: 248.2244 (d, parent ion) and 246.2119 (d, base peak).

***cis*-1,2-Di-1-piperidinocyclohexane (16).** From **12** (4.9 g, 0.02 mol) and 5% Pd/C (0.49 g) in ethyl acetate (50 mL), via the procedure for **7**, was obtained 3.37 g (67%) of **16**, bp 102–107 °C (0.18 Torr). ^1H NMR (90 MHz, $CDCl_3$): δ 2.85–2.25 (mu, 10 H), 2.20–1.10 (mu, 20 H, CH_2). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 64.53 (methinyl), 52.28, 26.86, 26.26, 25.11, 24.34. IR ($CDCl_3$): 2945 (s), 2864 (m), 1447 cm^{-1} (m). MS: 250.2411 (d, parent ion) and 124.1140 (d, base peak).

The cis stereochemistry was confirmed from NMR studies.

2-(1-Pyrrolidino)cyclohexanone. Via Heine's[13] procedure, **9** (3.49 g, 0.014 mol), pyrrolidine (1.97 g, 0.027 mol), and anhydrous methanol, 8 mL, were mixed and allowed to stir at room tem-

perature overnight, 14 h. Benzene (20 mL) was added to the now dark brown reaction mixture containing adipoin. The latter was transferred to a Dean-Stark apparatus, and the mixture was refluxed for 15 h under a static argon atmosphere. *Note*: this reaction was monitored by gas chromatography. The volatile components were removed at reduced pressure. The residue was vacuum distilled, bp 60-67 °C (0.23 Torr), giving 1.59 g of the title compound in 68% yield. ^{1}H NMR (90 MHz, $CDCl_3$): δ 3.19-1.38 (multiplet). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 211.71 (carbonyl), 72.45 (methinyl), 51.11, 40.57, 33.35, 28.37, 23.45, 22.62. IR ($CDCl_3$): 2962 (s), 1715 cm^{-1} (s). MS: 167.1318 (d, parent ion) and 110.0995 (d, base peak).

1-(1-Pyrrolidino)-6-(1-piperidino)cyclohex-1-ene. From 11 (4.68 g, 0.026 mol) and pyrrolidine (2.10 g, 0.03 mol) in benzene (20 mL) with *p*-toluenesulfonic acid, via the procedure for **6**, there was obtained 3.91 g (64%) of the title compound, bp 97-103 °C (0.45 Torr). ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.38 (tr, 1 H, 0.3 Hz, vinyl), 3.54-1.23 (mu, 25 H). ^{13}C NMR (20.1 MHz, $CDCl_3$ filtered through basic alumina): δ 143.47 (quat vinyl), 96.84 (vinyl), 59.99 (methinyl), 49.71, 47.63, 27.19, 25.22, 24.78, 23.53, 22.06, 21.28. IR ($CDCl_3$): 3043 (w), 2940 (s), 2860 (m), 2800 (m), 1625 cm^{-1} (m). MS: 234.2087 (d, parent ion) and 149.1227 (d, base peak).

1,6-Di-1-pyrrolidinocyclohex-1-ene (13). A mixture of anhydrous methanol (16 mL) bis(siloxene) **9** (15.25 g, 0.059 mol), and pyrrolidine (4.35 g, 0.061 mol) was stirred in a stoppered bottle for 20 h at room temperature under a static argon atmosphere.

Methanol and pyrrolidine were removed by rotary evaporation. To the residue were added benzene (50 mL), a few crystals of *p*-toluenesulfonic acid, and pyrrolidine (10 g, 0.14 mol). After refluxing this mixture for 63 h in a Dean-Stark apparatus, volatile components were removed under vacuum through a Vigreux column, and the residue was likewise fractionated, bp 92-100 °C (0.5 Torr), giving 8.56 g (66%) of clear **13**. The amino enamine was stored under argon in a 14/20 25-mL pear-shaped flask fitted with a glass stopcock and held in place with a spring clamp. ^{1}H NMR (90 MHz, $CDCl_3$): δ 4.39 (tr, 1 H, J = 0.4 Hz, vinyl), 3.58-0.94 (mu, 23 H). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 144.62 (quat vinyl), 96.57 (vinyl), 54.80 (methinyl), 48.84, 47.85, 25.23, 24.62, 23.91, 19.64. IR (neat) 3055 (w), 2947 (s), 1637 cm^{-1} (s). MS: 220.1937 (d, parent ion) and 149.1167 (d, base peak).

***cis*-1-(1-Piperidino)-2-(1-pyrrolidino)cyclohexane (17).** Hydrogenation of 1-(1-pyrrolidino)-6-(1-piperidino)cyclohex-1-ene (2.94 g, 0.013 mol) over 5% Pd/C (0.3 g) in ethyl acetate (50 mL), via the procedure for **7**, gave on workup 1.67 g (62%) of **17**, bp 90-95 °C (0.25 Torr). ^{1}H NMR (90 MHz, $CDCl_3$): δ 3.10-2.15 (mu, 10 H) and 2.14-1.10 (mu, 18 H). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 66.55, 63.60, 52.55, 51.84, 29.81, 26.58, 25.66, 23.14, 22.16. IR (neat) 2940 (s), 2865 (m), 2800 (m), 1453 cm^{-1} (w). MS: 236.2247 (d, parent ion) and 110.0961 (d, base peak).

This cis stereochemistry is assumed by analogy to the results with *cis*-1,2-dipiperidinocyclopentane.

***cis*-1,2-Di-1-pyrrolidinocyclohexane (18).** A mixture of adipoin (3.07 g, 0.026 mol), pyrrolidine (5.56 g, 0.078 mol), a few crystals of *p*-toluenesulfonic acid, and 40 mL of benzene was allowed to reflux for 50 h in a Dean-Stark apparatus, by which time gas chromatography indicated complete conversion of adipoin to the aminoenamine. The cooled reaction mixture was cannulated into a Parr jar and hydrogenated over 5% Pt on alumina, over a period of 10 h, via the procedure for **7**. The residue was vacuum distilled through a short-path distillation apparatus, giving 3.46 g (60%) of **18**, bp 90-98 °C (0.07 Torr). ^{1}H NMR (90 MHz, $CDCl_3$): δ 3.12-2.15 (mu, 10 H), 2.11-1.00 (mu, 16 H). ^{13}C NMR (20.1 MHz, $CDCl_3$): δ 66.30 (methinyl), 52.24, 28.90, 23.09. IR ($CDCl_3$): 2960 (s), 2883 (m), 2789 (s), 1460 cm^{-1} (m). MS: 222.2041 (d, parent ion) and 110.0976 (d, base peak).

The cis stereochemistry is assumed by analogy to the case of *cis*-1,2-dipiperidinocyclopentane.

Acknowledgment. This research was supported by the National Science Foundation, Grants CHE-8304636 and CHE-8605974. High-field NMR equipment used in this work was also financed in part by grants from the National Science Foundation. We are happy to acknowledge the technical advice from Dr. Charles Cottrell, Chemical Instrumentation Center, The Ohio State University.

Registry No. **2**, 55154-10-4; **5**, 6838-66-0; **6**, 118207-26-4; **7**, 26887-73-0; **7**·dipicrate, 118207-25-3; **9**, 6838-67-1; **11**, 118207-28-6; **12**, 118207-29-7; **13**, 118207-30-0; **14**, 26785-42-2; **15**, 89121-43-7; **16**, 26785-38-6; **17**, 118207-31-1; **18**, 26785-40-0; piperidine, 110-89-4; pyrrolidine, 123-75-1; 2-(1-pyrrolidino)cyclopentanone, 118207-27-5; adipoin dimer, 60308-50-1; 1,5-di-1-pyrrolidinocyclopent-1-ene, 118207-32-2; (*N*,*N*-dimethylamino)cyclopentanone, 79076-02-1; 1,5-di(*N*,*N*-dimethylamino)cyclopent-1-ene, 118207-33-3; dimethyl adipate, 627-93-0; 2-(1-pyrrolidino)-cyclohexanone, 118207-34-4; 1-(1-pyrrolidino)-6-(1-piperidino)-cyclohex-1-ene, 118207-35-5; adipoin, 533-60-8; dimethyl glutarate, 1119-40-0.

Supplementary Material Available: Atomic coordinates and all relevant details of X-ray crystallography of the dipicrate of **7** (11 pages). Ordering information is given on any current masthead page.

A Novel Synthesis of (±)-Abscisic Acid

Mauricio Gomes Constantino* and Pellegrino Losco

Departamento de Química da Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, Av. Bandeirantes, 3900, 14.049 Ribeirão Preto, SP, Brazil

E. E. Castellano

Instituto de Física e Química de São Carlos, Universidade de São Paulo, Caixa Postal 369, 13.560 São Carlos, SP, Brazil

Received April 28, 1988

A four-step synthesis of abscisic acid (1) is described, with a yield of 32.4%. The two starting materials are known compounds but are not commercially available: compound **2** is prepared in four steps from ethyl acetoacetate and mesityl oxide, and compound **3** is prepared in two steps from 3,3-dimethylacrylic acid. The synthesis involves a Reformatsky reaction, an epoxide formation, a ketal hydrolysis, and an elimination that accompanies an epoxide rearrangement.

Abscisic acid (1), also named Abscisin II, is a plant hormone that has a role in the control of several physiological processes such as abscision of leaves and seed germination.[1] It is largely distributed in higher plants and

0022-3263/89/1954-0681$01.50/0