1-Allylidene-2,2-dimethylcyclopropane (**10**).—This product formed in 60% yield from 1,1-dichloro-2,2-dimethyl-3-propylcyclopropane (**9**) after treatment with 3 equiv of base for 75 min at 25°; it was isolated by flash distillation.

Anal. Calcd for C_8H_{12}: C, 88.2; H, 11.2; mol wt, 108. Found: C, 88.5; H, 11.5, mol wt, 108 (mass spectrum).

Spectra follow: ir (film) 5.55, 6.19, 6.95 (broad), 7.27, 8.03, 8.89, 10.1 (very broad), and 11.15 μ (broad); nmr δ 0.98 (m, 2 H, cyclopropyl), 1.19 (s) and 1.23 (s, 6 H total, methyls), 4.85–5.5 (m, 2 H, $=CH_2$), and 6.0–6.8 (m, 2 H, $-CH=CH-$); λ_{max} 230 nm (ϵ 21,900). The nmr bands at δ 1.19 and 1.23 are interpreted as due to the *gem*-dimethyl on the syn and anti isomers. The area ratio of the δ 1.23 to 1.19 band was 1.2:1. It is not known which band corresponds to which isomer.

1-Methylene-2-propenylcyclopropane (**12**).—1,1-Dichloro-2-methyl-3-propylcyclopropane (**11**) afforded a major product in 40–50% yield when treated with a threefold excess of the base for 25 min at 25°. **12** was purified by preparative glpc, and showed strong infrared absorption at 10.22 μ, characteristic of methylenecyclopropanes. The nmr spectrum showed one proton signal at δ 0.98, 1.5, 2.2 (cyclopropyl), a methyl doublet at 1.74 (J = 6.5 cps), and an olefinic pattern extending from 4.6 to 5.7.

2-Methyl-2-hexen-4-yne (**8**).—1,1-Dichloro-2,2-dimethyl-3-propylcyclopropane (**7**) produced two products when treated with base for 25 min. The major product (57%) was isolated by preparative glpc and identified as **8** by its nmr spectrum:[12] signals at δ 1.92 (s, 3 H, $-C\equiv CCH_3$), 1.7 (m, 6 H, isopropylidene), and 5.48 (m, 1 H, olefinic). A second product, obtained in impure form, is provisionally identified as 1-chloro-2,2-dimethyl-3-ethylidenecyclopropane on the basis of an nmr singlet at δ 3.28 (-CHCl-) and by analogy to the formation of 1-chloro-2,2-dimethyl-3-methylenecyclopropane from 1,1-dichloro-2,2,3-trimethylcyclopropane.[13]

1-Ethylidene-2-isopropenylcyclopropane (**17**) **and 1-Isopropylidene-2-vinylcyclopropane** (**18**).—1,1-Dichloro-2-ethyl-3-isopropylcyclopropane (**16**) produced **17** (56%) and **18** (16%) when treated with base: nmr (**17**) δ 1.2 (cyclopropyl), 1.6 (3 H isopropenyl methyl), 1.8 (3 H, ethylidene methyl) overlapping a multiplet extending to 2.3 (cyclopropyl) 4.65 (2 H, methylene), and 5.8 (q, 1 H, olefinic); nmr (**18**) δ 0.6–2.3 (3 H, cyclopropyl), 1.78 (6 H, isopropylidene), 4.5–5.7 (3 H, vinyl).

1-Isobutylidene-2-isopropenylcyclopropane (**20**) was produced in 48% yield from 1,1-dichloro-2-isobutenyl-3-isopropylcyclopropane: nmr δ 1.05 (6 H, isopropyl methyls), 0.8–2.2 (3 H, cyclopropyl), 1.58 (3 H, isopropenyl methyl), 2.5 (1 H, isopropyl), 4.65 (2 H, methylene), and 5.72 (1 H, olefinic).

Bicyclo[10.1.0]trideca-1,10-diene (**22**).—Addition of 13,13-dichlorobicyclo[10.1.0]tridecane (**21**) to KO-*t*-Bu-DMSO provided **22** in 94% yield: nmr δ ~1.1, 1.4, 1.15 (~17 H), 4.74–6.1 (3 H); ir (film) prominent absorptions at 6.17, 6.87, 7.0, 7.6, 10.2, and 13.9 μ.

Registry No.—**2**, 19995-92-7; **4**, 22703-93-1; **10**, 19985-76-3.

Acknowledgment.—W. E. B. gratefully acknowledges the Research Corporation for partial support of this work.

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[12] I. A. Favorskaya, E. M. Auvinene, and Y. P. Artsybasheva, *Zh. Obshch. Khim.*, **28**, 1785 (1958); *Chem. Abstr.*, **52**, 1097*i* (1958).

[13] T. C. Shields and W. E. Billups, *Chem. Ind.* (*London*), 1999 (1967).

The Vinyl Anion. II

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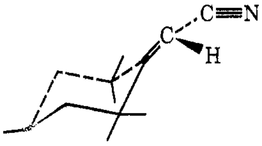
The exchange and racemization reactions of 2,2,4,6,6-pentamethylcyclohexylideneacetophenone (**1**) with sodium methoxide in methanol have been investigated. The ketone **1** exhibits only a moderate degree of retention of optical activity (30% at 50°), k_e/k_r = 1.43. This contrasts with the high degree of retention (>99% at 50°) observed with the corresponding 2,2,4,6,6-pentamethylcyclohexylideneacetonitrile (**2**). On the basis of primary hydrogen–deuterium and deuterium–tritium isotope effects, it is suggested that in both the base-catalyzed exchange and racemization reactions of **1** the rate-determining step is proton abstraction. Both (−)-**1** and its precursor (−)-2,2,4,6,6-pentamethylcyclohexylideneacetic acid [(−)-**3**] have been tentatively assigned the *R* configuration on the basis of their Cotton effects.

Recently this laboratory reported that the vinyl anion obtained by reaction of 2,2,4,6,6-pentamethylcyclohexylideneacetonitrile (**2**) with sodium methoxide in methanol was capable of maintaining its configuration (>99% retention at 50°). Moreover, based on the small kinetic isotope effect for the hydrogen isotope exchange reactions of **2**, it was proposed that proton abstraction was *not rate determining* in either the exchange or racemization reactions.[2]

These observations paralleled analogous data obtained in the investigation of the configurational stability of the cyclopropyl anion similarly derived from 1-cyano-2,2-diphenylcyclopropane (**4**) which indicated >99% retention at 50–75°.[3] In contrast to the behavior exhibited by the anion derived from **2** and **4**, however, the cyclopropyl anion generated from 1-benzoyl-2,2-diphenylcyclopropane (**5**) by base-catalyzed proton abstraction showed only moderate retention of optical activity (~27% retention at 75°). Further, the normal kinetic isotope effects observed in the isotope exchange reactions of **5** suggested that proton abstraction was rate limiting in both the exchange and racemization reactions.[4] This article presents our data on the rates of the sodium methoxide catalyzed exchange and racemization reactions of 2,2,4,6,6-pentamethylcyclohexylideneacetophenone (**1**).



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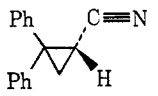

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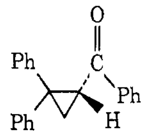

5

Results and Discussion

Synthesis.—The synthesis of racemic 2,2,4,6,6-pentamethylcyclohexylideneacetophenone is outlined in

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[1] National Science Foundation Predoctoral Fellow, 1970–1971; National Aeronautics and Space Administration Trainee, 1967–1970.

[2] H. M. Walborsky and L. M. Turner, *J. Amer. Chem. Soc.*, **94**, 2273 (1972).

[3] H. M. Walborsky and J. M. Motes, *ibid.*, **92**, 2445 (1970).

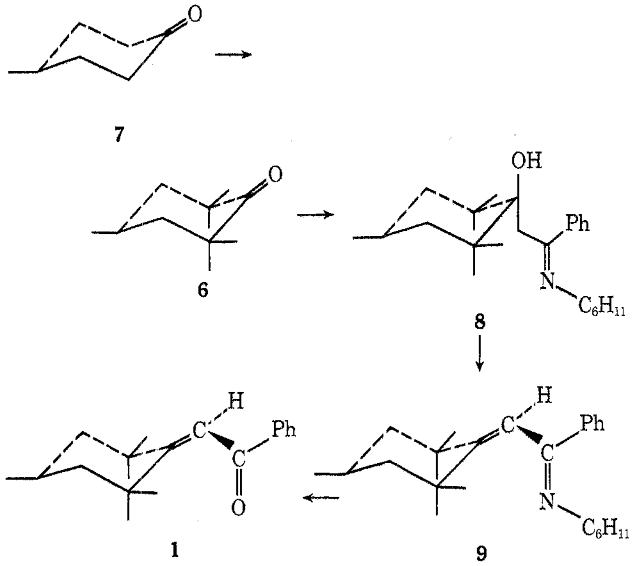
[4] J. M. Motes and H. M. Walborsky, *ibid.*, **92**, 3697 (1970).

Scheme I. The pentamethyl ketone **6** was obtained by a sodium hydride–methyl iodide alkylation of the commercially available 4-methylcyclohexanone (**7**).[5] Directed aldol condensation[6] of **6** with lithiated α-methylbenzylidene cyclohexylamine to yield the hydroxy imine **8** followed by dehydration with thionyl chloride–dimethylformamide gave the α,β-unsaturated imine **9**. Conversion of **9** to the desired acetophenone, **1**, was accomplished by refluxing with aqueous oxalic acid.

Scheme I

Synthesis of

2,2,4,6,6-Pentamethylcyclohexylideneacetophenone (1)

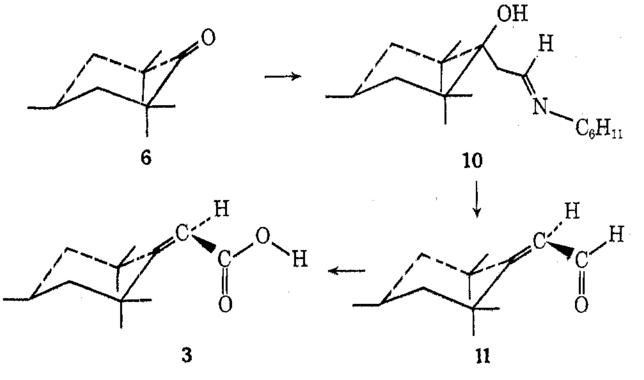


The optically active ketone, (−)-**1**, was obtained by treating (−)-2,2,4,6,6-pentamethylcyclohexylideneacetic acid with commercially available phenyllithium. The racemic acid was synthesized as in Scheme II.[7] Directed aldol condensation[6] of pentamethyl ketone **6** with lithiated ethylidenecyclohexylamine followed by steam distillation of the resulting hydroxy imine **10** from aqueous oxalic acid yielded the α,β-unsaturated aldehyde **11**.[2] Oxidation of **11** with silver oxide[8] gave racemic **1**, which was resolved through its brucine salt.[2]

Scheme II

Synthesis of

2,2,4,6,6-Pentamethylcyclohexylideneacetic Acid (3)



(−)-**1** has tentatively been assigned the *R* configuration on the basis of a comparison of the Cotton effects of its acid precursor (−)-**3**, and (−)-(*R*)-4-methylcyclohexylideneacetic acid,[9] (−)-**12** (Table I). The absolute configuration of (−)-**12** has been previously established by Gerlach[9] by means of a chemical correlation.

Table I

ORD–CD Data for

(−)-2,2,4,6,6-Pentamethylcyclohexylideneacetic Acid and (−)-4-Methylcyclohexylideneacetic Acid

Compd		Data
(−)-**1**	ORD	$[\alpha]_{220}^{25}$ −218.2 (*c* 1.34, MeOH)
	CD	$\Delta\epsilon_{243}^{25}$ + 3.12, $\Delta\epsilon_{208}^{25}$ −6.98 (*c* 1.34, MeOH)
(−)-(*R*)-**12**	ORD	Negative plain rotatory dispersion curve (MeOH)
	CD	$\Delta\epsilon_{280}^{25}$ +0.0103, $\Delta\epsilon_{226}^{25}$ −3.08 (EtOH)

The increased signal intensity observed for (−)-**1** relative to (−)-**12** is thought to be caused by increased steric distortion of the symmetry of the π-electron cloud upon introduction of additional methyl substituents into the cyclohexyl ring.[10]

The deuterated (**1**-*d*) and tritiated ketones (**1**-*t*) were synthesized by successive treatment of the protio ketone with sodium methoxide in methanol-*d* (-*t*), respectively.

Exchange and Racemization Rates.—The kinetic methods used are described in the Experimental Section. The second-order rate constants (Table II) were determined by dividing the pseudo-first-order rate constants by the base concentration. The first-order rate plots yielded straight lines in all cases studied.

Table II

Second-Order Rate Constants for the Exchange and Racemization Reactions of 2,2,4,6,6-Pentamethylcyclohexylideneacetophenone[a]

Reaction	Solvent	Temp, °C	k_2,[b] l. mol^{-1} sec^{-1}
H → D	MeOD	50.00 ± 0.01	8.80 ± 0.01 × 10^{-4}
D → H	MeOH	50.00 ± 0.01	6.75 ± 0.04 × 10^{-5}
T → H	MeOH	50.00 ± 0.01	3.55 ± 0.01 × 10^{-5}
H → D	MeOD	10.20 ± 0.10	1.21 ± 0.02 × 10^{-6}
D → H	MeOH	10.20 ± 0.10	7.93 ± 0.02 × 10^{-7}
T → H	MeOH	10.20 ± 0.10	3.42 ± 0.01 × 10^{-7}
Racemization	MeOD	50.00 ± 0.01	6.15 ± 0.01 × 10^{-4}
Racemization	MeOH	50.00 ± 0.01	2.90 ± 0.01 × 10^{-4}

[a] 1.0 *M* $NaOCH_3$; 0.05 *M* ketone. [b] Average rate constant ± standard deviation.

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[5] A. Haller, *C. R. Acad. Sci.*, **167**, 737 (1921).

[6] G. Wittig and H. Reiff, *Angew. Chem., Int. Ed. Engl.*, **7**, 7 (1968).

[7] See ref 2 for an alternative synthesis.

[8] A. Calieze and H. Schinz, *Helv. Chim. Acta*, **32**, 2556 (1949).

[9] The ORD–CD data for (−)-(*R*)-4-methylcyclohexylideneacetic acid were kindly supplied by Professor H. Gerlach, Erdg. Technische Hochscule, Zurich, Switzerland; see also H. Gerlach, *ibid.*, **49**, 6718 (1966).

[10] G. Snatzke, *Angew. Chem., Int. Ed. Engl.*, **7**, 14 (1968).

Exchange Reactions.—A general mechanism for the exchange reactions of a carbon acid may be written as that in eq 1.[2–4]

$$\mathrm{RH} + \mathrm{B}^- \underset{k_{-1}\mathrm{H}}{\overset{k_1\mathrm{H}}{\rightleftharpoons}} \mathrm{R}^-\cdots\mathrm{HB} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \mathrm{R}^-\cdots\mathrm{DB} \underset{k_{-1}\mathrm{D}}{\overset{k_1\mathrm{D}}{\rightleftharpoons}} \mathrm{RD} + \mathrm{B}^- \quad (1)$$

The rate law for the formation of the exchanged (deuterated) carbon acid is then given, under the experimental conditions of this work, by

$$k_{\mathrm{exptl}} = \frac{k_1 k_2}{k_{-1} + k_2} \quad (2)$$

For those reactions predominated by internal return, *i.e.*, $k_{-1} \gg k_2$, this expression simplifies to

$$k_{\mathrm{exptl}} = Kk_2 \quad (3)$$

where K is the equilibrium proton abstraction–recapture equilibrium constant. On the other hand, if proton abstraction is rate limiting, *i.e.*, $k_2 \gg k_{-1}$, eq 2 reduces to

$$k_{\mathrm{exptl}} = k_1 \quad (4)$$

Mechanisms typified by rate expressions eq 2 and 3 may be differentiated from that typified by eq 4 by the magnitude of primary kinetic isotope effects. Rate-limiting proton transfer will exhibit a normal primary isotope effect, while internal return and mixed or competitive mechanisms (*i.e.*, $k_1 \sim k_2$) will exhibit small kinetic effects in the absence of media and steric effects.[11] The experimentally observed kinetic isotope effects, uncorrected for solvent effects, are presented in Table III for the exchange reactions of 2,2-4,6,6-pentamethylcyclohexylideneacetophenone (**1**).

TABLE III

UNCORRECTED ISOTOPE EFFECTS[a]

Temp, °C	$k_{\mathrm{H}}{}^{\mathrm{MeOD}}/k_{\mathrm{D}}{}^{\mathrm{MeOH}}$	$k_{\mathrm{D}}{}^{\mathrm{MeOH}}/k_{\mathrm{T}}{}^{\mathrm{MeOH}}$
50.00 ± 0.01	13.0 ± 0.1	1.90 ± 0.08
10.20 ± 0.10	15.2 ± 0.2	2.32 ± 0.02

[a] 1.0 M $NaOCH_3$; 0.05 M ketone.

Theoretically, T, D, and H isotope effects are interrelated by

$$\left(\frac{k_{\mathrm{H}}}{k_{\mathrm{D}}}\right) = \left(\frac{k_{\mathrm{D}}}{k_{\mathrm{T}}}\right)^x \quad (5)$$

where $x = 2.26$ or 2.344.[12] Applying eq 5 to the data in Table III, we calculate from the T and D exchange data that at 50° $k_{\mathrm{A}}/k_{\mathrm{D}} = 4.3$–4.5. These values contrast with the experimentally determined ratio $k_{\mathrm{H}}{}^{\mathrm{MeOD}}/k_{\mathrm{D}}{}^{\mathrm{MeOH}} = 13.0$, suggesting the presence of a solvent isotope effect $k^{\mathrm{MeOD}}/k^{\mathrm{MeOH}} = 3.0$–2.9. This hypothesis is supported by the presence of an experimentally observed isotope effect in the racemization reactions $k_{\mathrm{rac}}^{\mathrm{MeOD}}/k_{\mathrm{rac}}^{\mathrm{MeOH}} = 2.12$. Moreover, solvent isotope effects of similar magnitude have been reported previously for this solvent system.[12b,13] These solvent isotope effects may be attributed to the weakening of the solvent–methoxide hydrogen bond and the increasing vibrational frequency of the oxygen–hydrogen (deuterium) bond as reaction progresses.[14] This view is supported by the recent work of Gold and Grist.[15]

The calculated $k_{\mathrm{H}}/k_{\mathrm{D}}$ values are presented in Table IV. All of these values lie in the normal high range indicative of substantial proton transfer at the transition state. Further, the magnitude of the primary isotope effect increases with decreasing temperatures, as would be expected for rate-limiting proton abstraction.[11]

TABLE IV

CALCULATED ISOTOPE EFFECTS[a]

Temp, °C	$(k_{\mathrm{D}}/k_{\mathrm{T}})^{2.26}$	$(k_{\mathrm{D}}/k_{\mathrm{T}})^{2.344}$
50.00 ± 0.01	4.3	4.5
10.20 ± 0.10	6.7	7.2

[a] 1.0 M $NaOCH_3$; 0.05 M ketone.

A mechanism consistent with rate-determining proton transfer is presented in Scheme III and is analogous to the scheme proposed for the cyclopropyl ketone **2**.[4] The first step involves the removal of the acidic proton by the active base, methoxide ion hydrogen bonded to one or more methanol molecules to form a hydrogen-bonded carbanion (k_1). Once the hydrogen-bonded carbanion is formed, the solvent exchange reactions (k_2 or k_3, k_4) occur in competition with the back reaction (k_{-1}) with the observed primary kinetic isotope effect requiring that $k_{-1} < k_2$ (k_3, k_4).

Racemization Reaction.—The data in Table I show that the reaction of (−)-**1** with sodium methoxide occurs with only a moderate degree (30%) of retention of optical activity, $k_{\mathrm{e}}/k_{\mathrm{r}} = 1.43$. This degree of retention of optical activity corresponds to 65% retention of configuration and 35% inversion. A possible reaction scheme is illustrated in Scheme IV, where S–OH signifies an aggregrate of hydrogen-bonded solvent molecules. The retention of optical activity is attributed to an internal return mechanistic component with racemization most probably occurring through the delocalized, planar carbanion.

As in the work with the vinyl nitrile, the observed $k_{\mathrm{e}}/k_{\mathrm{r}}$ ratio is not consistent with an addition–elimination mechanism such as that illustrated in Scheme V. In the absence of isotope effects the exchange rate for such a mechanism at the most would be only half as fast as the rate of racemization. Moreover, the

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(11) For an excellent review of isotope effects see (a) W. P. Jencks, "Catalysis in Chemistry and Enzymology," McGraw-Hill, New York, N. Y., 1969, Chapter 4, and references cited therein; (b) L. Melander, "Isotope Effects on Reaction Rates," Ronald Press, New York, N. Y., 1960. See also F. G. Bordwell and W. J. Boyle, *J. Amer. Chem. Soc.*, **93**, 512 (1971), and references cited therein.

(12) (a) C. G. Swain, E. C. Stivers, J. F. Reuwer, Jr., and L. J. Schaad, *ibid.*, **80**, 5885 (1958); (b) A. Streitwieser, Jr., W. B. Holyhead, A. H. Pudjaatmaka, P. H. Owens, T. L. Kruger, P. A. Rubenstein, R. A. MacQuarrie, M. L. Brokaw, W. K. C. Chu, and H. M. Niemeyer, *ibid.*, **93**, 5088 (1971).

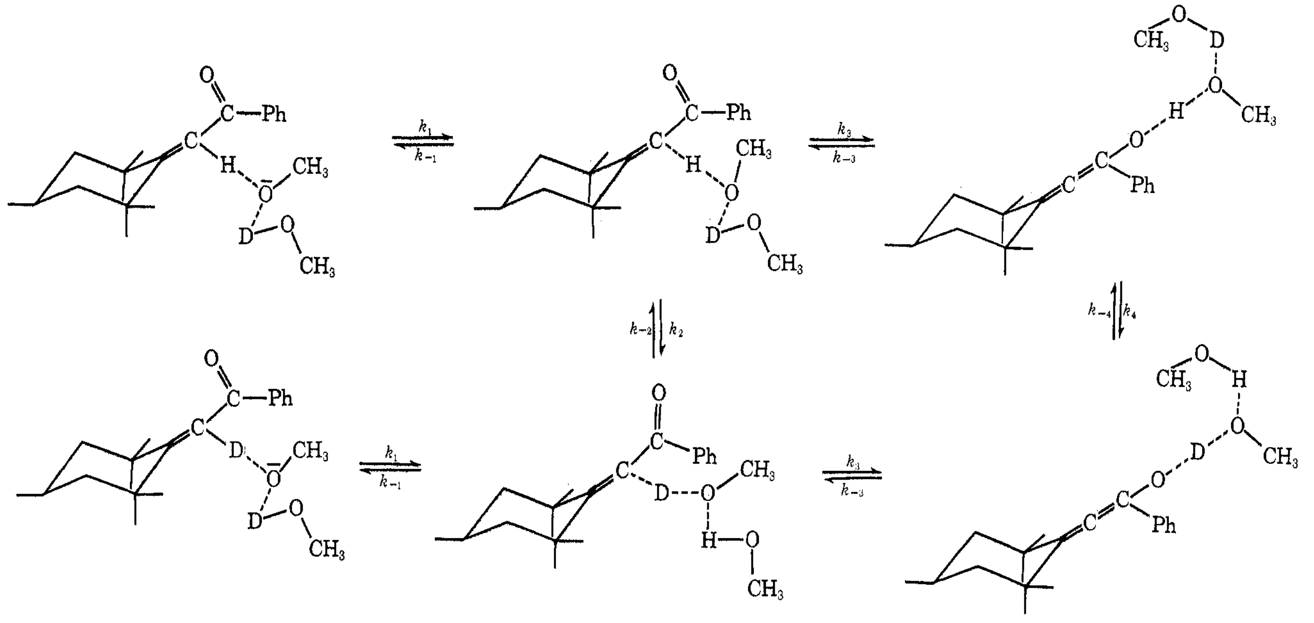
(13) (a) D. J. Cram, and R. T. Uyoda, *ibid.*, **86**, 544 (1964); (b) S. W. Ela and D. J. Cram, *ibid.*, **88**, 5791 (1966); (c) S. Andreades, *ibid.*, **86**, 2003 (1964).

(14) (a) C. A. Bunton and V. J. Shiner, Jr., *ibid.*, **83**, 3207 (1953); (b) P. M. Laughton and R. E. Robertson in "Solute–Solvent Interactions," J. F. Coetzee and C. D. Ritchie, Ed., Marcel Dekker, New York, N. Y., 1969, Chapter 7.

(15) V. Gold and S. Grist, *J. Chem. Soc. B*, 1665, 2272, 2282, 2285 (1971).

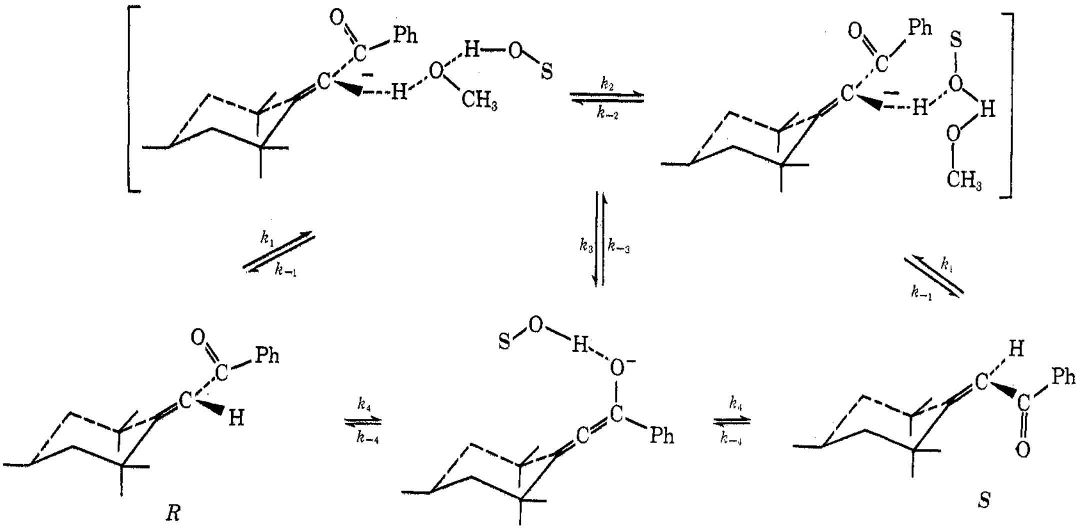
SCHEME III

EXCHANGE MECHANISM FOR 2,2,4,6,6-PENTAMETHYLCYCLOHEXYLIDENEACETOPHENONE (1)



SCHEME IV

RACEMIZATION MECHANISM FOR 2,2,4,6,6-PENTAMETHYLCYCLOHEXYLIDENEACETOPHENONE (1)



steric hindrance at the β carbon of the double bond minimizes the probability of addition.[16]

Comparison of Nitrile and Ketone.—Both the racemization and exchange data for the ketone **1** contrast sharply with that for the analogous nitrile **2**. The cause of this divergent behavior most likely lies in the differing acidities of the two compounds and the relative stabilities of the delocalized carbanions. Carbon acids stabilized by the carbonyl group are usually several pK_a units more acidic and have smaller recombination rates than those stabilized by cyano groups.[17] Moreover, the increased delocalization possible in the benzoyl ketone due to the phenyl ring shifts the equilibrium between the nonplanar localized and planar delocalized carbanion toward the planar anion relative to the equilibrium position in the nitrile system. The result is an increase in the rate of exchange ($k_{\text{H}\rightarrow\text{D}}^{\text{ketone}} \cong 100k_{\text{H}\rightarrow\text{D}}^{\text{nitrile}}$) and a shift in the stereochemical course of the reaction.

Direct comparison of the stereochemical stability of the cyclopropyl and vinyl ketones **1** and **5** is not possible because exchange and racemization data were not obtained under identical conditions. The close parallel between the behavior of the ketone and nitrile compounds in each of the two systems, however, makes an indirect comparison possible. In both the cyclopropyl and vinyl systems[2] the exchange reaction for the ketones proceeds with carbon–hydrogen bond breaking being rate determining. Further, in both systems the nitrile retains its configuration while under the same conditions the ketones undergo considerable racemization.[2-4]

Direct comparison of the exchange–racemization data for the nitriles shows that the cyclopropyl nitrile,

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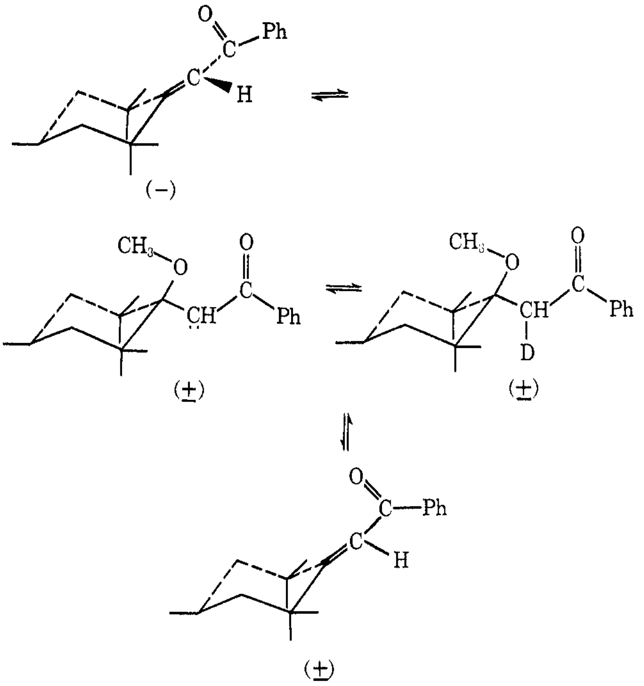
[16] For a discussion of the problem of the addition–elimination mechanism in evaluation of the stereochemical stability of the vinyl anion, see ref 2.

[17] (a) R. G. Pearson and R. L. Dillon, *J. Amer. Chem. Soc.*, **75**, 2439 (1955); L. A. Cohn and W. M. Jones, *ibid.*, **85**, 337, 3402 (1963).

SCHEME V

ADDITION–ELIMINATION MECHANISM FOR 2,2,4,4,4-PENTAMETHYLCYCLOHEXYLIDENEACETOPHENONE (1)



because of ring strain, is configurationally more stable than the analogous vinyl compound.[2] The close parallel in the internal behavior of the systems argues that the cyclopropyl ketone will likewise exhibit greater configurational stability than the analogous vinyl compound under identical conditions.

Experimental Section

Melting points were measured with a Mel-Temp apparatus and both melting and boiling points are uncorrected. Infrared spectra were determined using a Perkin-Elmer Model 257 spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian A-60 or Bruker 90-MHz spectrophotometer; chemical shifts are reported in parts per million downfield from tetramethylsilane and coupling constants are in hertz. Low-resolution mass spectra were obtained on a Nuclide electron impact mass spectrometer, and high-resolution mass spectra were obtained on an Associated Electronics Industries MS902 instrument. All mass spectra gave parent ions consistent with the expected molecular weight. Tritium counts were obtained with a Packard Tricarb liquid scintillation counter. Optical rotatory and circular dichroism spectra were recorded with a JASCO-5 and optical rotations at 5461 Å with a Bendix-Ericson Model 143A polarimeter. Microanalyses were performed by the Beller Laboratories, Gottingen, Germany.

Solvents.—Methyl alcohol-*t* (9800 cpm/mg) was prepared by the method of Streitwieser.[18] Methyl alcohol-*d* (>99.9% isotopically pure) was purchased from Diaprep. The deuterated and tritiated methanol were dried by distillation from a small amount of sodium, and reagent grade methanol was dried by distillation from magnesuim.

Stock base solutions of 1.0 *N* sodium methoxide in methanol (-*d*,-*t*) were prepared by adding a weighed amount of clean sodium metal to the anhydrous alcohol at −78° under an argon atmosphere. After all the sodium metal had reacted, the solution was allowed to warm to room temperature and transferred to a volumetric flask, which was diluted to the mark with anhydrous methanol. The stock solution was standardized with hydrochloric acid.

Exchange Method.—The stock solutions were prepared in volumetric flasks by adding the stock base solutions to a weighed amount of the vinyl compound. These solutions were shaken until all of the vinyl compound was dissolved. Portions (5 ml) were removed with a syringe and transferred to Pyrex screw cap vials with Teflon liners which were then placed in a constant-temperature bath at the appropriate temperature. Each tube was removed after a predetermined time and quenched in a Dry Ice–acetone bath before opening. The samples were acidified with dilute hydrochloric acid and extracted with pentane. The pentane extracts were combined and washed with 5% sodium bicarbonate solution and three portions of water. The pentane solution was dried over sodium sulfate and evaporated.

Quantitative Nuclear Magnetic Resonance Analysis.—For the hydrogen and deuterium exchange samples, the residue obtained above was dissolved in Spectrograde carbon tetrachloride containing tetramethylsilane as an internal standard and submitted to nmr analysis. The analysis was performed by integrating the phenyl and vinyl regions five times and averaging the areas obtained to determine the relative per cent deuterium in the sample. Excellent first-order rate plots were obtained and the first-order rate constants were determined by a least-squares fit of the experimental data. Second-order rate constants were calculated by dividing the first-order rate constants by the base concentration.

Radioactive Counting.—The relative tritium concentrations of kinetic samples were determined by scintillation counting. The unknown ketone was carefully weighed into a counting vial and 15.0 ml of the scintillation fluid [50 mg of 1,4-2-(5-phenyloxazoyl)-benzene and 4 g of 2,5-diphenyloxazole per liter of toluene] was added. The vial was capped, shaken to ensure solution, and placed in the scintillation counter. Two 2-min counts were taken after thermal equilibration of the sample. After adjustments were made for background radiation and quenching, the activity of the sample was determined.

Racemization Kinetics.—The rate of racemization of the ketone was determined directly on the reaction mixture by following the change in ellipticity of the sample with time using the JASCO-5. A 1.003-mm thermostated cell was used and the ellipticity was observed at 340 μ. The rate constants for the racemization and exchange reactions are listed in Table II.

2,2,4,6,6-Pentamethylcyclohexanone (6).—To a stirred suspension of 126 g of sodium hydride dispersion (57% in mineral oil) in 900 ml of dry dimethoxyethane (DME) at 0° under nitrogen was added a solution of 67.2 g (0.600 mol) of 4-methylcyclohexanone in 50 ml of dry DME. After 30 min, 250 ml of a solution of 426 g (3.00 mol) of methyl iodide in 750 ml of dry DME was added dropwise over a period of 12 hr. The reaction mixture was allowed to stir overnight at 0° and the addition sequence was repeated until all the methyl iodide solution had been added. The reaction mixture was then allowed to come to room temperature and stirred for an additional 24 hr. Water was added dropwise until hydrogen gas evolution ceased and the reaction mixture was poured onto ice, diluted with water, and extracted with five 200-ml portions of pentane. The combined pentane extracts were washed with saturated sodium chloride solution and dried over anhydrous sodium sulfate. Removal of the solvent under reduced pressure followed by distillation through a spinning band column gave 85.5 g (0.510 mol, 85.0%) of 2,2,4,6,6-pentamethylcyclohexanone: bp 68° (13 mm), 194–195° (760 mm) [lit.[1,8] bp 68° (13 mm)], ir (neat) 1700 ($C{=}O$), 1385 and 1370 cm^{-1} (*gem*-dimethyl).

***N*-α-Methylbenzylidenecyclohexylamine.**—*N*-α-Methylbenzylidenecyclohexylamine was prepared following the procedure of Tiollais.[19]

***N*-Cyclohexyl α-(1-Hydroxy-2,2,4,6,6-pentamethylcyclohexyl)-acetophenone Imine** (8).—To a stirred solution of 10.1 g (0.100 mol) of diisopropylamine in 50 ml of anhydrous ether at −10° under nitrogen was slowly added 55 ml of 2 *M* methyllithium in ether (Foote Chemical Co.). After the mixture was stirred for 15 min at −10° a solution of 20.1 g (0.100 mol) of *N*-α-methylbenzylidenecyclohexylamine in 20 ml of anhydrous ether was added and the reaction mixture was stirred for 10 min at 0°. The temperature was lowered to −70° and 16.8 g (0.100 mol) of 2,2,4,6,6-pentamethylcyclohexanone in 50 ml of dry ether was added dropwise. When the addition was completed, the reaction mixture was allowed to come to room temperature and was stirred for 1 hr. The reaction mixture was poured onto ice and extracted with three 50-ml portions of ether. The extracts were combined, washed with saturated sodium chloride solution, and

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[18] A. Streitwieser, Jr., L. Verbit, and P. Stang, *J. Org. Chem.*, **29**, 3706 (1964).

[19] R. Tiollais, *Bull. Soc. Chim. Fr.*, **14**, 708 (1947).

dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the crude product was recrystallized from low-boiling petroleum ether to yield 22.1 g (0.600 mol, 60.0%) of hydroxy imine **8**: mp 73.0–75.0; ir (CCl_4) 3200 (OH), 1650 (C═N), 1395 and 1382 (*gem*-dimethyl), 1240 cm^{-1} (CO); nmr (CCl_4) δ 7.3–7.1 (m, 5 H), 2.6 (s, 2 H), 1.8–0.8 (m, 31 H).

Anal. Calcd for $C_{25}H_{39}NO$: C, 81.31; H, 10.57; N, 3.79. Found: C, 81.20; H, 10.54; N, 3.70.

***N*-Cyclohexyl α-(2,2,4,6,6-Pentamethylcyclohexylidene)acetophenone Imine** (**9**).—To a solution of 2 ml of *N*,*N*-dimethylformamide in 10 ml of thionyl chloride at 0°, under nitrogen, was added 1.00 g (2.72 mmol) of **8**. After the reaction mixture was stirred for 1 hr at room temperature, it was poured onto ice and diluted with water. Solid sodium carbonate was added until carbon dioxide was no longer evolved and the reaction mixture was extracted with three 10-ml portions of pentane. The extracts were combined, shaken with water and 10% sodium bicarbonate solution, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the crude product was recrystallized from *N*,*N*-dimethylformamide to give 0.700 g (2.00 mmol, 73.5%) of **9**: mp 81.0–81.5°; ir (CCl_4) 3045 (OH), 1680 (C═N), 1625 (C═C), 1382, and 1370 cm^{-1} (*gem*-dimethyl); nmr (CCl_4) δ 8.0–7.0 (m, 4 H), 5.9 (s, 1 H), 2.3–0.7 (m, 31 H).

Anal. Calcd for $C_{25}H_{37}N$: C, 85.41; H, 10.61; N, 3.98. Found: C, 85.41; H, 10.71; H, 3.91.

2,2,4,6,6-Pentamethylcyclohexylideneacetophenone (**1**).—A mixture of 36.9 g (100 mmol) of **9** and 25.2 g (200 mmol) of oxalic acid dihydrate in 200 ml of water was refluxed for 36 hr. The reaction mixture was cooled and extracted with three 50-ml portions of pentane. The pentane extracts were combined, washed with 10% sodium carbonate solution and saturated sodium chloride solution, and then dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the crude product was distilled to give 32.4 g (120 mmol, 60.0%) of 2,2,4,6,6-pentamethylcyclohexylideneacetophenone: bp 120° (0.025 mm); ir (neat) 1670 (C═O), 1620 (C═C), 1385 and 1370 cm^{-1} (*gem*-dimethyl); nmr (CCl_4) δ 8.0–7.2 (m, 4 H), 5.35 (s, 1 H), 1.8–0.7 (m, 20 H).

Anal. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69. Found: C, 84.51; H, 9.80.

Ethylidenecyclohexylamine.—Ethylidenecyclohexylamine was prepared following the procedure of Tiollais.[19]

2,2,4,6,6-Pentamethylcyclohexylideneacetaldehyde (**11**).—To a stirred solution of 1.01 g (0.100 mol) of diisopropylamine in 50 ml of anhydrous ether at −10°, under nitrogen, was slowly added 50 ml of 2.0 *M* methyllithium in ether (Foote Chemical Co.). After the mixture was stirred for 15 min at −10° a solution of 12.5 g (0.100 mol) of ethylidenecyclohexylamine, bp 47.5–48.5°, in 20 ml of ether was added and the reaction mixture was stirred for 10 min at 0°. The temperature was lowered to −70° and 16.8 g (0.100 mol) of 2,2,4,6,6-pentamethylcyclohexanone in 50 ml of anhydrous ether was added dropwise. When the addition was completed, the solution was allowed to come to room temperature and stirred for 1 hr. The reaction mixture was poured onto ice and extracted with three 50-ml portions of pentane. The extracts were combined, shaken with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure to yield 28.5 g (92.0 mmol, 92.0%) of crude adduct: ir (neat) 3300 (OH), 1710 (C═N), 1380 and 1375 (*gem*-dimethyl), 1200 cm^{-1} (CO); nmr (CCl_4) δ 8.2 (t, 1 H), 4.9 (s, 1 H), 2.5 (d, 2 H), 2.2–0.8 (m, 31 H). The crude hydroxy imine adduct was hydrolyzed upon steam distillation from oxalic acid to yield 18.1 g (90.0 mmol, 90.0%) of 2,2,4,6,6-pentamethylcyclohexylideneacetaldehyde: ir (neat) 1670 (C═O), 1595 (C═C), 1385 and 1370 (*gem*-dimethyl), 1225 cm^{-1} (CO); nmr (CCl_4) δ 6.07 (d, 1 H, J = 8.0 Hz), 2.1–0.8 (m, 20 H). Ir and nmr are identical with those reported in the literature.[2]

2,2,4,6,6 Pentamethylcyclohexylideneacetic Acid (**3**).—To a solution of 15.5 g (80.0 mmol) of 2,2,4,6,6 pentamethylcyclohexylideneacetaldehyde in 36.0 ml of ethanol was added a solution of 28.0 g (0.170 mol) of silver nitrate dissolved in the minimum amount of water. The mixture was cooled with stirring to −10° and a solution of 16.8 g (0.300 mol) of potassium hydroxide in 280 ml of water was added at a rate such that the temperature was maintained between 0 and 10°. The reaction mixture was then *vigorously* stirred at room temperature for 2 weeks and decanted, and the precipitate was washed with hot water. The decanted solution and washings were combined and extracted with three 50-ml portions of ether. The ether extracts were combined, washed with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. Evaporation of the solvent under reduced pressure gave 6.00 g (31.0 mmol) of unreacted aldehyde. Acidification of the aqueous solution obtained above, followed by extraction with three 50-ml portions of pentane, drying over sodium sulfate, evaporation of solvent, and recrystallization of the crude product from methanol–water gave 6.50 g (31.0 mmol, 39.0%) of 2,2,4,6,6-pentamethylcyclohexylideneacetic acid: mp 91–93° (lit.[3] mp 91–93°); ir (neat) (CCl_4) 3500 (OH), 1690 (C═O), 1620 (C═C), 1382 and 1368 cm^{-1} (*gem*-dimethyl); nmr (CCl_4) δ 12.0 (s, 1 H), 5.77 (s, 1 H), 2.0–0.8 (m, 20 H). Ir and nmr were identical with those reported in the literature.[2]

(−)-2,2,4,6,6-Pentamethylcyclohexylideneacetophenone.—To a solution of 20.0 g (95.0 mmol) of (−)-2,2,4,6,6-pentamethylcyclohexylideneacetic acid in anhydrous ethyl ether, $[\alpha]^{24}_{5461}$ −60.3 ± 0.3 (*c* 5.0, $CHCl_3$), at ambient temperature was added over a 30-min period 13.6 ml of 2.2 *M* phenyllithium in benzene–ether (Foote Chemical Co.). Stirring was continued for 1 hr, after which the reaction mixture was hydrolyzed by pouring it into an ice-cold saturated ammonium chloride solution which was extracted with three 10-ml portions of ether. The extracts were combined, shaken with water and saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The solvent was removed under reduced pressure and the residue was distilled to yield 1.89 g (6.80 mmol, 70.0%) of (−)-2,2,4,6,6-pentamethylcyclohexylideneacetophenone, $[\alpha]^{24}_{5461}$ −47.0 ± 0.3 (*c* 5.0, $CHCl_3$). Boiling points, ir, nmr, and mass spectra were identical with those of the racemic ketone.

Anal. Calcd for $C_{19}H_{26}O$: C, 84.39; H, 9.69. Found: C, 84.53; H, 9.68.

α-Deuterio-2,2,4,6,6-Pentamethylcyclohexylideneacetophenone (**1**-*d*).—A 1.0 *N* solution of sodium methoxide in methanol-*d* (10 ml) was added *via* syringe to a culture tube containing 1.00 g (3.70 mmol) of 2,2,4,6,6-pentamethylcyclohexylideneacetophenone. The tube was flushed with nitrogen, fitted with a Teflon-lined cap, and placed in an oil bath at 90° for 24 hr. The tube was removed from the bath and cooled to 0°, 1 ml of deuterium oxide was added, and the resulting solution was extracted with three 5-ml portions of pentane. The pentane extracts were combined, shaken with saturated sodium chloride solution, and dried over anhydrous sodium sulfate. The pentane was removed under reduced pressure and the residue was distilled to give 0.750 g (2.80 mmol, 75.0%) of α-deuterio-2,2,4,6,6-pentamethylcyclohexylideneacetophenone, which was shown by nmr analysis to have 99% deuterium in the α position: bp 120° (0.025 mm); ir (neat) 1670 (C═O), 1605 (C═C), 1385 and 1370 cm^{-1} (*gem*-dimethyl); nmr (CCl_4) δ 8.0–7.2 (m, 4 H), 1.8–0.7 (m, 20 H).

α-Tritio-2,2,4,6,6-pentamethylcyclohexylideneacetophenone (**1**-*t*).—α-Tritio-2,2,4,6,6-pentamethylcyclohexylideneacetophenone was prepared in a manner exactly analogous to the preparation of the α-deuterio-2,2,4,6,6-pentamethylcyclohexylideneacetophenone above, yield 75%, 271 cpm/mg.

Registry No.—**1**, 35740-80-8; (−)-**1**, 35820-70-3; **1**-*d*, 35740-81-9; **1**-*t*, 35820-71-4; **3**, 35820-72-5; **6**, 29668-29-9; **8**, 35740-39-7; **9**, 35867-15-3.

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