Reactions Involving Electron Transfer. II. Reductions of Enones with Alkali Metal Solutions[1]

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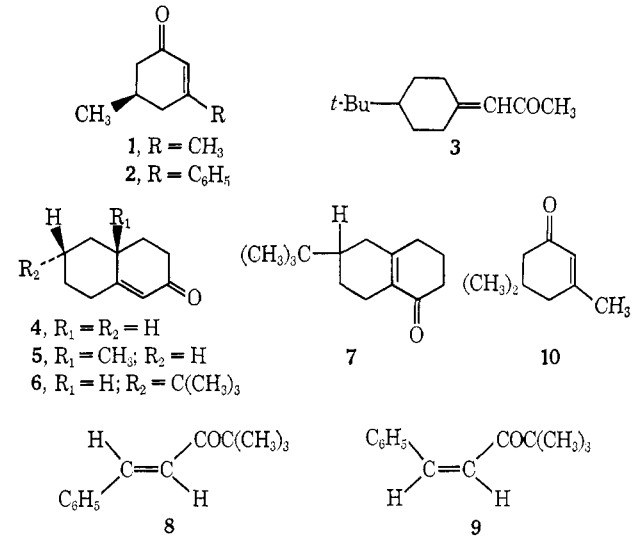
Abstract: The members of a representative series of α,β-unsaturated ketones **1–10** have been reduced with solutions of sodium or lithium in hexamethylphosphoramide (HMP) or liquid NH_3. In general, reductions with sodium in HMP yield reduction products containing a greater proportion of the less stable epimer than is found in reductions with sodium or lithium in liquid ammonia. The factors which appear most effective in increasing the proportion of the less stable epimer from Na–HMP reductions include (1) use of low temperatures (−33 to −78°), (2) the presence of a proton donor in the reduction mixture, (3) the use of a cosolvent such as THF, and (4) the presence of excess dissolved sodium throughout the reduction. As noted in the accompanying paper, use of low temperatures with no proton donor present in Na–HMP reduction mixtures favors the conversion of enones such as **8** and **9** to dihydrodimers **50** and **51** in a process that is at least partially stereospecific.

In the preceding paper[3] we summarized the similarities between solutions of alkali metals (especially Na and Li) in liquid ammonia[4] and the corresponding metal solutions in hexamethylphosphoramide (HMP).[5] As part of an exploration of uses of these metal solutions in synthesis, we wished to learn whether reductions of α,β-unsaturated carbonyl compounds (enones) with Na–HMP solutions[6] would offer the high degree of stereoselectivity often observed in the reduction of enones to saturated carbonyl compounds with Li or Na in liquid ammonia. In particular, the use of metal–ammonia reductions of the C=C of enones to yield products with the more stable configuration at the carbon atom β to the carbonyl group has been widely exploited in stereospecific synthesis.[7] In this paper we have compared the stereochemical results obtained when a number of representative α,β-unsaturated ketones were reduced either with metal–ammonia solutions or with metal–HMP solutions.

Preparation of the Starting Enones and Their Reduction Products. Of the enones **1–9** (Scheme I) selected for study, only compounds **6**, **7**, and **9** had not been described previously. The *cis*-ketone **9** was obtained by photoisomerization of the corresponding *trans*-isomer **8** and the *t*-butyloctalone derivatives **6** and **7** were obtained by the sequence illustrated in Scheme II.

Scheme I



Although the stereoisomeric reduction products **15–20** (Scheme III) had been characterized and authentic samples were available *via* previously described procedures, it was necessary to prepare and characterize authentic samples of the reduction products **21–26**. We also prepared authentic samples of ketones **27–29** to establish the absence of these substances in reduction mixtures obtained from unsaturated ketones **1** and **3**. Earlier studies of the Clemmensen reduction of α,β-unsaturated ketones[8] had demonstrated the presence of such rearranged reduction products presumably derived from intermediate cyclopropanols. In no instance did we detect these by-products in the metal–ammonia and metal–HMP reductions studied in this paper.

Authentic samples of the *trans*-cyclohexanone derivatives **19** and **23** were obtained by the previously discussed[9] additions of $LiCuMe_2$ and of $LiCuPh_2$ to

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(2) (a) National Institutes of Health Predoctoral Fellow, 1966–1969; (b) National Institutes of Health Predoctoral Fellow, 1968–1969.

(3) K. W. Bowers, R. W. Giese, J. Grimshaw, H. O. House, N. H. Kolodny, K. Kronberger, and D. K. Roe, *J. Amer. Chem. Soc.*, **92**, 2783 (1970).

(4) (a) M. C. R. Symons, *Quart. Rev.* (London), **13**, 99 (1959); (b) U. Schindewolf, *Angew. Chem. Intern. Ed. Engl.*, **7**, 190 (1968).

(5) (a) H. Normant, *ibid.*, **6**, 1046 (1967); (b) H. Normant, *Bull. Soc. Chim. Fr.*, 791 (1968).

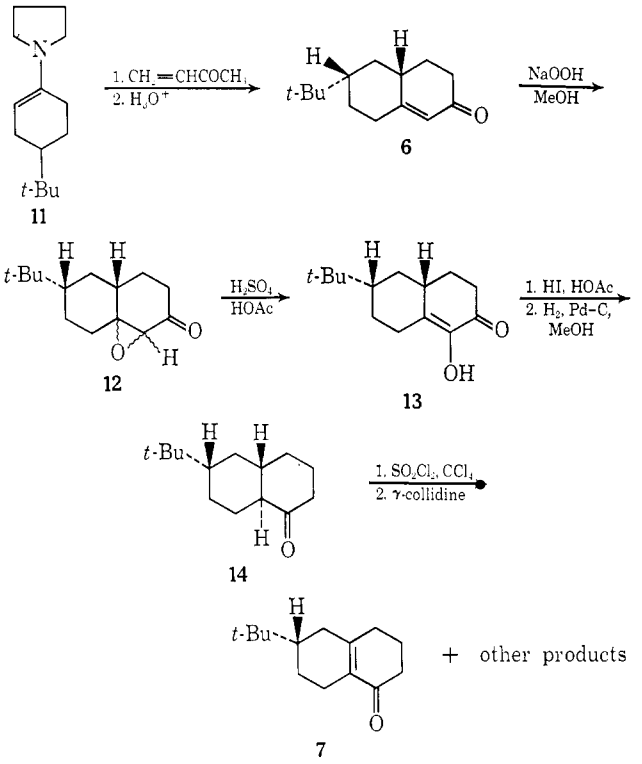
(6) For a previous study see P. Angibeaud, M. Larcheveque, H. Normant, and B. Tchoubar, *ibid.*, 595 (1968).

(7) (a) A. J. Birch and H. Smith, *Quart. Rev.* (London), **4**, 69 (1950); (b) H. Smith, "Organic Reactions in Liquid Ammonia," Interscience Publishers, Inc., New York, N. Y., 1963, pp 142–147, 151–185; (c) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., 1965, pp 50–70; (d) M. Smith in "Reduction," R. L. Augustine, Ed., Marcel Dekker, Inc., New York, N. Y., 1968, pp 95–170.

(8) (a) B. R. Davis and P. D. Woodgate, *J. Chem. Soc.*, 5943 (1965); (b) *ibid.*, *C*, 2006 (1966); (c) B. R. Davis and P. G. Woodgate, *Chem. Commun.*, **No. 3**, 65 (1966).

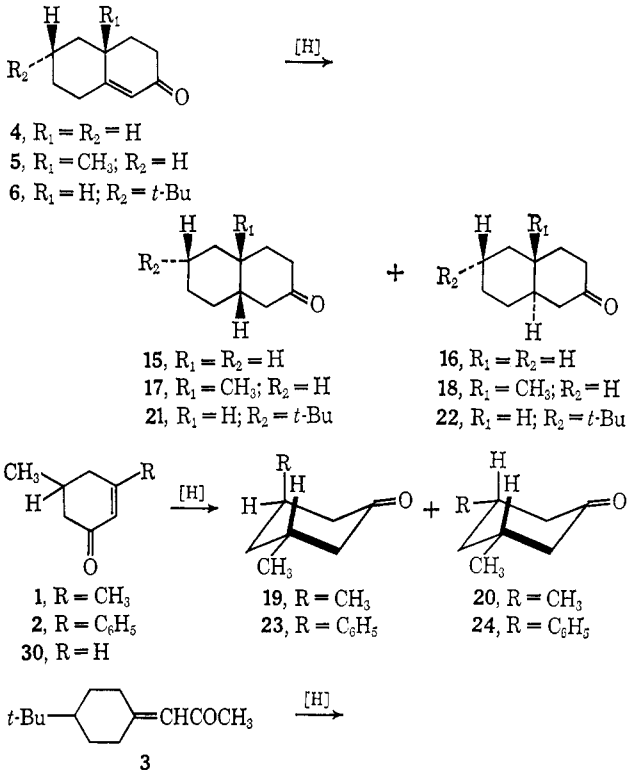
(9) (a) H. O. House, W. L. Respess, and G. M. Whitesides, *J. Org. Chem.*, **31**, 3128 (1966); (b) N. L. Allinger and C. K. Riew, *Tetrahedron Lett.*, **No. 12**, 1269 (1966); (c) H. O. House and W. F. Fischer, Jr., *J. Org. Chem.*, **33**, 949 (1968).

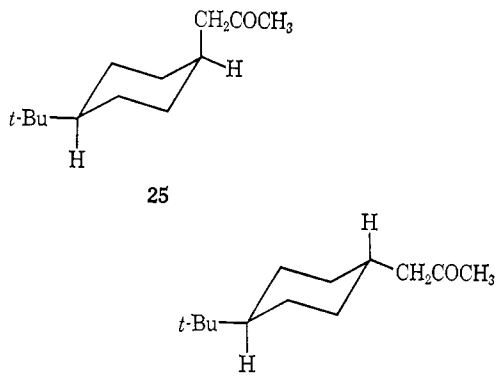
Scheme II

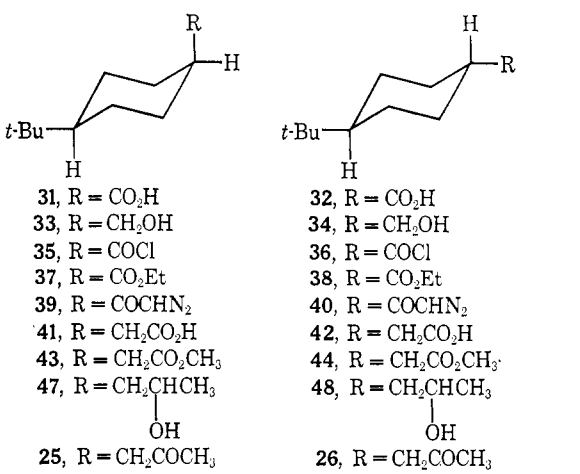


11 6 12 13 14 7

Scheme III







5-methyl-2-cyclohexenone (**30**). The *cis*-isomers **20** and **24** were available by reduction of the corresponding enones **1** and **2** with Li in ammonia. The isomeric 4-*t*-butylcyclohexyl derivatives **25** and **26** were obtained from the known acids **31** and **32**[10] by application of the Arndt–Eistert reaction sequence followed by reaction of the intermediate acids **41** and **42** with methyllithium to form the methyl ketones.

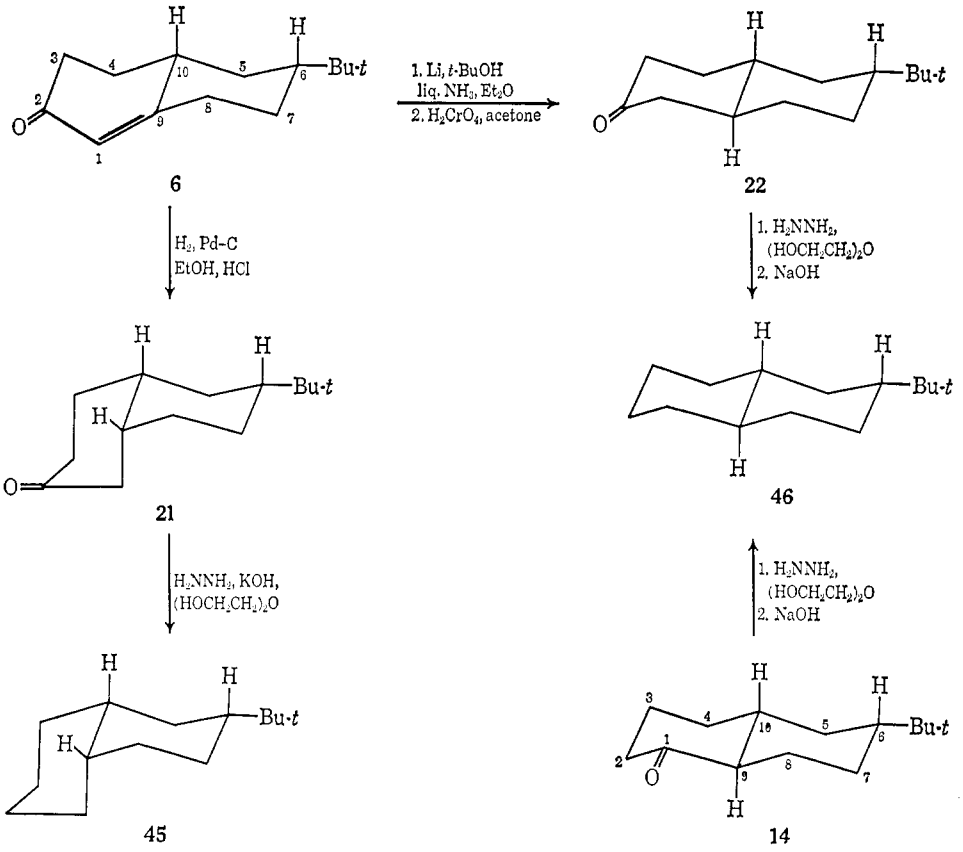
Recovery of primarily the unchanged octalone **6** (Scheme IV) from equilibration experiments provided convincing evidence that this material possesses the indicated *cis*-stereochemical relationship (both substituents equatorial) at C-6 and C-10. This material behaved like previously studied 1-octal-2-one derivatives (*e.g.*, **4** and **5**) in yielding primarily the product **21** with a *cis*-fused ring junction from catalytic hydrogenation in acidic medium[11] and primarily the *trans*-fused product **22** from reduction with lithium in liquid ammonia.[7,12] Supporting evidence for the assignment of the stereochemistry indicated in structure **22** to the product from metal–ammonia reduction was obtained by conversion of this ketone **22** to the same hydrocarbon **46** which was produced by the Wolff–Kishner reduction of the 1-decalone derivative **14**. This latter ketone **14** had been formed (Scheme II) from the more stable octalone **6** by a sequence which allowed equilibration at C-9 of ketone **14**; consequently, the ketone **14** can be assigned the *trans*-fused configuration in which all substituents occupy equatorial positions.

(10) See H. O. House and T. M. Bare, *J. Org. Chem.*, **33**, 943 (1968), and references cited therein.

(11) (a) R. L. Augustine, *ibid.*, **23**, 1853 (1958); **28**, 152 (1963); (b) R. L. Augustine and A. D. Broom, *ibid.*, **25**, 802 (1960); (c) R. L. Augustine, D. C. Migliorini, R. E. Foscante, C. S. Sodano, and M. J. Sisbarro, *ibid.*, **34**, 1075 (1969).

(12) (a) M. J. T. Robinson, *Tetrahedron*, **21**, 2475 (1965); (b) H. A. Smith, B. J. L. Huff, W. J. Powers, and D. Caine, *J. Org. Chem.*, **32**, 2851 (1967); (c) S. K. Malhotra, D. F. Moakley, and F. Johnson, *Tetrahedron Lett.*, **No. 12**, 1089 (1967).

Scheme IV



Monomeric Reduction Products from the Enones and Metals. The stereochemical results obtained when ketones **1**–**6** were reduced with solutions of metals in either liquid ammonia or HMP are compared in Table I. Reduction of each of the octalones **4**–**6**, with Li and *t*-BuOH in liquid ammonia, yielded the corresponding decalones which contained <2% of the *cis*-fused isomers **15**, **17**, and **21**. These results agree with Robinson's[12a] reduction of the octalones **4** and **5** with Na and MeOH in liquid ammonia to give mixtures containing 1.0% of **15** or 1.3% of **17**. In each case examined the proportion of the product with the less stable configuration at the β position was greater for reductions conducted in HMP solution. This stereochemical difference became preparatively significant for the ketones **2** and **3** where a significant percentage of the less stable isomer (**23** or **25**) was produced even from reductions with Li in ammonia. Since this stereochemical difference was particularly apparent with the cyclohexylidene ketone **3**, the effects of reaction conditions on the stereochemistry of metal–HMP reductions were explored with this ketone (Table I, entries 9–17). The proportion of the less stable axial reduction product **25** was particularly high (>70%) when the reduction was performed at low temperatures (−33 to −78°) with *t*-BuOH, excess Na, and THF cosolvent present throughout the reaction (see Table I, entries 13–17). These reaction conditions were achieved by adding the unsaturated ketone to a cold solution of Na and *t*-BuOH in HMP. That the stereochemical difference between Li–ammonia and Na–HMP reductions should not be ascribed to the use of different metals was shown (Table I, entries 9 and 12) by reducing the ketone **3** with either Na or Li in ammonia–*t*-BuOH–THF mixtures to form practically the same proportions of reduction products **25** and **26**.

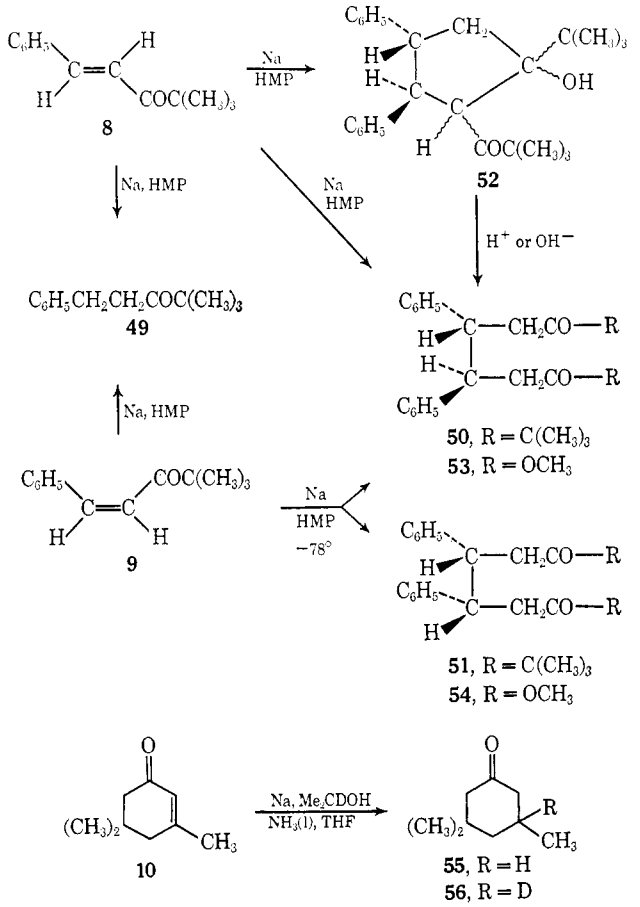
In all cases better yields of reduction products were obtained with proton donor (*e.g.*, *t*-BuOH) present during reduction. As has been noted by others,[12a,b] in the absence of a proton donor we frequently recovered substantial amounts of starting ketone and obtained lower material balances. The remaining material was invariably present in higher molecular weight by-products. We believe these results are caused by a combination of the subsequently discussed dimerization and by formation of enolate anions from the starting ketone when no proton donors of acidity comparable to the starting ketone are present to protonate the initially formed anion radicals. In the accompanying paper[3] we have cited evidence indicating that the hydrogen added to the β position in these reductions is derived from a proton donor rather than a hydrogen atom donor. An additional piece of evidence is provided by the reduction of isophorone (**10**, Scheme V) with Li and Me_2CDOH (a donor for either a proton or a deuterium atom) in liquid ammonia to yield the nondeuterated product **55** (not **56**).

Dimeric Reduction Products from the Enones and Metals. The formation of dimeric reduction products was explored with reductions of the benzylidene ketones **8** and **9** (Scheme V). As noted in the accompanying study[3] of an aliphatic enone, the formation of one or more of the dimeric products **50**–**52** in addition to the monomeric reduction product **49** was especially favorable when the ketone **8** (or **9**) was reduced with Na in HMP at low temperatures and in the absence of a relatively acidic proton donor. The dimerization stereochemistry also paralleled our accompanying study

Table I. Reduction of the Ketones **1–6** with Sodium or Lithium

	Reaction conditions	Temp, °C	Products (% yield)	Fraction of less stable epimer in the reduced product
1.	**1** added to Li + *t*-BuOH in NH_3(l)–THF	−33	**19**(10) + **20**(70)	12% of **19**
2.	**1** added to Li in NH_3(l)–THF	−33	**1**(3) + **19**(4) + **20**(46)	8% of **19**
3.	Li soln added to **1** + *t*-BuOH in NH_3(l)–THF	−33	**19**(4) + **20**(61)	6% of **19**
4.	**1** added slowly to Na + *t*-BuOH (3 equiv) in HMP–THF	0	**19**(13) + **20**(16)	18% of **19**
5.	**1** added to Na + *t*-BuOH (1 equiv) in HMP–THF	0	**19**(4) + **20**(25)	14% of **19**
6.	Na soln added to **1** + *t*-BuOH in HMP–THF	0	**19**(4) + **20**(20)	20% of **19**
7.	**2** added to Li + *t*-BuOH in NH_3(l)–THF	−33	**23**(11) + **24**(70)	14% of **23**
		−78	**23**(9) + **24**(75)	12% of **23**
8.	Na soln added to **2** + *t*-BuOH in HMP–THF	−33	**2**(5) + **23**(33) + **24**(50)	40% of **23**
9.	**3** added to Li + *t*-BuOH in NH_3(l)–THF	−33	**25**(15) + **26**(73)	17% of **25**
10.	**3** added to Li in NH_3(l)–THF	−33	**3**(6) + **25**(8) + **26**(64)	11% of **25**
11.	Li soln added to **3** + *t*-BuOH in NH_3(l)–THF	−33	**3**(41) + **25**(3) + **26**(31)	9% of **25**
12.	**3** added to Na + *t*-BuOH in NH_3(l)–THF	−33	**25**(10) + **26**(84)	11% of **25**
13.	**3** added to Na + *t*-BuOH in HMP–THF	0	**25**(44) + **26**(49)	47% of **25**
		−33	**25** (60) + **26**(24)	71% of **25**
		−78	**3**(25) + **25**(41) + **26**(15)	73% of **25**
14.	**3** added to Na + *t*-BuOH (1 equiv) in HMP–THF	−33	**25**(60) + **26**(35)	63% of **25**
15.	**3** added to Na + *t*-BuOH (1 equiv) in HMP–THF	0	**25**(30) + **26**(49)	38% of **25**
16.	**3** added slowly to Na + *t*-BuOH (3 equiv) in HMP–THF	0	**25**(35) + **26**(50)	41% of **25**
17.	Na soln added to **3** + *t*-BuOH in HMP–THF	0	**25**(22) + **26**(73)	24% of **25**
18.	**4** added to Li + *t*-BuOH in NH_3(l)–THF	−33	**15**(<2) + **16**(>98)	<2% of **15**
19.	**4** added to Na + *t*-BuOH in HMP–THF	−33	**4**(27) + **15**(2) + **16**(23)	7% of **15**
20.	**4** added to Na + *t*-BuOH in HMP	0	**4**(10) + **15**(3) + **16**(43)	6% of **15**
21.	**5** added to Li + *t*-BuOH in NH_3(l)–THF	−33	**17**(<2) + **18**(96)	<2% of **17**
22.	**5** added to Na + *t*-BuOH in HMP	0	**5**(39) + **17**(8) + **18**(53)	13% of **17**
23.	**6** added to Li + *t*-BuOH in NH_3(l)–THF	−33	**21**(<2) + **22**(97)	<2% of **21**
24.	**6** added to Na + *t*-BuOH in HMP–THF	−33	**6**(23) + **21**(2) + **22**(72)	2% of **21**
25.	**6** added to Na + *t*-BuOH in HMP	0	**6**(5) + **21**(1) + **22**(48)	2% of **21**

Scheme V



since reduction of the *trans*-ketone **8** with Na and HMP at −33 or −78° yielded either the racemic-dimer **50** or the related aldol-product **52**. Reduction of the *cis*-ketone **9** at −78° yielded a mixture of comparable amounts of the racemic-dimer **50** and the *meso*-dimer **51**. Since reconversion of the *cis*-ketone **9** to the more stable *trans*-isomer **8** was especially easy, we are uncertain how much isomerization of **9** → **8** may have occurred in the reaction mixture before dimerization was complete.

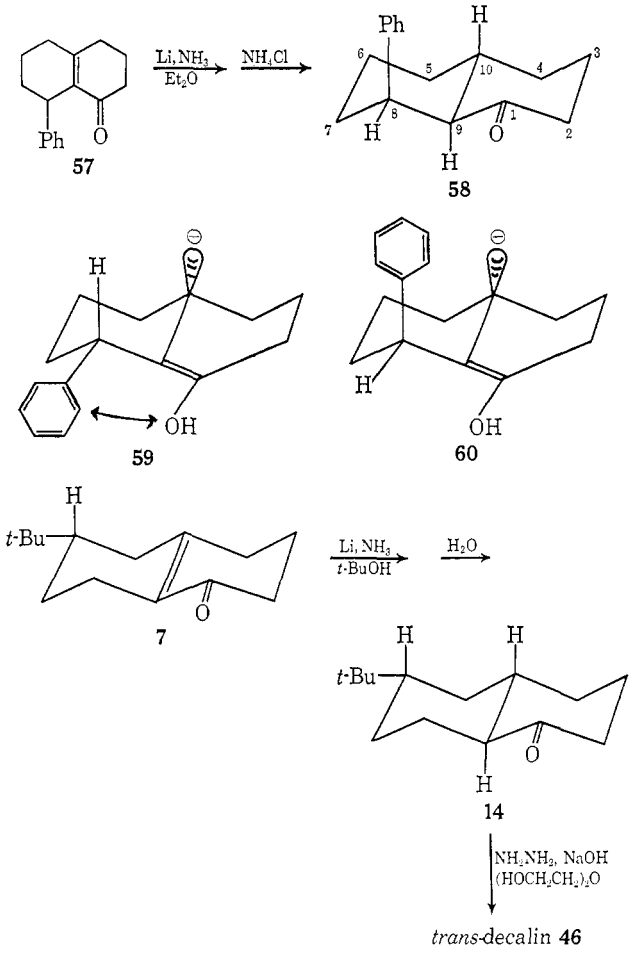
The structure and stereochemistry of the dimeric ketones **50** and **51** were established by synthesis involving reaction of the known[13] *meso* (**54**) and racemic (**53**) diesters with *t*-BuLi. The esters **53** and **54** were obtained along with methyl hydrocinnamate by the previously described[13] reduction of methyl cinnamate with Al amalgam in moist ether. Interestingly, this Al–Hg reduction in H_2O–Et_2O of a *trans*-α,β-unsaturated ester (analogous to ketone **8**) is reported[13] to yield comparable amounts of the stereoisomeric dimers **53** and **54**.

Reduction of Δ[9,10]-Octal-1-one Derivatives. In an earlier study,[14a] we noted that reduction of the Δ[9,10]-octalone derivative **57** (Scheme VI) with Li in NH_3 yielded the decalone **58** in which the nonketonic ring either must be in a boat conformation or carry an axial phenyl substituent at C-8. This reduction to an apparently less stable configuration at C-10 was attributed[14a] to the existence of the intermediate allylic anion in conformation **60** to avoid a serious nonbonded interaction (heavy arrow in structure **59**) present when the phenyl group is equatorial (more recently termed

(13) (a) M. P. Oommen and A. I. Vogel, *J. Chem. Soc.*, 2148 (1930); (b) A. L. Wilds and R. E. Sutton, *J. Org. Chem.*, **16**, 1371 (1951); (c) samples of the *meso* (**51**, reported mp 214°) and racemic (**50**, reported mp 148–149°) dimers have also been described by J. Simonet, *Compt Rend.*, **263**, 1547 (1966); **264**, 1962 (1967); J. Simonet, Ph.D. Dissertation, University of Clermont-Ferrand, 1965. We are grateful to Dr. Simonet for sending us a copy of his Ph.D. Dissertation.

(14) (a) H. O. House and H. W. Thompson, *J. Org. Chem.*, **28**, 360 (1963); (b) F. Johnson, *Chem. Rev.*, **68**, 375 (1968).

Scheme VI



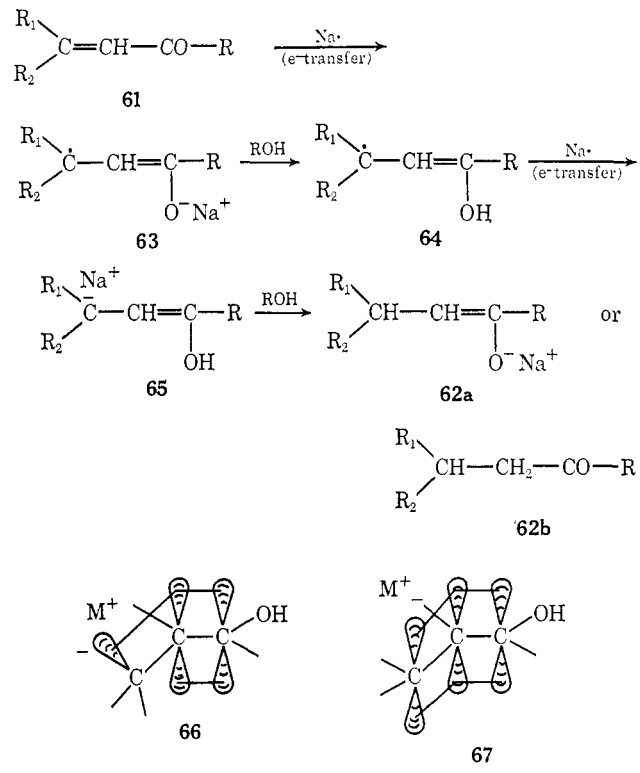
A[1,3] strain).[14b] To verify that this unusual reduction stereochemistry **57** → **58** was not a property of substituted $\Delta^{9,10}$-octalones, we examined the Li–NH_3 reduction of the octalone **7**, where nonbonded interaction of the type indicated in structure **59** is absent. From the reduction of **7** the major product (*ca.* 96%) was the normal *trans*-fused ketone **14** with an equatorial substituent.

Discussion of Stereochemical Results. As discussed in our accompanying paper,[3] we believe that the series of steps leading from an enone **61** (Scheme VII) to a monomeric reduction product **62** involves the consecutive transfers of an electron (**61** → **63**), a proton (**63** → **64**), and an electron (**64** → **65**), to form an allylic carbanion or organometallic intermediate **65**. The stereochemistry of these enone reductions at the β-carbon atom is presumably determined by the reaction of this allylic intermediate **65** with a proton donor.

In the absence of contrary experimental evidence, we subscribe to the view[15] that such an allylic carbanion or organometallic intermediate is best described as a system with a pyramidal (**66**) rather than a planar (**67**) carbanion with a decided preference for the indicated conformation in which overlap between the carbanion orbital and the π orbital of the double bond is maintained.[15c] This geometrical arrangement corresponds to the one suggested for the isoelectronic enamines and

(15) (a) D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press, New York, N. Y., 1965, pp 47–84, 175–210; (b) P. E. Verkade, K. S. DeVries, and B. M. Wepster, *Rec. Trav. Chim. Pays-Bas*, **84**, 1295 (1965); (c) G. Stork and S. Darling, *J. Amer. Chem. Soc.*, **86**, 1761 (1964).

Scheme VII



anilines;[16] in the present case the presence of a nearby metal cation offers an additional factor favoring the existence of the allylic intermediates with a pyramidal carbanion as in structure **66**. Most of the stereochemical results observed in the reduction of enones with metal solutions would appear to be explicable in terms of the reaction of a proton donor with the more stable epimer of the allylic intermediate **66** by a process which involves retention of configuration at carbon. However, it is clearly desirable to know more about the behavior of such allylic intermediates before offering a detailed discussion of the stereochemistry of these reductions. It is of interest to note that the conditions (low temperature, presence of THF cosolvent, excess Na) most favorable to the formation of the less stable epimer **25** in reductions of the enone **3** with Na–HMP–*t*-BuOH solutions are also conditions which might be expected to favor ion pairing between the allylic anion and the metal cation. These same conditions in the absence of a proton donor such as *t*-BuOH favor the formation of dimeric reduction products from enones.

Experimental Section[17]

Preparation of the Unsaturated Ketones 1–6. We have described the preparations and physical properties of ketones **1**,[9c] **2**,[3] **3**,[9a]

(16) (a) B. M. Wepster, *Progr. Stereochemistry*, **2**, 99–156 (1958); (b) W. D. Gurowitz and M. J. Joseph, *J. Org. Chem.*, **32**, 3289 (1967); (c) A. Mannschreck and U. Koelle, *Tetrahedron Lett.*, **No. 10**, 863 (1967); (d) Y. Shvo, E. C. Taylor, and J. Bartulin, *ibid.*, **No. 34**, 3259 (1967).

(17) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with a Perkin-Elmer, Model 237, infrared recording spectrophotometer, fitted with a grating. The ultraviolet spectra were determined with a Cary spectrophotometer, Model 14. The nmr spectra were determined at 60 MHz with a Varian, Model A-60 or Model T-60, nmr spectrometer. The chemical shift values are expressed either in cycles per second or δ values (parts per million) relative to a tetramethylsilane internal standard. The mass spectra were obtained with an Hitachi (Perkin-Elmer) mass spectrometer. Unless otherwise stated, all re-

and **5**[18] in previous publications and followed literature procedures[19] to obtain the octalone **4**, bp 70–71° (0.1 mm) [lit.[19b] bp 75–78° (0.2 mm)]. A solution of 21.1 g (0.102 mol) of the pyrrolidine enamine **11**[20] in 70 ml of PhH was maintained at 30° with external cooling over 25 min while 7.30 g (0.104 mol) of methyl vinyl ketone was added dropwise and with stirring. The resulting solution was refluxed for 21 hr. Then an aqueous buffer (pH 5) from 4.2 g of NaOAc, 8.3 ml of HOAc, and 8.3 ml of H_2O was added and refluxing was continued for 3.25 hr. The benzene extracts of the reaction mixture were washed successively with aqueous 10% HCl, aqueous $NaHCO_3$, and aqueous NaCl and then concentrated. Distillation of the crude liquid product (21.2 g) separated 1.07 g of 4-*t*-butylcyclohexanone and 14.8 g (71%) of a mixture of the $\Delta^{1,9}$-octalone isomer **6** and the corresponding $\Delta^{9,10}$ isomer: bp 110–115° (0.05 mm); $n^{26.5}$D 1.5100; ir (CCl_4) 1720 (C=O), 1680 (conj C=O), and 1625 cm^{-1} (C=C); uv (95% EtOH) 238 (ε 12,000) and 298 mμ (ε 380). When the mixture was repeatedly crystallized from hexane at −20°, the pure conjugated ketone **6** was obtained as white prisms: mp 27.5–29°; ir (CCl_4) 1680 (conj C=O) and 1625 cm^{-1} (conj C=C); uv (95% EtOH) 238 (ε 15,000) and 307 mμ (ε 65); nmr (CCl_4) δ 5.65 (1 H, br s, vinyl CH), 1.0–2.5 (12 H, m, aliphatic CH), and 0.90 (9 H, s, $(CH_3)_3C$); mass spectrum, *m/e* (rel intensity) 206 (44, M^+), 150 (75), 57 (100), and 41 (61).

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.80; H, 10.78.

Preparation of the Cyclohexanones 23 and 24. The preparation and characterization of authentic samples of the 3,5-dimethylcyclohexanones **19** and **20** are described elsewhere.[9b,c]

To a cold (−78°) solution of 80 mmol of Li in 100 ml of liquid NH_3 was added, dropwise and with stirring, a solution of 3.66 g (19.6 mmol) of the cyclohexenone **2** and 3.00 g (40.5 mmol) of *t*-BuOH in 10 ml of THF. The resulting solution was allowed to stand for 5 min and then excess solid NH_4Cl was added and the NH_3 was allowed to evaporate. The residual material was partitioned between Et_2O and H_2O and the organic phase was dried and concentrated. A solution of the residual liquid in cold (0°) acetone was treated with 5 ml of 8 *N* H_2CrO_4 solution (Jones reagent)[21] and then stirred at 0° for 5 min and treated with excess Me_2CHOH. The resulting mixture was concentrated and the residue was partitioned between H_2O and Et_2O. The organic phase was washed successively with H_2O, aqueous $NaHCO_3$, and H_2O and then dried and concentrated. The residual yellow oil (4.73 g) was distilled in a short-path still (0.5 mm and 78–95°) to separate 3.24 g of the crude *cis*-ketone **24** as a colorless liquid which crystallized when cooled to 0°. At Dry Ice temperatures a pentane solution of this crude product deposited 2.28 g (62.5%) of the ***cis*-ketone 24** as white crystals, mp 34–36.5°. Recrystallization raised the melting point to 37.2–37.5°; ir (CCl_4) 1720 cm^{-1} (C=O); uv (95% EtOH) series of weak maxima (ε 223 or less) in the region 240–270 mμ with a maximum at 288 mμ (ε 50); nmr (CCl_4) δ 7.22 (5 H, br s, aryl CH), 1.3–3.0 (8 H, aliphatic CH), and 0.9–1.2 (3 H, br, CH_3); mass spectrum, *m/e* (rel intensity) 188 (42, M^+), 131 (100), 104 (47), 91 (29), 41 (24), and 39 (23).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.85; H, 8.29.

To a cold (0°) solution of $LiCuPh_2$ prepared from 124 mmol of PhLi and 8.90 g (62.0 mmol) of CuBr in 118 ml of Et_2O was added a solution of 6.64 g (60.3 mmol) of 5-methyl-2 cyclohexenone (**30**) in 50 ml of Et_2O. After the resulting mixture had been stirred for 15 min at 0°, excess aqueous solution (pH ~8) prepared from NH_4Cl and NH_3 was added and air was passed through the solution for a short time to complete the oxidation of insoluble Cu(I) species to the soluble Cu(II)–NH_3 complex. The organic layer was separated, combined with the Et_2O extract of the aqueous phase, and then washed with aqueous NH_4Cl, dried, and concentrated. The residual yellow oil (12.66 g) was distilled in a short-path still (0.09 mm and 96–110°) to separate 7.61 g of crude *trans*-ketone **23**. An ether solution of this material was washed with aqueous 5% NaOH to remove traces of phenol. Although separation of the *cis*- and *trans*-isomers **24** and **23** by glpc was difficult, on one long (6 m) column (adipic acid ester of polyethylene glycol) partial separation was achieved with the *trans*-ketone **23** being eluted faster than the *cis*-ketone **24**. We estimate that the crude distilled product from the $LiCuPh_2$ addition contained more than 90% of the *trans*-isomer **23**. To obtain the pure *trans*-ketone a 1.21-g (8.15 mmol) sample of the crude product was added to 0.70 g (10 mmol) of $HONH_3Cl$ in 2.5 ml of aqueous EtOH and then a solution of 0.40 g (10 mmol) of NaOH in 3.7 ml of aqueous EtOH was added. The solution, from which crystalline oxime began to precipitate, was adjusted to pH 5–6 by adding HOAc, and then 20 ml of H_2O was added. The resulting mixture was stirred for 30 min and then the crude oxime was collected as 1.22 g (73.5%) of white crystals, mp 92–93°. This material was recrystallized from aqueous EtOH to separate 1.19 g (71.5%) of oxime isomers as white needles melting within the range 82–95°. A 1.66-g (8.17 mmol) sample of recrystallized oxime in 60 ml of aqueous 30% $(CO_2H)_2$ was refluxed for 1 hr and then steam distilled. The Et_2O extract of the steam distillate was dried, concentrated, and distilled in a short-path still (0.05 mm and 90–95°) to separate 1.01 g of the ***trans*-ketone 23** as a colorless liquid: n^{23}D 1.5356–1.5360; ir (CCl_4) 1720 cm^{-1} (C=O); uv (95% EtOH) series of weak maxima (ε 285 or less) in the region 240–270 mμ with a maximum at 286 mμ (ε 112); nmr (CCl_4) δ 7.20 (5 H, br s, aryl CH), 2.9–3.5 (1 H, m, benzylic CH), 1.4–2.7 (7 H, m, aliphatic CH), and 0.8–1.1 (3 H, m, CH_3); mass spectrum, *m/e* (rel intensity) 188 (16, M^+) 131 (100), 105 (24), 104 (57), and 91 (25).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.93; H, 8.61.

Comparison of the ir spectra of purified samples of the *cis*- and *trans*-ketone isomers **24** and **23** indicates that each sample must contain less than 5% of its epimer as an impurity.

Preparation of the Cyclohexylcarbinyl Ketones 25 and 26. Samples of *trans*- (**32**, mp 176–177°, lit. mp 174–175°,[22e] 176–177°[22a,c]) and *cis*-4-*t*-butylcyclohexanecarboxylic acids (**31**, mp 116–117°, lit. 117–118,[22b,c,d] 117.5–118°[22a,e]) were prepared as previously described.[10,22] A sample of each acid **31** or **32** was reduced with $LiAlH_4$ in Et_2O solution to yield the corresponding carbinol **33** or **34**. The ***trans*-carbinol 34** was isolated after short-path distillation as a colorless liquid: n^{27}D 1.4650 (lit.[23] n^{20}D 1.4683); ir (CCl_4) 3620 and 3400 (broad) cm^{-1} (free and assoc OH); nmr (CCl_4) δ 3.62 (1 H, br, OH), 3.29 (2 H, d, J = 5.0 Hz, CH_2OR), 0.8–2.0 (10 H, m, aliphatic CH), and 0.84 (9 H s, $(CH_3)_3C$). The ***cis*-carbinol 33** was collected from a sublimation (1 mm and 45°) as white prisms: mp 58.5–59.5° (lit.[23] mp 56–57°); ir (CCl_4) 3625 and 3400 (broad) cm^{-1} (free and assoc OH); nmr (CCl_4) δ 3.77 (1 H, br, OH), 3.47 (2 H, d, J = 7.0 Hz, CH_2OR), 0.8–2.0 (10 H, m, aliphatic CH), and 0.83 (9 H, s, $(CH_3)_3C$). On glpc (TCEP column) the retention times were 40 min for the *trans*-carbinol **34** and 44 min for the *cis*-carbinol **33**.

A solution of 3.474 g (18.8 mmol) of the *trans*-acid **32** in 15 ml of CH_2Cl_2 and 7.67 g (64.3 mmol) of $SOCl_2$ was allowed to stand at 25–30° for 36 hr and then concentrated and distilled in a short-path still (0.6 mm and 140–150°). The ***trans*-acid chloride 36** was collected as 3.00 g (79%) of colorless liquid: n^{26}D 1.4699; ir (liquid film) 1800 cm^{-1} (COCl) with a band at 975 cm^{-1} not present in the spectrum from the *cis*-isomer **35**. The same procedure with 3.669 g (19.8 mmol) of the *cis*-acid **31**, 15 ml of CH_2Cl_2, and 6.87 g (57.8 mmol) of $SOCl_2$ yielded 3.52 g (86%) of the ***cis*-acid chloride 35** as a colorless liquid: n^{26}D 1.4729; ir (liquid film) 1810 cm^{-1} (COCl) with a band at 835 cm^{-1} not present in the spectrum from the *trans*-isomer **36**. To demonstrate the absence of appreciable epimerization during the preparation of the acid chlorides **35** and **36** a sample (252–265 mg) of each distilled acid chloride was added to excess EtOH. The resulting mixtures were stirred for 5 min and then treated with saturated aqueous $NaHCO_3$. After the resulting solutions had been concentrated to remove volatile solvents, Et_2O solutions of the residual organic products were dried, concentrated, and distilled in a short-path still (0.35 mm and 89–95°). The ***trans*-ethyl ester 38** [lit.[24] bp 74–78° (0.4–0.7 mm), n^{20}D 1.4522], obtained in 48% yield from the *trans*-acid chloride **36**, contained (glpc, TCEP)

actions involving strong bases, metals, or organometallic intermediates were performed under a nitrogen atmosphere.

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column) 1.6% of the more rapidly eluted *cis*-ester **37**. Similarly, the *cis*-**ethyl ester 37** [lit.[24] bp 89–90° (2.5 mm), n^{20}D 1.4532], obtained in 49% yield from the *cis*-acid chloride **35**, contained only 1.2% of the more slowly eluted *trans*-ester **38**.

To a cold (0°) solution of 81 mmol of CH_2N_2 in 250 ml of Et_2O was added dropwise with mixing, a solution of 3.00 g (15 mmol) of *trans*-acid chloride **36** in 25 ml of Et_2O. After the solution had been allowed to stand at 0° for 14 hr, the volatile solvents were evaporated and the yellow crystalline residue was recrystallized from hexane. The *trans*-**diazo ketone 40** was collected as fractions of yellow plates: mp 61.5–63° or 63–64°, yield 4.26 g (85%); ir (CCl_4) 2120 and 1645 cm^{-1} (α-diazo ketone); uv (95% EtOH) 249 (ϵ 10,800) and 271 mμ (shoulder, ϵ 8760); nmr (CCl_4) δ 5.29 (1 H, s, $COCHN_2$), 0.8–2.2 (10 H, m, aliphatic CH), and 0.85 (9 H, s, $(CH_3)_3C$); mass spectrum, no molecular ion and abundant fragments at *m/e* 137, 81, 57, 41, 29, and 28. Similarly, reaction of 3.52 g (17 mmol) of the *cis*-acid chloride **35** with 68 mmol of CH_2N_2 in 350 ml of Et_2O yielded, after crystallization from hexane, 3.18 g (90%) of the *cis*-**diazo ketone 39** as fractions of yellow plates: mp 34–36° or 36.5–37.5°; ir (CCl_4) 2120 and 1645 cm^{-1} (diazo ketone); uv (95% EtOH) 250 (ϵ 10,200) and 270 mμ (shoulder, ϵ 7900); nmr (CCl_4) δ 5.33 (1 H, s, $COCHN_2$), 0.8–2.5 (10 H, m, aliphatic CH), and 0.82 (9 H, s, $(CH_3)_3C$); mass spectrum, no molecular ion and abundant fragments at *m/e* 81, 57, 44, 41, and 28.

To a solution of 2.88 g (13.8 mmol) of the *cis*-diazoketone **39** in 25 ml of anhydrous MeOH was added, with continuous stirring, three drops of a solution prepared by dissolving 200 mg of anhydrous $PhCO_2Ag$ in 3 ml of Et_3N.[25] An additional 4 ml of this catalyst solution was added dropwise over the next 20 min at such a rate as to maintain vigorous nitrogen evolution and gentle refluxing of the reaction mixture. The resulting suspension of black solid (and colloidal material) was filtered and concentrated. An Et_2O solution of the residue was dried, concentrated, and distilled in a short-path still (0.35 mm and 90–100°) to separate 2.34 g (80%) of the *cis*-**ester 43** as a colorless liquid: n^{25}D 1.4584; ir (liquid film) 1740 cm^{-1} (ester C=O); nmr (CCl_4) δ 3.59 (3 H, s, OCH_3), 1.0–2.3 (12 m, aliphatic CH), and 0.84 (9 H, s, $(CH_3)_3C$); mass spectrum, no molecular ion and abundant fragments at *m/e* 157, 156, 81, 74, 57, 56, and 41.

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.36; H, 11.25.

The corresponding reaction of 2.18 g (10.5 mmol) of the *trans*-diazo ketone **40** with 20 ml of MeOH in the presence of 2 ml of the $PhCO_2Ag$–Et_3N catalyst solution yielded, after short-path distillation (0.35 mm and 90–100°), 1.44 g (65%) of the *trans*-**ester 44** as a colorless liquid: n^{25}D 1.4543; ir (liquid film) 1740 cm^{-1} (ester C=O); nmr (CCl_4) δ 3.59 (3 H, s, OCH_3), 0.8–2.2 (12 H, m, aliphatic CH), and 0.86 (9 H, s, $(CH_3)_3C$); mass spectrum, no molecular ion and abundant fragments at *m/e* 157, 81, 74, 57, 56, and 41.

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.53; H, 11.39. Found: C, 73.33; H, 11.45.

After a solution of 2.30 g (10.8 mmol) of the *cis*-ester **43** and 0.80 g (20 mmol) of NaOH in 3 ml of H_2O and 7 ml of MeOH had been stirred at 25–30° for 5 days, the crude acidic product was isolated in the usual way. The pure *cis*-**acid 41** crystallized from hexane as 1.27 g (60%) of white needles: mp 98–99° (lit.[26] mp 96–98.8°); ir (CCl_4) 2800–3300 (assoc OH) and 1705 cm^{-1} (carboxyl C=O); nmr (CCl_4) δ 11.8 (1 H, s, OH), 1.0–2.5 (12 m, aliphatic CH), and 0.83 (9 H, s, $(CH_3)_3C$); mass spectrum, no molecular ion with abundant fragments at *m/e* 143, 81, 57, 56, and 41. The corresponding reaction of 1.40 g (6.6 mmol) of the *trans*-ester **44** with 0.40 g (10 mmol) of NaOH yielded 0.86 g (66%) of the *trans*-**acid 42** as fractions of white needles from hexane: mp 95–96° or 96–96.5° (lit.[26] mp 95.5–96°); ir (CCl_4) 2700–3400 (assoc OH) and 1705 cm^{-1} (carboxyl C=O); nmr (CCl_4) δ 10.1 (1 H, s, OH), 0.7–2.3 (12 m, aliphatic CH), and 0.83 (9 H, s, $(CH_3)_3C$); mass spectrum, no molecular ion with abundant fragments at *m/e* 143, 81, 57, 56, and 41.

To a cold (0°) solution of 399 mg (2.01 mmol) of the *cis*-acid **41** in 7 ml of Et_2O was added, dropwise and with stirring over 15 min, 4.26 ml of an Et_2O solution containing 4.42 mmol of MeLi. The resulting suspension was stirred at 25–30° for 3.5 hr and then added, dropwise, to a vigorously stirred aqueous solution (pH 7) of NH_4Cl and NH_3. The neutral organic product was extracted with Et_2O, dried, concentrated, and distilled in a short-path still (0.8 mm and 95–120°). The distillate, 365 mg of colorless liquid, contained (in order of elution from glpc, Carbowax 20M) *ca.* 91% of the *cis*-ketone **25** and *ca.* 9% of a component believed to be the corresponding tertiary alcohol. A hexane solution of the product when cooled to −78° deposited the crystalline *cis*-ketone **25** which was collected at low temperatures. The *cis*-**ketone 25** remelted at 5–8° to a colorless liquid which no longer contained the alcohol impurity: ir (CCl_4) 1715 cm^{-1} (C=O); nmr (CCl_4) δ 0.8–2.4 (12 H, m, aliphatic CH) with superimposed singlets at 2.03 (3 H, $COCH_3$) and 0.84 (9 H, $(CH_3)_3C$); mass spectrum, *m/e* (rel intensity) 196 (1, M^+), 81 (38), 80 (30), 59 (50), 58 (30), 57 (82), 43 (100), and 41 (53).

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.61; H, 12.35.

The same procedure was applied to the reaction of 359 mg (1.80 mmol) of the *trans*-acid **42** with 3.80 mmol of MeLi in 10.8 ml of Et_2O. The distilled product, 320 mg of colorless liquid, contained (in order of elution from glpc, Carbowax 20M) *ca.* 89% of the *trans*-ketone **26** and *ca.* 11% of a component believed to be the corresponding tertiary alcohol. Since low-temperature crystallization did not separate the pure ketone **26** efficiently, a sample of the pure *trans*-**ketone 26** was collected (glpc) as a colorless liquid: mp 24–25°; ir (CCl_4) 1720 cm^{-1} (C=O); nmr (CCl_4) δ 0.8–2.4 (12 H, m, aliphatic CH) with superimposed singlets at 2.00 (3 H, $COCH_3$) and 0.83 (9 H, $(CH_3)_3C$); mass spectrum, *m/e* (rel intensity) 196 (1, M^+), 81 (22), 59 (30), 57 (51), 43 (100), and 41 (27).

Anal. Calcd for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.46; H, 12.21.

A solution of 196.1 mg (1.03 mmol) of the unsaturated ketone **3** in 5.5 ml of EtOH was hydrogenated at 23.5° and atmospheric pressure over 35 mg of a 5% Pd–C catalyst. The hydrogen uptake (25.6 ml or 0.94 equiv) ceased after 5 min and the reaction mixture was filtered and concentrated. Both the nmr spectrum (CCl_4) and glpc (TCEP column) of the crude product indicated the presence of a mixture of the *cis*-ketone **25** (34%, first eluted) and the *trans*-ketone **26** (66%, second eluted).

To a solution of 50 mg (1.32 mmol) of $LiAlH_4$ in 10 ml of Et_2O was added 82 mg (0.418 mmol) of the *trans*-ketone **26**. The resulting solution was stirred at 25–30° for 5 min, H_2O was added to destroy the excess hydride, and the resulting mixture was partitioned between Et_2O and dilute aqueous H_2SO_4. The organic phase was washed successively with aqueous NaCl and with aqueous $NaHCO_3$ and then dried and concentrated to leave 82.2 mg of the crude alcohol **48**, mp 55–57°. Sublimation (0.1 mm and 50–55°) afforded 72.2 mg (88%) of the pure *trans*-**alcohol 48** as white needles: mp 56–57°; ir (CCl_4) 3600 cm^{-1} (OH); nmr (CCl_4) δ 3.72 (1 H, m, >CHOR), 1.87 (1 H, s, OH), 0.8–2.0 (12 H, m, aliphatic CH), 1.13 (3, H, d, J = 6.5 Hz, CH_3), and 0.82 (9 H, s, $(CH_3)_3C$); mass spectrum, no molecular ion with abundant fragments at *m/e* 123, 81 67, 57, 56, 55, 45, and 41.

Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.59; H, 13.08.

The corresponding reaction of 50 mg (1.32 mmol) of $LiAlH_4$ with 77.5 mg (0.395 mmol) of the *cis*-ketone **25** yielded 79.0 mg of crude liquid product from which the pure alcohol **47** was separated by glpc (silicone SE-52). A collected sample of the pure *cis*-**alcohol 47** was obtained as a colorless liquid: mp *ca.* 22°; ir (CCl_4) 3600 cm^{-1} (OH); nmr (CCl_4) δ 3.76 (1 H, m, >CHOR), 0.8–2.0 (13 H, OH and aliphatic CH), 1.17 (3 H, d, J = 6.0 Hz, CH_3), and 0.85 (9, H, s, $(CH_3)_3C$); mass spectrum, no molecular ion with abundant fragments at *m/e* 123, 82, 81, 80, 67, 57, 56, 55, and 41.

Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.58; H, 13.33.

On an 8-m glpc column (TCEP) the carbinols **47** and **48** are partially resolved with the *trans*-isomer **48** being eluted more rapidly than the *cis*-epimer **47**.

Preparation of the Possible Rearranged Products 27–29. Authentic samples of the methyl ketones **27** and **28** were available from other work.[10] Reaction of isophorone (**10**) with $Pb(OAc)_4$ as previously described[27] yielded 6-acetoxy-3,5,5-trimethyl-2-cyclohexenone: mp 75.5–76.2° (lit.[27] mp 77–77.5°); ir (CCl_4) 1755 (ester C=O), 1695 (conj C=O), and 1635 cm^{-1} (conj C=C); nmr (CCl_4) δ 5.78 (1 H, m, vinyl CH), 5.05 (1 H, s, COCHOR), 1.8–2.8 (2 H, m, CH_2), 2.12 (3 H, s, $OCOCH_3$), 1.93 (3 H, br s, vinyl CH_3), 1.07 and 0.94 (two 3 H, s, CH_3). Hydrolysis of this product with aqueous HCl[27] produced 6-hydroxy-3,5,5-trimethyl-2-cyclohexenone: mp 44–45° (lit.[27] mp 45–46°); ir (CCl_4) 3460 (assoc OH), 1680 (conj C=O), and 1635 cm^{-1} (conj C=C), which was

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heated with powdered NaOH.[27] The acidic product was 1-hydroxy-2,2,4-trimethylcyclopentanecarboxylic acid: mp 88–89° (lit.[27] 89–90°); ir (CCl_4) 3590, 3540, 2800–3200 (free and assoc OH), and 1695 cm^{-1} (carboxyl C=O). A solution of 1.006 g (5.83 mmol) of this hydroxy acid and 2.601 g (5.87 mmol) of $Pb(OAc)_4$ in 25 ml of PhH was refluxed for 2.5 hr and then cooled, filtered, washed with aqueous $NaHCO_3$, dried, concentrated, and distilled in a short-path still (760 mm and 100–130°) to give a mixture (glpc, TCEP column) of benzene and the ketone **29**. The **cyclopentanone 29** was collected (glpc) as a colorless liquid: $n^{29}D$ 1.4249 (lit.[28] $n^{20}D$ 1.4294); ir (CCl_4) 1740 cm^{-1} (cyclopentanone C=O); nmr (CCl_4) δ 1.0–2.8 (5 H, m, aliphatic CH), 1.11 (3 H, d, J = 7 Hz, CH_3), 1.02, and 0.96 (two 3 H, s, CH_3); mass spectrum, molecular ion at m/e 126 with abundant fragments at 111, 69, 56, and 41. A sample of this ketone was converted in 63% yield to its **2,4-dinitrophenylhydrazone** (red needles from MeOH), mp 164.5–165.5° (lit.[28] mp 164.5–165°). On the glpc column (TCEP) used for analysis of the reduction products **19** and **20**, the retention times were: **29**, 9.0 min, **20**, 21 min, and **19**, 24 min. Similarly, the retention times on the same glpc column used to study the reduction of the unsaturated ketone **3** were **27**, 92 min; **28**, 150 min; **26**, 171 min; and **25**, 179 min.

Preparation of the Decalones 15–18, 21, and 22. A solution of 2.3 g (0.33 g-atom) of Li in 500 ml of liquid NH_3 was treated with a solution of 17.0 g (82.5 mmol) of the conjugated ketone **6** and 8.7 ml (90 mmol) of *t*-BuOH in 100 ml of Et_2O. After the resulting blue solution had been stirred for 2 min, solid NH_4Cl was added to consume the excess Li and the NH_3 was allowed to evaporate. The residue was partitioned between H_2O and Et_2O and the organic layer was washed with aqueous NaCl, dried, and concentrated. A solution of the residue in cold (0°) acetone was oxidized with excess 8 *N* H_2CrO_4[21] at 0° for 15 min and then the excess oxidant was destroyed with Me_2CHOH. The resulting mixture was concentrated and the residue was partitioned between H_2O and Et_2O. After the Et_2O layer had been washed and dried, concentration left 14.0 g of crude yellow solid. Recrystallization from hexane afforded 13.3 g (78.5%) of the *trans*-fused ketone **22** as white prisms, mp 56–58°. Recrystallization raised the melting point to 58–59°: ir (CCl_4) 1715 cm^{-1} (C=O); nmr (CCl_4) δ 0.9–2.6 (15 H, m, aliphatic CH) and 0.93 (9 H, s, $(CH_3)_3C$); mass spectrum, m/e (rel intensity), 208 (22, M^+), 153 (20), 152 (47), 57 (100), and 41 (28).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.43; H, 11.39.

A solution of 10.3 g (50 mmol) of the unsaturated ketone **6** and 5 ml of aqueous 3 *M* HCl in 50 ml of EtOH was hydrogenated at 26.5° and 1 atm pressure over 1.03 g of a 5% Pd–C catalyst. The reaction was stopped after 1150 ml (0.92 equiv) of H_2 had been consumed. After the mixture had been filtered and concentrated, distillation of the residue (9.66 g) separated 8.77 g (85%) of colorless liquid, bp 72–75° (0.1 mm), which contained (glpc, silicone XE-60) 93% of the *cis*-fused ketone **21** and 7% of the isomer **22**. Fractional distillation with a Teflon spinning band column afforded a fraction, bp 79° (0.12 mm), $n^{25}D$ 1.4899, which contained (glpc, silicone XE-60) 99% of the desired ketone **21**: ir (CCl_4) 1712 cm^{-1} (C=O); nmr (CCl_4) δ 0.9–2.6 (15 H, m, aliphatic CH) and 0.93 (9 H, s, $(CH_3)_3C$); mass spectrum, m/e (rel intensity), 208 (21 M^+), 153 (25), 152 (100), 109 (45), 96 (25), 94 (39), 57 (78), 55 (23), and 41 (37).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.96; H, 11.71.

With the glpc column (silicone XE-60) used for analyses these ketones and an internal standard (naphthalene) had the following retention times: naphthalene, 7 min; *trans*-fused ketone **22**, 37 min; *cis*-fused ketone **21**, 42 min; unsaturated ketone **6**, 65 min.

Samples of *trans*-2-decalone [**16**, bp 118.5–120° (25 mm), $n^{23.5}D$ 1.4817, lit.[11a] $n^{23}D$ 1.4820] and *cis*-2-decalone [**15**, bp 64–65° (0.7 mm), $n^{23.5}D$ 1.4910, lit.[11a] $n^{25}D$ 1.4904] were prepared as previously described.[11a,29] Analyses of these ketones and an internal standard (naphthalene) were performed by glpc (silicone SE-30), the following retention times being observed: naphthalene, 11 min; *trans*-ketone **16**, 20 min; *cis*-ketone **15**, 24 min; unsaturated ketone **4**, 27 min.

Reduction of the 9-methyloctalone **5** with Li and *t*-BuOH in liquid ammonia followed by the usual isolation procedure afforded the *trans*-ketone **18**: bp 60–61° (0.3 mm); $n^{25}D$ 1.4892 [lit.[30] bp 130° (20 mm), $n^{24}D$ 1.4862]; ir (CCl_4) 1710 cm^{-1} (C=O); nmr (CCl_4) δ 0.7–2.8 m with a superimposed singlet at 1.00 (CH_3C). Hydrogenation of the octalone **5** over a 5% Pd–C catalyst in EtOH containing aqueous HCl yielded the *cis*-ketone **17** which crystallized from hexane as white plates: mp 47.5–48.5° (lit.[31] mp 46°); ir (CCl_4) 1715 cm^{-1} (C=O); nmr (CCl_4) δ 0.7–2.8 m with superimposed singlet at 1.10 (CH_3C). Although glpc analysis (silicone XE-60 column) could be used to analyze mixtures of an internal standard (diphenylmethane, ret time 11 min), the mixture of saturated ketones **17** and **18** (17 min), and the unsaturated ketone (27 min), separation of the isomeric saturated ketones **17** and **18** by glpc was unsuccessful. Consequently, an analytical scheme was devised for mixtures of the ketones **17** and **18** in which the nmr spectrum of a CCl_4 solution of the mixture was scanned (50 cycle sweep) and the areas under the singlet at δ 1.00 (from **18**) and 1.10 (from **17**) were integrated with a planimeter. This method was calibrated with a series of known mixtures prepared from authentic samples and allowed us to determine the composition of mixtures of **17** and **18**. A similar analytical procedure has been described by Robinson.[12a]

Preparation of the Decalin Derivatives 45 and 46. A solution of 1.53 g (7.35 mmol) of the *trans*-fused ketone **22** (purity 90%) and 2.05 g (34.8 mmol) of 85% H_2NNH_2 in 15 ml of $(HOCH_2CH_2)_2O$ was refluxed for 1 hr and then 0.89 g (22 mmol) of NaOH was added. Water was allowed to distill from the mixture and the reaction mixture was heated to 210° for 3 hr. After the resulting solution had been cooled, it was partitioned between aqueous HCl and Et_2O, and the Et_2O layer was washed with aqueous NaCl and then dried and concentrated. Distillation of the residual liquid (1.30 g) in a short-path still (100–110° and 0.05 mm) afforded 1.12 g (78.5%) of colorless liquid, $n^{26}D$ 1.4725, which contained (glpc, silicone XE-60) one major component (>99%), the hydrocarbon **46**. The pure hydrocarbon **46** was collected (glpc) as a colorless liquid: $n^{28.5}D$ 1.4720; ir (CCl_4) no OH, C=O, or C=C absorption in the 3- and 6-μ regions; nmr (CCl_4) δ 0.6–2.4 m with a superimposed singlet at 0.83 [$(CH_3)_3C$]; mass spectrum, m/e (rel intensity), 194 (24, M^+), 138 (70), 137 (77), 136 (88), 95 (71), 81 (77), 67 (36), 57 (80), 56 (100), and 41 (47).

Anal. Calcd for $C_{14}H_{26}$: C, 86.51; H, 13.49. Found: C, 86.60; H, 13.27.

A similar reduction of 1.885 g (9.06 mmol) of the *cis*-fused ketone **21** with 1.22 g (19 mmol) of KOH, 1.22 ml (20.8 mmol) of 85% hydrazine, and 20 ml of $(HOCH_2CH_2)_2O$ yielded after short-path distillation (90–120° and 0.04 mm), 890 mg (47%) of colorless liquid which contained (glpc, silicone XE-60) >97% of the *cis*-fused hydrocarbon **45**. A collected (glpc) sample of the hydrocarbon **45** was obtained as a colorless liquid: $n^{28.5}D$ 1.4781; ir (CCl_4) no OH, C=O, or C=C absorption in the 3- and 6-μ regions; nmr (CCl_4) δ 0.6–2.2 m with a superimposed singlet at 0.83 [$(CH_3)_3C$]; mass spectrum, m/e (rel intensity), 194 (18, M^+), 138 (32), 137 (100), 136 (88), 95 (75), 81 (85), 67 (38), 57 (56), 56 (60), and 41 (43).

Anal. Calcd for $C_{14}H_{26}$: C, 86.51; H, 13.49. Found: C, 86.84; H, 13.38.

The two hydrocarbons had the following retention times on glpc (silicone XE-60): **46**, 21.5 min; **45**, 24.0 min.

Preparation of the Epoxy Ketone 12. To a cold (15°) solution of 108.7 g (0.526 mol) of the unsaturated ketone **6** (which contained some of the $\Delta^{9,10}$ isomer) and 151 ml (1.58 mol) of aqueous 30% H_2O_2 in 530 ml of MeOH was added, dropwise and with stirring over 1.5 hr, a solution containing 10.5 g (0.262 mol) of NaOH in 44 ml of H_2O while the temperature of the reaction mixture was maintained at 18–22°. The resulting mixture was stirred at 25° for 4.3 hr and then diluted with H_2O and extracted with Et_2O. The Et_2O extract was washed with aqueous NaCl, dried, and concentrated to leave 88.3 g of the product as a semisolid. Recrystallization from pentane separated 53.2 g (46%) of the epoxide **12** as white plates; mp 70–72°. After recrystallization the sample melted at 72–72.5°: ir (CCl_4) 1720 cm^{-1} (C=O); uv (95% EtOH) 298 mμ (ϵ 38.5); nmr (CCl_4) δ 2.87 (1 H, s, epoxide CH), 0.9–2.4 (12 H, m, aliphatic CH), and 0.88 (9 H, s, $(CH_3)_3C$); mass spectrum, m/e (rel intensity) 222 (19, M^+), 57 (100), 55 (28), 46 (67), and 39 (23).

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.44; H, 10.03.

Preparation of the Enolic Diketone 13. To a solution of 50.7 g (0.228 mol) of the epoxide **12** in 250 ml of HOAc was added, dropwise and with stirring over 1 hr while the reaction temperature was

(28) S. F. Birch and E. A. Johnson, *J. Chem. Soc.*, 1493 (1951).

(29) H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 1341 (1965).

(30) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler, and W. M. McLamare, *J. Amer. Chem. Soc.*, **74**, 4223 (1952).

(31) (a) E. C. duFeu, F. J. McQuillin, and R. Robinson, *J. Chem. Soc.*, 53 (1937); (b) R. B. Woodward, *J. Amer. Chem. Soc.*, **62**, 1208 (1940).

kept at 22°, a solution of 50 ml of concentrated H_2SO_4 in 250 ml of HOAc.[32] The resulting green fluorescent solution was allowed to stand at 22° for 30 min and then diluted with H_2O and cooled to 0°. The crude solid product was collected, dissolved in Et_2O, and washed successively with H_2O, aqueous $NaHCO_3$, and aqueous NaCl. After the organic solution had been dried and concentrated, the residual solid (49.0 g, mp 120–148°) was recrystallized from hexane to separate 27.9 g (55%) of the enolic diketone **13** as white needles, mp 154–156°. The product melted at 155–156° after recrystallization: ir (CCl_4) 3430 (assoc OH), 1675 (conj C=O), and 1650 cm^{-1} (enol C=C); uv (95% EtOH) 276 mμ (ε 12,400); nmr (pyridine-d_5), δ 0.8–3.6 m with superimposed singlet at 0.80 [$(CH_3)_3C$]; mass spectrum, *m/e* (rel intensity), 222 (47, M^+), 166 (38), 165 (40), 112 (37), 86 (39), 84 (60), 57 (100), 49 (90), 43 (56), and 41 (58).

Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.65; H, 10.13.

Preparation of the Decalone 14. A mixture of 11.11 g (50 mmol) of the enolic diketone **13**, 50 ml (380 mmol) of aqueous 57% HI, and 250 ml of HOAc was refluxed[33] for 3 hr under N_2 and then poured with a cold (5°) solution of 200 g of NaOH and 50 g of $NaHSO_3$ in 1200 ml of H_2O. The crude solid product was collected from the cold mixture and then dissolved in hexane and washed successively with aqueous $NaHSO_3$, H_2O, aqueous NaOH, H_2O, and aqueous NaCl. After the hexane solution had been dried and concentrated, the residual yellow solid (9.185 g) was distilled in a short-path still (80° and 0.05 mm) to separate 8.57 g (84%) of the crude ketone **14** as a pale yellow solid, mp 65–72°. The ir absorption (CCl_4, 1715 (s), 1665 (w), and 1636 (w)), uv (95% EtOH, maximum at 246 mμ), and glpc (silicone XE-60) of this crude product suggested the presence of 3–4% of an α,β-unsaturated ketone with the same glpc retention time as the octalone **7**; however neither of the β-decalones **21** or **22** was detected by glpc. A solution of 15.51 g (*ca.* 74 mmol) of the crude ketone **14** from the above reaction and a comparable reduction in 500 ml of MeOH was hydrogenated at 25–30° and 1 atm over 944 mg of a 5% Pd–C catalyst. After the H_2 uptake (95 ml or 4.2 mmol) ceased, the mixture was filtered and concentrated. The ketone **14** separated from the MeOH solution as 15.43 g of pale yellow solid, mp 67–73°. Recrystallization from MeOH at low temperatures gave the pure ketone **14**: 74–75.5°; ir (CCl_4) 1715 cm^{-1} (C=O); uv (95% EtOH), 286 mμ (ε 27); nmr (CCl_4) δ 0.7–2.5 m with a superimposed singlet at 0.85 [$(CH_3)_3C$]; mass spectrum, *m/e* (rel intensity), 208 (69, M^+) 152 (88), 110 (36), 57 (100), and 41 (38).

Anal. Calcd for $C_{14}H_{24}O$: C, 80.71; H, 11.61. Found: C, 80.81; H, 11.65.

A solution of 1.55 g (7.43 mmol) of the ketone **14** and 2.24 g (38.1 mmol) of 85% H_2NNH_2 in 20 ml of $(HOCH_2CH_2)_2O$ was refluxed for 1 hr and then 1.04 g (26 mmol) of NaOH was added. Water was distilled from the mixture and it was heated to 200–210° for 3 hr. After following the previously described isolation procedure, the product was collected from short-path distillation (100–110° and 0.05 mm) as 1.12 g (78%) of colorless liquid, $n^{28.5}D$ 1.4720, which contained (glpc, silicone XE-60) more than 98% of the *trans*-fused decalin **46**, identified with the previously described sample by comparison of glpc retention times and ir and mass spectra.

Preparation of the Octalone 7. To a solution of 15.32 g (73.4 mmol) of the ketone **14** in 50 ml of CCl_4 was added, dropwise over 20 min, a solution of 12.3 g (91 mmol) of SO_2Cl_2 in 30 ml of CCl_4. The resulting solution was stirred at 25–30° for 7 hr, subjected to reduced pressure to remove part of the HCl, again stirred at 25–30° for 0.5 hr, and then concentrated under reduced pressure. The crude α-chloro ketone product [18.25 g of liquid, ir (CCl_4) 1725 and 1745 (sh) cm^{-1} (C=O)] was mixed with 12.2 g (101 mmol) of γ-collidine and heated to 180° at which point a vigorous reaction occurred and a solid separated. The mixture was heated at 180° for 10 min and then cooled and extracted with hexane to leave the insoluble γ-collidine hydrochloride. The hexane solution was washed successively with aqueous HCl and aqueous NaCl and then dried and concentrated. The crude product (15.09 g of yellow liquid) was distilled to separate 11.76 g of colorless liquid, bp 96–104° (0.05 mm) which contained (glpc, silicone XE-60) primarily the desired $\Delta^{9,10}$-ketone **7** (ret time 25.4 min) accompanied by a second component (ret time 23.6 min) believed to be the corresponding $\Delta^{8,9}$ isomer and several minor components. A solution of 11.64 g (*ca.* 56 mmol) of this mixture and 1.31 g (18.5 mmol) of pyrrolidine in 10 ml of Et_2O was stirred at 26° for 21 hr and then diluted with Et_2O and washed successively with aqueous HCl and aqueous NaCl. After the Et_2O solution had been dried and concentrated, the residual yellow oil (9.87 g containing 86% of **7** by glpc) crystallized on standing. Recrystallization from hexane at low temperatures (*ca.* −20°) separated the pure enone **7** as white plates: mp 41.7–42.5°; ir (CCl_4) 1670 (conj C=O) and 1645 cm^{-1} (conj C=C); uv (95% EtOH) 245 mμ (ε 13,000); nmr ($CDCl_3$) δ 0.9–2.6 (13 H, m, aliphatic CH) and 0.90 (9 H, s, $(CH_3)_3C$); mass spectrum, *m/e* (rel intensity), 206 (36, M^+), 150 (33), 149 (100), 135 (32), 91 (22), 57 (30), and 41 (25).

Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.17; H, 10.66.

Preparation of the Benzylidene Ketones 8 and 9. The preparation and spectroscopic properties of *trans*-benzalpinacolone (**8**), mp 42–43°, are described elsewhere.[3,34] A solution of 20.0 g (106 mmol) of the *trans*-ketone **8** in 40 ml of pentane was swept with N_2 and then irradiated in a quartz vessel with 254-mμ light from a Rayonet photochemical reactor. The composition of the solution was determined (glpc, silicone SE-52) at time intervals for the content of *cis*-ketone **9** (ret time 5 min) and *trans*-ketone **8** (ret time 7 min). After a 41-hr irradiation period, a constant composition (*ca.* 40% **9** and 60% **8**) was obtained. Fractional crystallization from pentane at −78° separated part of the crystalline *trans*-isomer **8** to leave a mixture containing 72% of the *cis*-isomer **9** in the pentane mother liquor. Although the *cis*-ketone **9** was rather easily isomerized to **8** on glpc, use of relatively low (160–180°) column and injection port temperatures permitted collection of the pure *cis*-ketone **8** as a yellow liquid: ir (CCl_4) 1690 (conj C=O) and 1605 cm^{-1} (br conj C=C and phenyl); uv (95% EtOH) 283 (ε 8480); nmr (CCl_4) δ 7.0–7.8 (5 H, m, aryl CH), 6.69 (1 H, d, J = 12.6 Hz, vinyl CH), 6.32 (1 H, d, J = 12.6 Hz, vinyl CH), and 1.13 (9, H, s, $(CH_3)_3C$); mass spectrum, *m/e* (rel intensity), 188 (10, M^+), 132 (13), 131 (100), 103 (32), 77 (19), 57 (12), and 41 (11).

Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.57. Found: C, 82.99; H, 8.60.

A solution of 5.0 g (27 mmol) of the ketone **8** in 35 ml of EtOH was hydrogenated over 0.5 g of 5% Pd–C catalyst, the H_2 uptake (630 ml of 0.97 equiv) being complete after 30 min. The crude liquid product (4.85 g) was distilled in a short-path still (0.2 mm and 100–110°) to separate the ketone **49** as a colorless liquid: $n^{25}D$ 1.4949 (lit.[35] $n^{25}D$ 1.4949); ir (CCl_4) 1715 cm^{-1} (C=O); nmr (CCl_4) δ 7.13 (5 H, br s, aryl CH), 2.5–2.9 (4 H, m, CH_2), and 1.01 (9 H, s, $(CH_3)_3C$); mass spectrum, molecular ion at *m/e* 190 with abundant fragments at *m/e* 133, 105, 91, 57, 44, and 41.

Preparation of the Dimeric Reduction Products 50–52. A cold (0°) solution of 5.016 g (26.8 mmol) of the unsaturated ketone **8** in 25 ml of THF was stirred over 2.0 g (91 mg-atom) of Na slices for 5 hr and then the reaction solution was decanted from the unchanged Na and poured into H_2O. The colorless crystalline precipitate (4.953 g, mp 115–135°) which separated was recrystallized from EtOH to separate 517 mg (10%) of one stereoisomer of the aldol condensation product **52** as white needles: mp 173–174°; ir (CCl_4) 3420 (assoc OH) and 1670 cm^{-1} (C=O, presumably shifted to lower frequency by intramolecular H bonding); uv (95% EtOH) series of weak peaks (ε 500 or less) in the region 250–270 mμ with intense end absorption; nmr ($CDCl_3$) δ 7.10 (10 H, br s, aryl CH), 5.30 (1 H, s, OH lost after exchange with D_2O), 1.0–4.0 (5 H, m, aliphatic CH), 0.93 (9 H, s, $(CH_3)_3C$), and 0.68 (9 H, s, $(CH_3)_3C$).

Anal. Calcd for $C_{26}H_{34}O_2$: C, 82.49; H, 9.05. Found: C, 82.23; H, 9.12.

A solution of 411 mg (1.09 mmol) of the crystalline aldol product and several milligrams of TsOH in benzene was refluxed for 12 hr and then cooled, washed with aqueous $NaHCO_3$, dried, and concentrated. The residual solid (503 mg) was recrystallized from EtOH to separate 327 mg (80%) of the dimer **50**, mp 146–148°. An additional recrystallization afforded the pure racemic dihydrodimer **50** as white needles from EtOH: mp 147–148°; ir (CCl_4) 1705 cm^{-1} (C=O); uv (95% EtOH) series of weak peaks (ε 401 or less) in the region 240–270 mμ; nmr ($CDCl_3$) δ 6.8–7.3 (10 H, m, aryl CH), 2.4–3.9 (6 H, m, aliphatic CH), and 0.98 (18 H, s, $(CH_3)_3C$).

Anal. Calcd for $C_{26}H_{34}O_2$: C, 82.49; H, 9.05. Found: C, 82.67; H, 9.21.

(32) This general procedure was described by K. Heusler, J. Kalvoda, P. Wieland, G. Anner, and A. Wettstein, *Helv. Chim. Acta*, **45**, 2575 (1962).

(33) This reduction procedure has been described by W. Reusch and R. LeMahieu, *J. Amer. Chem. Soc.*, **86**, 3068 (1964).

(34) G. A. Hill and G. M. Bramann, "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1941, p 81.

(35) E. Berliner and F. Berliner, *J. Amer. Chem. Soc.*, **72**, 222 (1950).

Following previously described procedures,[13] a solution of methyl cinnamate in moist Et_2O was reduced over excess Al–Hg to yield a mixture of methyl hydrocinnamate and the stereoisomeric dihydrodimers **53** and **54**. A combination of fractional crystallization and distillation separated the *meso*-dimer **54** as colorless needles, mp 175–177° (lit.[13b] 177–177.5°) [ir ($CHCl_3$) 1735 cm^{-1} (C=O); nmr ($CDCl_3$) δ 7.24 (10 H, m, aryl CH), 3.30 (6 H, s, OCH_3), 3.0–3.6 (2 H, m, benzyl CH), and 2.3–2.6 (4 H, m, CH_2CO)], and the racemic dimer **53** as colorless prisms, mp 72–74° (lit.[13] 73–74°) [ir ($CHCl_3$) 1730 cm^{-1} (C=O); nmr ($CDCl_3$) δ 6.7–7.4 (10 H, m, aryl CH), 3.50 (6 H, s, OCH_3), 3.2–3.8 (2 H, m, benzyl CH), and 2.5–3.0 (4 H, m, CH_2CO)]. A mixture of 1.362 g (4.18 mmol) of the *meso*-diester **54** and 250 ml of cold (−78°) pentane was treated with 7.5 ml of a pentane solution containing 9.2 mmol of *t*-BuLi and the resulting mixture was stirred for 12 hr during which time it was allowed to warm to 25–30°. After H_2O had been added the mixture was filtered to remove the bulk of the insoluble unchanged diester **54** and the filtrate was partitioned between H_2O and Et_2O. The Et_2O solution was dried and concentrated to leave 670 mg of solid which contained (glpc) a mixture of the diketone **51**, the diester **54**, and several unidentified components. Recrystallization (EtOH) gave 139 mg of solid which contained (glpc, silicone SE-52) the diester **54** (*ca.* 20%, ret time 9.2 min) and the diketone **51** (*ca.* 80%, ret time 13.4 min). After the crude product had been saponified for 2.5 hr with 0.5 g of KOH and 1 ml of H_2O in 50 ml of boiling EtOH, the crude neutral product recovered (102 mg) no longer contained (glpc) the diester **43**. Recrystallization (EtOH) afforded the pure *meso*-diketone **51** as colorless needles: mp 212–212.5°; ir ($CHCl_3$) 1700 cm^{-1} (C=O); uv (95% EtOH) series of weak maxima (ε <425) in the region 240–270 mμ; nmr ($CDCl_3$) δ 7.30 (10 H, m, aryl CH), 1.6–3.8 (6 H, m, aliphatic CH_2), and 0.72 (18 H, s, $(CH_3)_3C$).

Anal. Calcd for $C_{26}H_{34}O_2$: C, 82.49; H, 9.05. Found: C, 82.19; H, 8.92.

Application of the same procedure to a mixture of 102 mg (0.313 mmol) of the racemic diester **53** and 0.37 mmol of *t*-BuLi in 150 ml of pentane yielded, after saponification, 52 mg of crude neutral product as a yellow oil. Recrystallization (EtOH) afforded 11 mg of the racemic diketone **50** as needles, mp 147–148°, which was identified with the previously described sample by comparison of ir spectra and glpc retention times and by a mixture melting point.

A cold (−78°) solution of Na in HMP–THF was prepared by adding a precooled (0°) solution of 10.2 mg-atom of Na in 30 ml of HMP–THF (2:1, v/v) to 70 ml of cold (−78°), stirred THF. A precooled (−78°) solution of 642.6 mg (3.42 mmol) of the unsaturated ketones (68% *cis* **9** and 32% *trans* **8**) in 5 ml of THF was added and the resulting blue solution was stirred for 3 min and then quenched with H_2O. Following the usual isolation procedure, the crude product was oxidized with excess H_2CrO_4[21] in acetone and then the crude neutral organic product was separated as 621 mg (94%) of crystalline solid, mp 130–184°, which contained (glpc in order of elution, silicone SE-52) 5% of the monomer **49**, 43% of the *meso*-dimer **51** (ret time 23 min), and 51% of the racemic dimer **50** (26 min). This mixture was fractionally crystallized (EtOH) to separate 122.9 mg (19% yield) of the *meso*-dimer **51**, mp 211–212°, which was identified with the previously described sample by a mixture melting point and comparison of ir spectra.

In another reduction a cold (−33°) solution of 117.5 mg (0.625 mmol) of the *trans*-ketone **8** and 1.90 g (16 mmol) of *t*-BuOH in 10 ml of HMP–THF (3:2, v/v) was treated with 4.5 ml of a HMP–THF (2:1, v/v) solution containing 1.62 mg-atom of Na. The resulting yellow solution was quenched with water and the organic product was mixed with an internal standard (*p*-dibromobenzene) and analyzed (glpc, silicone SE-52, temperature programmed from 90–220°). The crude product contained *p*-dibromobenzene (ret time 14 min), the ketone **49** (34% yield, 23 min), the starting ketone **8** (17% recovery, 27 min), a minor unidentified component (45 min), and the racemic dimer **50** (10% yield, 59 min). Collected samples of products **8**, **49**, and **50** were identified with authentic samples by comparison of ir spectra and glpc retention times. From a reduction of 4.164 g (22.1 mmol) of the ketone **8** with 620 mg (90 mg-atom) of Li, 2.29 g (30.9 mmol) of *t*-BuOH, and 5 ml of THF in 50 ml of liquid NH_3 following the usual procedure, the crude product (3.911 g of yellow oil) contained the saturated ketone **49** (*ca.* 19% of the mixture), the dimer **50** (*ca.* 30% of the mixture), and several unidentified components.

Reduction of 3,5,5-Trimethyl-2-cyclohexenone (10) with Li–NH_3–Me_2CDOH. To a cold (−78°) solution of 254 mg (1.84 mmol) of the unsaturated ketone **10** and 1.0 ml of Me_2CDOH[3] in 2.0 ml of liquid NH_3 was added 4.0 mmol of Li wire and the mixture was stirred at −78°. The initially yellow solution assumed a blue color indicative of excess Li in solution after 5 min and the entire mixture partially solidified after an additional 8 min. The mixture was allowed to melt (at which time the blue color was discharged) and then the NH_3 was evaporated and the residual white solid was partitioned between H_2O and Et_2O. An internal standard (*n*-butylbenzene) for glpc analysis was added and the organic phase was dried, concentrated, and dissolved in cold (0°) acetone. Excess aqueous H_2CrO_4[21] was added to reoxidize any alcohols present to ketones. After the resulting solution had been stirred at 0° for 5 min, Me_2CHOH was added to destroy the excess oxidant and the resulting mixture was partitioned between H_2O and Et_2O. The Et_2O phase was washed with aqueous $NaHCO_3$, dried, and concentrated to leave 540 mg of colorless oil which contained (in order of elution by glpc, silicone XE-60) *n*-butylbenzene, 3,5,5-trimethylcyclohexanone (**55**, 84% yield), and the starting unsaturated ketone **10** (9% recovery). A collected sample of the reduction product **55** was identified with an authentic sample[9c] by comparison of mass spectra and glpc retention times. The mass spectrum indicated that the product contained less than 2% of deuterated species.

Reduction of the Unsaturated Ketones 1–6. The reductions with Li or Na in liquid NH_3 were accomplished by distilling the NH_3 (from a solution of Na in NH_3) into the reaction vessel and then adding successively 3–20 equiv of Na or Li and in certain cases (see Table I), 2–20 equiv of *t*-BuOH. The resulting solutions (under a Dry Ice reflux condenser) were treated with a THF solution containing 1 equiv of one of the unsaturated ketones **1–6** and the resulting solutions were stirred at −33° for 30–120 min. After the excess metal present in all cases had been consumed by the addition of excess H_2O, the NH_3 was allowed to evaporate and the residue was partitioned between H_2O and Et_2O. For small scale reactions (1–2 mmol of unsaturated ketone) an internal standard was added at this time. After the usual H_2CrO_4 oxidation procedure, the crude neutral product was either analyzed by glpc (small scale reactions) or distilled in a short-path still and then analyzed by glpc. The glpc columns and internal standards used for the decalones **15–18**, **21**, and **22** were described in a previous section of this paper. For analysis of the dimethylcyclohexanones **19** and **20** either *n*-butylbenzene or pentamethylbenzene was used as an internal standard; the relative retention times (glpc, TCEP column) were: *n*-butylbenzene, 7 min; ketone **20**, 17 min; ketone **19**, 19 min; pentamethylbenzene, 25 min; and ketone **1**, 53 min. The distilled mixture (**19** + **20**) was collected as a colorless liquid: bp 130–150°; $n^{26.2}D$ 1.4399; yield 80%.

For analyses of mixtures of the methylphenylcyclohexanones **23** and **24**, benzyl was added as an internal standard. On one glpc column (Carbowax 20 M), the relative retention times were: bibenzyl, 3 min; ketones **23** and **24** (not resolved), 6 min; and ketone **2**, 12 min; with the second glpc column (8 m, neopentylglycol adipate) the retention times were: bibenzyl, 120 min; ketone **23**, 234 min; and ketone **24**, 244 min. The distilled mixture (**23** + **24**) was collected from short-path distillation (135–145° and 2 mm) as a colorless liquid: $n^{26.2}D$ 1.5300; yield 81%.

Mixtures of the cyclohexyl derivatives **25** and **26** were mixed with *p*-dibromobenzene as an internal standard. The relative retention times (glpc, TCEP column) were: *p*-dibromobenzene, 84 min; the *trans*-ketone **26**, 160 min; the *cis*-ketone **25**, 166 min; and the unsaturated ketone **3** (or its double bond isomer),[9a] 205 min. The product (**25** + **26**) from a preparative reaction was isolated from a short-path distillation (145–160° and 2 mm) as a colorless liquid: $n^{26.2}D$ 1.4589; yield 87%.

The products from these reductions, summarized in Table I, were identified with the previously described authentic samples by comparison of glpc retention times and ir spectra of collected samples.

For small scale (*ca.* 1 mmol of unsaturated ketone) reductions, solutions of Na in HMP–THF (2:1, v/v for 0°, 3:2, v/v for −33°, and 1:4, v/v for −78°) were prepared and standardized by titration with pinacolone as previously described.[3] Aliquots of the solution containing 3–10 equiv of Na were treated with 1 equiv of the unsaturated ketone. In certain cases (see Table I) 20 equiv of *t*-BuOH was added prior to mixing the ketone with the Na solution. After the reaction mixtures had been stirred for 10–15 min, the excess metal was consumed by addition of H_2O or MeOH and the mixture was partitioned between H_2O and either Et_2O or pentane. An appropriate internal standard was added, the crude product was oxidized with H_2CrO_4 in the usual way, and then the organic product was analyzed by glpc as previously described.

The following example illustrates the procedure followed for reduction on a larger scale (these reactions listed as slow additions

in Table I). A solution of the ketone **3** (2.56 g or 12.8 mmol) in 10 ml of HMP was added, dropwise and with stirring over 1.5 hr, to a cold (0°) mixture containing 2.0 g (87 mg-atom) of Na (partially dissolved), 30 ml of HMP, and 3.7 ml (2.9 g or 39 mmol) of *t*-BuOH. The resulting blue mixture containing some undissolved Na was stirred for 10 min and then methanol was added to destroy the excess Na and the resulting mixture was partitioned between pentane and H_2O. After an acetone solution of the crude neutral product had been oxidized with aqueous H_2CrO_4, distillation in a short-path still (1 mm and 140–150°) separated 2.32 g (91%) of a mixture of ketones containing (glpc) 62% of the *trans*-isomer **26** and 38% of the *cis*-isomer **25**.

Reduction of the Octalone 7 with Li and NH_3. After a solution of 1.063 g (5.16 mmol) of the ketone **7**, 1.35 ml (15 mmol) of *t*-BuOH, and 111 mg (16 mg-atom) of Li in 100 ml of liquid NH_3 and 20 ml of THF had been stirred under reflux for 1 hr, the excess Li was consumed by addition of 1.5 ml of H_2O and the NH_3 was allowed to evaporate. After the residue had been partitioned between aqueous NaCl and Et_2O, the organic layer was dried and concentrated to leave 1.031 g of yellow crystals (mp 54–65°). After the usual oxidation (H_2CrO_4 in acetone), the crude neutral product (969 mg, mp 57–68°) was distilled in a short-path still (90–100° and 0.05 mm) to separate 832 mg (77.5%) of pale yellow solid, mp 56–69°, which exhibited (glpc, silicone XE-60) one major peak (>96%) corresponding to the ketone **14**. The crude ketonic product (1.500 g or 7.19 mmol) from a comparable Li–NH_3–THF reduction was treated with 2.02 g (34.3 mmol) of 85% H_2NNH_2 and 1.10 g (27.5 mmol) of NaOH in 20 ml of diethylene glycol as previously described. The crude product was collected from short-path distillation (90–100° and 0.05 mm) as 1.120 g (80%) of colorless liquid, $n^{27}D$ 1.4730, which contained (glpc, silicone XE-60) one major component (*ca.* 95%). A collected (glpc) sample of this major component was identified with the *trans*-decalin **46** by comparison of glpc retention times and ir and mass spectra.

Hydrochlorination of Cyclohexene in Acetic Acid. Kinetic and Product Studies[1]

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Abstract: The reaction of cyclohexene with HCl in acetic acid yields cyclohexyl chloride (C) and cyclohexyl acetate (A) under conditions of kinetic control. The reaction rate and product composition have been studied as a function of the concentration of cyclohexene, HCl, water, and tetramethylammonium chloride (TMAC). The effect of temperature as well as the deuterium isotope effect (k_H/k_D = 1.3) in DCl–DOAc have been determined. The ratio of C to A was found (1) to be low (~3.0) at low [HCl] and in the absence of water or TMAC, (2) to increase significantly with the HCl concentration, with the water concentration, and with the TMAC concentration, and (3) to vary significantly with the temperature. These observations differentiate the reaction of cyclohexene from the reactions of styrene and *t*-butylethylene studied previously under similar conditions and indicate that the reaction of cyclohexene, unlike styrene and *t*-butylethylene, does not occur exclusively *via* a carbonium ion mechanism. Analysis of the rate and product data shows that there are two terms in the rate law, one involving acid and olefin and another involving acid, olefin, and dissociated chloride ion. The latter term corresponds to a termolecular mechanism leading to the formation of cyclohexyl chloride. The effect of water on the rate and product distribution is associated with its effect upon the ionization and dissociation of HCl.

This is the second in a series of studies undertaken to determine the mechanism involved in the *anti* addition of acids to olefins. In the first paper,[3] it was shown that styrene and *t*-butylethylene react with HCl in acetic acid *via* a mechanism involving rate-limiting formation of a carbonium chloride ion pair intermediate. Rapid collapse with the counterion, rapid collapse with solvent, or rapid rearrangement and collapse of this intermediate lead to the observed products. Recent studies by Pocker and coworkers[4] on HCl addition to olefins in nitromethane as solvent are in general accord with a carbonium ion mechanism. This type of mechanism is consistent with the nonstereospecific or preferential *syn* addition of acids to olefins but provides no rationalization for stereospecific *anti* addition.

(1) (a) Reported in part at the 155th National Meeting of the American Chemical Society, San Francisco, Calif., April 1968. (b) Taken in part from the Ph.D. Thesis of Michael W. Monahan, University of California, San Diego, Calif., 1968.

(2) (a) Alfred P. Sloan Foundation Fellow, 1966–1968; (b) National Defense Education Act Predoctoral Fellow.

(3) R. C. Fahey and C. A. McPherson, *J. Amer. Chem. Soc.*, **91**, 3865 (1969).

(4) Y. Pocker, K. D. Stevens, and J. J. Champoux, *ibid.*, **91**, 4199 (1969); Y. Pocker and K. D. Stevens, *ibid.*, **91**, 4205 (1969).

In this paper we report rate and product studies for the hydrochlorination of cyclohexene in acetic acid and show that the reaction of cyclohexene differs from that of *t*-butylethylene and of styrene in several important respects. In the following paper we examine the stereochemistry of addition to cyclohexene-1,3,3-d_3 and show that cyclohexene reacts almost entirely by a different mechanism from that involved for *t*-butylethylene and styrene.

Results

General Procedure. The reaction of cyclohexene with HCl in acetic acid occurs slowly at 25° to yield cyclohexyl acetate (A) and cyclohexyl chloride (C). The reaction kinetics were studied by the method of initial rates. After 1–5% reaction, portions of the reaction were quenched and worked up, and the composition was analyzed by glpc. The concentrations of A