trans-Di-*tert*-butylcyclopropanone. Preparation, Properties, Resolution, and Reaction with Nucleophiles[1]

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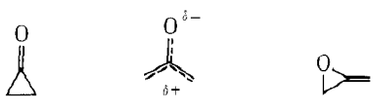
trans-Di-*tert*-butylcyclopropanone (1) has been prepared by reaction of potassium *tert*-butoxide with α-bromodineopentyl ketone. Partial resolution has been effected by reaction with *d*-amphetamine and with diisopinylcampheylborane. Reaction of 1 with water affords the hydrate (rates and equilibrium constants are reported in Table I). Reaction of 1 with alcohols affords the hemiketals, isolable for primary alcohols (relative rates of formation of hemiketals in alcohol solution at 25° follow: methanol, 90; ethanol, 20; isopropyl alcohol, 1; *tert*-butyl alcohol, 0). The rate of reversion of the methanol hemiketal to 1 in methanol has been determined by use of deuterium-labeled hemiketal. Under basic conditions the hemiketals are converted to the ring-opened Favorskii ester **2**, under acidic conditions to α-alkoxy ketone **3**. Reaction of 1 with potassium *tert*-butoxide in *tert*-butyl alcohol-*O*-*d* affords ester 3 of deuterium content d_0 3%, d_1 50%, d_2 31%, d_3 16%, pointing to some attack at α hydrogen. The cyclopropanone is stable to oxygen; the hydrate and hemiketals are not.

The cyclopropanone functionality has been an elusive one. Considerable interest attaches to this class, however, because of the possible breadth of reactions associated with the carbonyl group in a three-membered ring and the synthetic relevance to the Favorskii reaction. Cyclopropanones might be expected to possess three points of reactivity: (1) the carbonyl group, (2) the hydrogens α to the carbonyl group, and (3) the C-2–C-3 bond. The possibility of reactivity of C-2–C-3 is associated with the question of small-ring valence isomerization of the type shown in eq 1.



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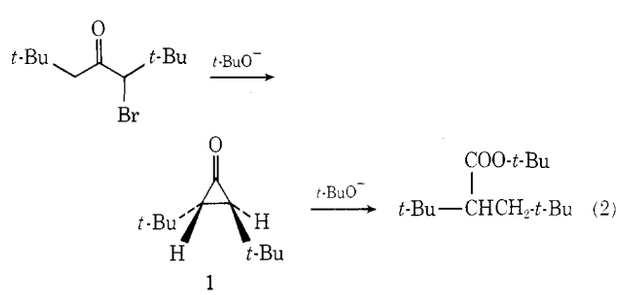
Various aspects of cyclopropanone reactions have been examined and reviewed[2] over the past few years, primarily with cyclopropanones containing small substituents. The high reactivity of these cyclopropanones has precluded isolation and has often involved special methods of preparation.[2a,3] In 1967 we reported the preparation of *trans*-di-*tert*-butylcyclopropanone,[4a] an isolable cyclopropanone of moderate stability. In this and following papers[5] we describe the preparation, properties, and a number of reactions of this cyclopropanone.

Preparation and Properties. *trans*-Di-*tert*-butylcyclopropanone may be prepared by the action of potassium *tert*-butoxide on α-bromodineopentyl ketone. The reaction may be carried out heterogeneously in ether or homogeneously in *tert*-butyl alcohol (eq 2). The latter case corresponds to conditions of the Favorskii reaction.[6] Use of 1 equiv of base affords the cyclopropanone; use of even a small excess of base results in complete conversion to the ester. Assignment of the trans structure, originally made



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on nmr evidence of the hemiketal from benzyl alcohol,[4] is confirmed by the partial resolution of the cyclopropanone (see below).

Chart I

Physical Data for *trans*-Di-*tert*-butylcyclopropanone (1)

mp 24–26°, bp 75–77° (20 mm)
d 0.8380 (26°)
^{1}H nmr (CCl_4) 0.96 (s, 18 H), 1.55 (s, 2 H)
^{13}C nmr (CS_2, downfield from TMS) 28.4 (CH_3), 30.1 [$C(CH_3)_3$], 30.8 (C_2 and C_3), 215.2 ppm (C_1)
ir (CCl_4) 1822 cm^{-1}
uv (isooctane) λ_{max} 354 nm (ε 33)
RD and CD (0.053 *M* in isooctane at 25°; values are for a sample of ~9% optical purity)
RD $[\Phi]_{450}$ +96°, $[\Phi]_{400}$ +221°, $[\Phi]_{373}$ +530°, $[\Phi]_{328}$ −483°, $[\Phi]_{285}$ −267°
CD $[\theta]_{396}$ 0°, $[\theta]_{354}$ +870°, $[\theta]_{285}$ 0°; bandwidth at half-maximum 41 nm
Major species in mass spectrum at 70 eV: *m/e* (rel intensity) 168 (1.7, molecular ion), 125 (75), 83 (100), 70 (90), 69 (91), 57 (90), 55 (90), 41 (90)

The n → π* maximum at 354 nm is at considerably longer wavelength than that for other ketones (cyclobutanone, 290 nm;[7a] cyclohexanone, 285 nm;[7b] tetrapropylcyclohexanone, 310 nm),[7b] and indeed somewhat longer than other cyclopropanones (cyclopropanone, 310 nm; tetramethylcyclopropanone, 340 nm).[2a] The ^{13}C nmr shows the carbonyl carbon at 215.2 ppm (downfield from TMS)[7c] *vs.* cyclopropenone C-1 155.1, C-2 158.3,[8] cyclobutanone 208.2,[9] cyclopentanone 213.9 ppm.[9]

The cyclopropanone 1 has been partially resolved by asymmetric destruction with *d*-amphetamine.[4b] The RD and CD values are summarized in Chart I. The degree of optical purity was determined by reduction to the corresponding cyclopropanol and determination of enantiomeric composition by the methods of Dale, Dull, and Mosher[10] (conversion to the diastereomeric esters with optically pure 2-methoxy-2-phenyl-3,3,3-trifluoropropanoyl chloride and nmr analysis) and of Whitesides and Lewis[11] (nmr analysis with optically active lanthanide shift reagent). Both methods indicate an optical purity of 9 ± 1%. (+)-Cyclopropanone of 90–100% optical purity was obtained by partial reduction with (+)-diisopinocampheylborane,[12] but the product from this route was much harder to purify.

The RD and CD values given in Chart I are for cyclopropanone 1 of 9% optical purity, indicating values for optically pure 1 of $[\Phi]_{373}$ +5890°, $[\theta]_{354}$ +9660°; differential dichroic absorption, Δε 2.92; optic anisotropy, Δε/ε 0.089; molecular amplitude, a_{obsd} +112°, *a* (calculated from $a = 0.0122[\theta]$) +117°.[13] The absolute configuration of the cyclopropanone is not known. The configuration of (+)-1 as *R,R* (shown in eq 2) is that suggested by the octant rule.

Table I
Hydration of *trans*-Di-*tert*-butylcyclopropanone (1) in Aqueous Dioxane

A. Rates

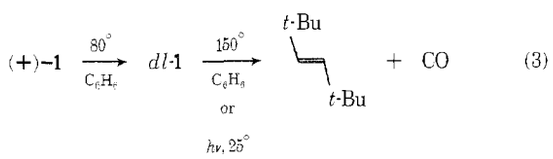
[H_2O], M	[1], M[a]	$k \times 10^5$, sec^{-1} 46°	80°
1.46	0.0367	2.3	4.4
2.33	0.0381	6.4	13.6
2.76	0.0501	8.7	17.8

B. Equilibria[b]

[H_2O], M	[1], M[a]	K[b], M^{-1} 27°	46°	80°
1.46	0.0367	8.6	5.3	2.3
2.33	0.0435	7.8	5.0	2.1
2.76	0.0501	7.4	5.3	2.1
6.73	0.3035	4.7		
10.51	0.282	2.3	2.0	
13.42	0.262	2.1	1.9	

[a] Initial concentration, moles/liter. [b] 1 + H_2O ⇌ hydrate.

(+)-Cyclopropanone 1 racemizes at 80°.[4b,c] A detailed study is reported in a forthcoming paper.[5] At higher temperatures the cyclopropanone decomposes cleanly to *trans*-di-*tert*-butylethylene and carbon monoxide ($t_{1/2}$ 9.5 hr in benzene at 150°), eq 3. Irradiation at 25° also effects clean decarbonylation.



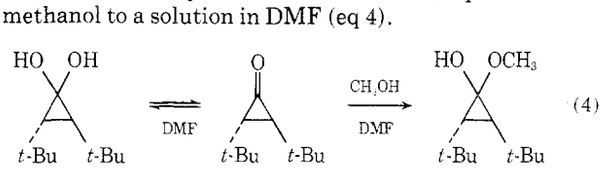
(3)

Reaction with Nucleophiles. General Considerations. Cyclopropanone 1 has two features of consequence in reactions with nucleophiles. The contraction of the C–C–C angle of the ketone from the preferred 120° to 60° provides strong driving force for nucleophilic addition to the carbonyl group. The trans-oriented *tert*-butyl groups, however, shield the carbonyl from attack. The net effect is a carbonyl group that might be expected to be inert toward large nucleophiles but reactive toward small ones.

A variety of results are obtained upon addition to the carbonyl group. The adduct may be stable, or may undergo ring opening at C_{1-2}, ring expansion, fragmentation, or dehydration. Reaction with water and alcohols are considered in this paper. In a following paper we describe examples in which addition is followed by some of the other possibilities.

Reaction with Water. The cyclopropanone hydrates readily. The hydrate, a solid of mp 105–107°, decomposes in air (see below). It is also sensitive to acids and bases. In a vessel of carefully cleaned surface a solution of the hydrate in dioxane or DMF was unchanged after 3 days at 80°. Heating an aqueous dioxane solution of the hydrate containing acid results in clean conversion to a α-hydroxydineopentyl ketone.

Reversibility of hydrate formation is seen in the conversion (slow) of the hydrate to the hemiketal upon addition of methanol to a solution in DMF (eq 4).



(4)

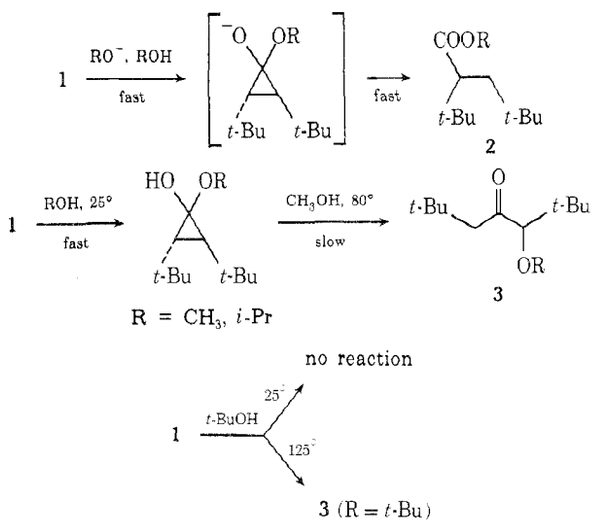
A brief study has been made of the hydration of the cyclopropanone in degassed aqueous dioxane. Rate and equilibria data are summarized in Table I. The data were obtained by determination of cyclopropanone concentration by ultraviolet analysis at 354 nm.

The principal conclusions are that hydration does not go to completion in aqueous dioxane at low water concentration; *e.g.*, at 2.33 M water in dioxane, $t_{1/2}$ for hydration is 3 hr at 46°, and at equilibrium approximately 8% of the initial cyclopropanone remains as free cyclopropanone. Increase in temperature shifts the equilibrium toward free cyclopropanone. The concentration equilibrium "constant" is shifted to lower values by increasing water content, a not unexpected type of change in view of the substantial medium changes involved.[14]

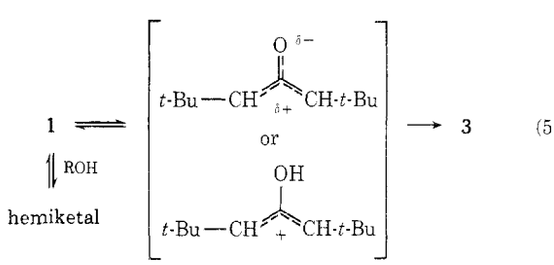
Reaction with Alcohols. The cyclopropanone reacts rapidly with primary alcohols, more slowly with secondary alcohols, and is unreactive with *tert*-butyl alcohol at 25°. The hemiketals from the primary alcohols may be isolated. The hemiketals and the hydrate are unstable in the presence of oxygen.

Under neutral conditions in a degassed solution containing an excess of the alcohol, no further change in the hemiketals is observed at 25°. Upon heating, the hemiketal is converted to the α-alkoxy ketone and/or the Favorskii ester. Under basic conditions the hemiketal undergoes rapid ring opening to the Favorskii ester. Under acid conditions α-alkoxy ketone is formed. Both hemiketal formation and conversion to alkoxy ketone are accelerated by acid.

Chart II



The results are summarized in Chart II. Conversion of hemiketal under basic conditions (*i.e., via* the alkoxide species) to ester is rapid, and is easily understood.[15,16] Conversion of hemiketal to alkoxy ketone is slow, and the mechanism is less apparent. It probably involves reversion to the cyclopropanone, ring opening to oxyallyl species or the corresponding protonated form, and capture by solvent (eq 5).[17,18]



(5)

The rates of addition of methanol to cyclopropanone 1

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EXPERIMENTAL SECTION

Dineopentyl Ketone. -- The iron carboxylate pyrolysis procedure was used.[23] 3,3-Dimethylbutyric acid (58.1 g, 0.5 mol), iron powder (15.4 g, 0.274 mol, Fisher electrolytically reduced) and boric acid (approx 15 mg) were heated at reflux under N_2 for 4 hr. The pot temp was raised to 360° and the volatile components were collected by distillation. Pyrolysis began at 275°. The distillate was added to pentane, filtered, washed with 1N NaOH, dried ($MgSO_4$), concentrated and distilled: fraction 1, bp 65–75°C/95 mm, 1 g, identified by ir and nmr as methyl neopentyl ketone; Fraction 2, bp 105–115°C/95 mm, 14 g (20% yield), dineopentyl ketone (lit.[25] 75–79 at 20 mm). Fraction 3, bp 115–120°C/95 mm, 3 g, identified as 2-*tert*-butyl-5-neopentylfuran: ir (CCl_4) 3100 (w), 2960 (s), 1930 (s), 1475 (m), 1460 (s), 1390 (m), 1360 (s), 1275 (s), 1225 (s), 1200 (s), 1140 (s), 1025 (s), 1010 (s), 965 (s) cm^{-1}; nmr (CCl_4) δ 5.7 (2H, s), 2.4 (2H, s), 1.25 (9H, s), 0.90 (9H, s); mass spectrum, *m/e* (rel intensity) 194(18), 179(23), 138(17), 137(100), 123(33), 122(20), 95(10), 57(15), 43(56), 41(13); uv (isooctane) λ_{max} 224 nm (log ε = 4).

Anal. Calcd for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.28; H, 11.58.

Fraction 4, bp 120–125°C/95 mm, 4 g, was identified by ir and nmr as *tert*-butylacetic anhydride.

Dineopentyl ketone was also prepared by the slow addition of ethereal neopentylmagnesium chloride solution to 3,3-dimethylbutyryl chloride.[25]

α-Bromodineopentyl Ketone. -- To a 12.61 g (0.074 mol) sample of dineopentyl ketone in 50 ml of CCl_4 was added a solution of bromine (11.85 g, 0.072 mol) in 60 ml CCl_4 over a period of 30 min while flushing with nitrogen to help eliminate the hydrogen bromide. After addition was completed, more nitrogen was flushed for 45 hr. The CCl_4 was evaporated and the product distilled, affording 14.0 g (0.056 mol) of α-bromodineopentyl ketone in 78% yield: bp 46–47° (0.11 mm); ir (CCl_4), 1722, 1710 cm^{-1}; nmr (CCl_4), 1.05 (s, 9H), 1.18 (s, 9H), 2.5 (s, 2H), 4.1 (s, 1H).

Anal. Calcd for $C_{11}H_{21}BrO$: C, 53.02; H, 8.50; Br, 32.07. Found: C, 53.19; H, 8.48; Br, 32.34.

The residue was found to be mostly one component. Crystallization from pentane afforded a white solid α,α'-dibromodineopentyl ketone, mp 70–71° (lit.[25] 70–71°).

trans-2,3-Di-tert-butylcyclopropanone (1). -- To α-bromodineopentyl ketone (33.6 g, 0.135 mol) in a flame-dried flask (N_2) equipped with magnetic stirrer over an ice-water bath was slowly added (30 min) 128 ml of a solution of 1.0 M potassium *tert*-butoxide in *tert*-butyl alcohol (prepared by the addition of potassium metal to freshly distilled, sodium dried *tert*-butyl alcohol and scandardized by back titration of an aliquot acidified with an aliquot of 0.1 N HCl). When the mixture solidified, the ice-bath had to be removed. The mixture was concentrated (ca 60°C, 45 mm) and trap-to-trap distilled (0.1 mm, 25–100°C). Recrystallization of the distillate from pentane (−78°C) yielded 10.8 g (75% yield) of cyclopropanone 1. The yield is variable (30–75%). It is imperative not to exceed 0.95 equivalents of base and to add the base slowly. Physical data on the cyclopropanone are summarized in Chart I.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.70; H, 12.06.

Partial Resolution of trans-2,3-Di-tert-butylcyclopropanone by d-Amphetamine. -- d-Amphetamine (1.10 ml, 1.03 g, 7.6 mmol) was added to trans-2,3-di-tert-butylcyclopropanone (3.9 g, 23 mmol) (N_2). After completion of reaction the mixture was trap-to-trap distilled at 50°C and 0.1 mm yielding the cyclopropanone, and approximately 200 mg of a second phase (water). The organic fraction was separated and found to be greater than 98% cyclopropanone, $[\alpha]^{25}_{436}$ +76° (c 0.5, CCl_4). From another run, $[\alpha]^{25}_{436}$ +98° (c, 0.44 in isooctane), $[\alpha]^{23}_{373}$ +344° (c, 0.28 in isooctane). Additional RD and CD data are summarized in Chart I.

The residue from the trap-to-trap distillation was added to 2 ml of pentane and cooled to −78°C. The resulting precipitate was recrystallized from pentane (−78°C) to yield 600 mg of waxy solid, mp 37.5–46°C, trans-2,3-di-tert-butyl-N-(1-methyl-2-phenylethyl) cyclopropanimine. A second recrystallization (pentane, −20°C) raised the melting point to 39–40°C. Sublimation (40°C) yielded material of mp 44–46.5°: ir (CCl_4) 3030 (w), 2970 (s), 1775 (m) cm^{-1}, nmr (CCl_4) δ 7.07 (5H, s), 3.30 (1H, m), 2.75 (2H, d, see below), 1.34 (3H, d, J = 6Hz), 0.90 (9H, s), 0.70 (9H, s).

Anal. Calcd for $C_{20}H_{31}N$: C, 84.14; H, 10.95; N, 4.91. Found: C, 83.95; H, 11.15; N, 5.06.

Nmr analysis (C_6D_6, Varian HA-100) indicated that the downfield part of the "doublet" at δ 2.75 was actually two lines. When the multiplet at δ 3.30 was irradiated, the pattern at δ 2.75 merged to two lines of approximately equal intensity, separated by 2 Hz. This observation suggests that the imine sample is a mixture of low diastereomeric purity; attempted fractional crystallization of the diastereomers was unsuccessful.

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Partial resolution of the cyclopropanone was also effected by use of l-α-phenylethyl serine and by d-α-(1-naphthyl) ethylamine.

trans-2,3-Di-tert-butylcyclopropanol was prepared by reduction of the cyclopropanone with $LiAlH_4$, mp 49–51°, nmr (CCl_4) 3.28 (1H, doublet of doublets), 1.0 and 0.87 (two sharp peaks of equal area), integrated area from 0.7 to 1.1 is 20 H; 9 for each of two different *tert*-butyl groups and 2 for the cyclopropyl hydrogens.

Anal. Calcd for $C_{11}H_{22}O$: C, 77.57; H, 13.02. Found: C, 77.47; H, 13.19.

Determination of Optical Purity. NMR Method of Whitesides and Lewis.[11] To a solution of trans-2,3-di-tert-butylcyclopropanol in CCl_4 (obtained by $LiAlH_4$ reduction of cyclopropanone of $[\alpha]^{25}_{373}$ +344° (c, 0.28 in isooctane)) was added tris-[3-(*tert*-butylhydroxymethylene)-d-camphorate] europium (III). In the presence of approximately 0.2M europium compound, the signal for the *tert*-butyl group *trans* to the hydroxyl (originally at δ 0.82) appears as a broad singlet at δ 0.15, and the *tert*-butyl group *cis* to the hydroxyl (originally at δ 1.02) appears as an enantiomeric pair of signals at 1.98 and 2.10. Integration of the signals at a sweep width of 100 Hz using a planimeter indicated a ratio of 54.7/45.3 or a percent optical purity of 9.24%. Analysis of the same solution at 100 MHz gave a separation of 12 Hz and an optical purity of 9.6%.

Nmr Method of Dale, Dull, and Mosher.[10] trans-2,3-Di-tert-butylcyclopropyl α-methoxy-α-trifluoromethylphenylacetate. -- To trans-2,3-di-tert-butylcyclopropanol (85 mg, 0.5 mmol) was added a mixture of the acid chloride of (+)-MTPA (255.6 mg, 0.9 mmol) and pyridine (0.5 ml, freshly distilled from CaH_2). After 1 hr, water (1 ml) was added and the mixture extracted with ether (20 ml). The ether extracts were washed with dil aq HCl, sat'd aq $NaHCO_3$ soln, and water, dried ($MgSO_4$), and concentrated. The mixture of diastereomeric esters was purified by preparative gc, mp 72–78°C: ir (CCl_4) 3060 (w), 3030 (w), 2950 (s), 2905 (m), 2865 (m), 1730 (s), 1440 (m,b), 1368(w), 1360 (m), 1230 (s,b), 1185 (s), 1165 (s), 1115 (m), 1100 (m), 1075 (w), 1050 (w), 1015 (m), 960 (w), 912 (w), 890 (w); nmr (neat, CCl_4) δ 7.37 (5H, s, broad), 4.13 (1H, m), 3.57 (3H, s, broad), 0.87 and 0.80 (two sharp signals of equal area, integrated area from 0.6 to 1.0 is 20H; 9 for each of two different *tert*-butyl groups and 2 for the cyclopropyl hydrogens); fluorine, 56.45 MHz, CCl_4/C_6F_6) two diastereomeric CF_3 singlets 91 ppm downfield from C_6F_6 and separated by 0.25 ppm (14.1 Hz).

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Anal. (Mixture of Diastereomers): Calcd for $C_{24}H_{35}O_2F_3$: C, 65.20; H, 7.56. Found: C, 65.07; H, 7.57.

When the diastereomeric esters were prepared starting from (+)-trans-2,3-di-tert-butylcyclopropanone, $[\alpha]^{23}_{373}$ +344° (C, 0.28 isooctane), resolved by partial asymmetric destruction with 0.33 equivalents of d-amphetamine and of (−)-α-methoxy-α-trifluoromethylphenylacetyl chloride,[10] measurement of the relative intensities of the diastereomeric CF_3 signals gave an optical purity of 9.21% (planimeter) or 9.42% (peak height) for the cyclopropanone. (The peak farthest downfield from C_6F_6 was the more intense).

Asymmetric Reduction of trans-2,3-Di-tert-butylcyclopropanone with Diisopinocampheylborane. -- To a solution of (−)-2-pinene (2.46 g, 18.1 mmol, 10% excess) in 3 ml of THF (freshly distilled from $LiAlH_4$) was added 3.62 ml of 1.06N diborane in THF (0.85 mol of BH_3) at 0°C. After 4 hr at 0°C the mixture was cooled to −78°C and trans-2,3-di-tert butylcyclopropanone (2.78 g, 16.5 mmol) was added. When the mixture was warmed to 0° the precipitated organoborane quickly dissolved. The solution was maintained at 0° for 2 hr and at room temperature for an additional 2 hr, concentrated, and trap-to-trap distilled. The distillate (analyzed by glc, uv, and ir) contained approx equal amounts of the cyclopropanone and 2-pinene (total; 1.6 g). Attempted fractional crystallization at −78°C was not successful. The cyclopropanone could be purified by gc without recrystallization under the following conditions: 2' × 1/4" column of 20% SE 30 on 60/80 mesh Chromosorb W, 80°C, 150 cc He/min, injector at 70°C, detector at 65°C, retention time = 5 min. Cyclopropanone which was collected neat decomposed rapidly (as did samples of racemic material) so that it was necessary to collect it directly into isooctane solution $[\alpha]^{25}_{373}$ +43.950° (c 0.28, isooctane). For cyclopropanone of 9.21% optical purity, $[\alpha]^{25}_{373}$ +344° (c 0.28, isooctane) so that the optical purity of the recovered cyclopropanone is approximately 100% ±12%).

Decomposition of trans-di-tert-butylcyclopropanone, Thermal. -- A solution of 0.1470 g (0.88 mmol) of the cyclopropanone and 0.2409 g n-pentane in 3.0 ml benzene (freshly distilled from sodium) in Pyrex tubes was degassed and sealed (−78°, 0.05 mm), and heated at 150±4°. Analysis (glc, SE 30 on Chromosorb W, 70°) showed the disappearance of the cyclopropanone ($t_{1/2}$, 9.5 hr) and the appearance of *trans*-1,2-di-*tert*-butylethylene (95% after 45.5 hr at 150°), identified as the *trans* isomer by comparison of ir and nmr spectra with those of authentic samples. No other products were observed.

Photochemical. -- A solution of 0.0155 g (0.092 mmol) of the cyclopropanone and 0.0145 g n-decane was degassed and sealed in Pyrex tubes and irradiated at ambient temperature with a 275 watt General Electric sunlamp. Analysis (glc) after 6 hr showed only the cyclopropanone (52%: retention time, 7 min) and *trans*-1,2-di-*tert*-butylethylene (48%: retention time, 2 min). In a parallel experiment a solution of 1 in CCl_4 was degassed, sealed and irradiated under the above conditions. Analysis (nmr) after 6 hr showed the cyclopropanone and *trans*-1,2-di-*tert*-butylethylene only.

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Stability of Cyclopropanone 1 in Dioxane at 100°. -- A 0.0374 M solution of cyclopropanone 1 in dioxane (distilled from sodium and benzophenone) was degassed and sealed in a Pyrex uv cell, λ_{max} = 290 nm (ε = 41.0). Only 20% of the cyclopropanone was destroyed in 30 days at 100°. Analysis by glc indicated the only product was *trans*-di-*tert*-butylethylene.

In Triethylamine. -- A sealed tube containing the cyclopropanone and triethylamine was heated to 100° for 2 hr. Infrared analysis indicated no reaction had occurred.

Di-α-t-butylcyclopropanone Hydrate. -- All glassware employed in this experiment was soaked for two days in distilled water which had been distilled from $KMnO_4$ and stored in a drying oven prior to use. A mixture of 0.158 g (1.0 mmole) of cyclopropanone 1, 0.40 g (22 mmole) of distilled water and 3.0 ml of dioxane in a 25 ml flask was allowed to stand at room temperature under a positive nitrogen pressure for 48 hr. The addition of 10 ml of water afforded a white fluffy precipitate, isolated by filtration under a nitrogen atmosphere and dried under a stream of rapidly flowing nitrogen. The solid, 0.162 g (0.87 mmole), 87% yield, mp 105–107 (sealed tube) shows ir bands in CCl_4 at 3750 cm^{-1} and 3360 cm^{-1}. Exposure of a 25-mg sample of the hydrate to the air for 30 min resulted in complete destruction. The infrared spectrum of the residue shows two strong carbonyl peaks at 1790 cm^{-1} and 1700 cm^{-1}.

Formation of α-Hydroxydineopentyl Ketone from trans-Di-tert-butylcyclopropanone. -- A solution of cyclopropanone 1 (152 mg, 0.90 mmol) in 3 ml of 90% aqueous dioxane containing 5 mg of toluenesulfonic acid monohydrate (0.026 mmol) was degassed, sealed in a Pyrex tube, and heated at 80° for 60 hr. The organic material was extracted with ether, washed once with water and dried with K_2CO_3. Evaporation of the solvents yielded an oil which gave a single peak on glc. Sublimation yielded α-hydroxyneopentyl ketone: mp 40–42°; ir (CCl_4) 3480 m broad, 2950 s, 1705 s, 1480 s, 1395 m, 1365 s, 1060 s, 1020 cm^{-1}; nmr (CCl_4) 0.90 (9H, s), 1.00 (9H, s), 2.53 (2H, ABqdn = 10 Hz, J = 16 Hz), 4.3 (concentration-dependent (1H, broad)), 3.90 (1H, broad) ppm identical with an authentic sample prepared by hydrolysis of α-acetoxyneopentyl ketone.

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Methanol Hemiketal of trans-di-tert-butylcyclopropanone. -- A solution of 0.158 g (1.0 mmole) of cyclopropanone (99% pure by vpc) and 0.32 g (10 mmole of methyl alcohol distilled from sodium was allowed to react at room temperature under a positive nitrogen pressure for two hr. The excess methanol was removed under reduced pressure, affording 0.195 g (97%) of a white crystalline solid, mp 94–96° (sealed tube): ir (CCl_4) 3370 (s), 3360 (br), and 3125 (s) cm^{-1}; nmr ($CDCl_3$), 0.93 and 1.00 (double, 20 H), 2.87 (s, 1H), 3.40 (s, 3H).

Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.07. Found: C, 72.08; H, 12.08.

The material decomposed when exposed to the atmosphere for several hours. A degassed solution of the hemiketal in deuterochloroform was unchanged after heating for three days at 80°.

Benzyl Alcohol Hemiketal of trans-2,3-Di-t-butylcyclopropanone. -- The cyclopropanone (0.1372 g, 0.955 mmol) and benzyl alcohol (0.101 g, 0.935 mmol) were mixed neat. After 2 hr the reaction mixture was filtered, affording 0.1665 g (65% yield) of crude product, mp 93–98°. Recrystallization gave pure *trans*-2,3-di-t-butylcyclopropanone benzyl alcohol hemiketal, mp 102–103°, ir (CCl_4) 3550 (no carbonyl absorption); nmr (CCl_4), 0.97 and 1.02 (two sharp peaks of equal area) integrated area from 0.6 to 1.6 is 20 H; 9 for each of two different t-butyl groups and 2 for the cyclopropyl hydrogens) 2.8 (s, 1H), 4.6 (quartet, 2H), 7.2 (s, 5H).

Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.21; H, 10.23; mol. wt., 276. Found: C, 78.04; H, 10.35; mol. wt. 279.

The hemiketal was found to be unstable in solution: ir and nmr spectra had to be measured immediately after the solid had been dissolved.

Reaction of trans-di-tert-butylcyclopropanone with potassium tert-butoxide. -- Addition of the cyclopropanone to tert-BuOH-tert-BuOK results in rapid conversion to the ester, *tert*-butyl 2-*tert*-butyl-4,4-dimethylpentenoate: ir (CCl_4) 1725 (s), nmr (CCl_4) 0.88 (s, 9H), 0.92 (s, 9H), 1.43 (s, 9H), 1.8–2.1 (multi, 2H).

Anal. Calcd for $C_{18}H_{34}O_2$: C, 74.43; H, 12.48. Found: C, 74.42; H, 12.30.

With tert-butyl alcohol. -- A sample of the cyclopropanone in t-BuOH was degassed, sealed, and heated at 100° for 6 days. Evaporation of the solvent and analysis (glc) indicated a single product, identified as α-*tert*-butoxydineopentyl ketone: ir (CCl_4) 2960 (s), 1710 (s), 1475 (m), 1365 (s), 1390 (s), 1380 (s), 1020 cm^{-1}; nmr (CCl_4) 0.90 (9H, s), 1.00 (9H, s), 1.10 (9H, s), 2.43 (2H, ABqdn = 19 Hz, J = 19 Hz), 3.27 (1H, s) ppm; uv (*tert*-butanol) λ_{max} = 305 (ε = 92.5).

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Anal. Calcd for $C_{15}H_{30}O_2$: C, 74.33; H, 12.47. Found: C, 74.28; H, 12.42.

With t-butyl. -- Cyclopropanone 1 in $BuOt$, degassed and sealed, heated at 80° for 60 hr, afforded a single product, 2-methoxy dineopentyl ketone: ir (CCl_4) 2960 (s), 1710 (s), 1480 (s), 1360 (s), 1215 (s), 1120 (m), 1095 (s) cm^{-1}; nmr (CCl_4) 0.90 (9H, s), 1.00 (9H, s), 1.16 (3H, s), 2.32 (2H, s), 3.03 (1H, s), 3.36 (2H, m) ppm.

Anal. Calcd for $C_{13}H_{26}O_2$: C, 72.83; H, 12.25. Found: C, 72.78; H, 12.45.

With isopropyl alcohol, acidic conditions. -- Cyclopropanone 1 in 1 ml of a 1.7×10^{-2} M solution of toluenesulfonic acid monohydrate in 2-propanol degassed and sealed, heated at 80° for 2.5 hr, afforded a single product α-isopropoxydineopentyl ketone: ir (CCl_4) 2960 (s), 1710 (s), 1470 (m), 1360 (s), 1182 (s) cm^{-1}; nmr (CCl_4) 0.90 (9H, s), 1.00 (9H, s), 1.11 (6H, sd), 2.33 (2H, partially resolved ABq), 3.10 (1H, s), 3.40 (1H, septet) ppm.

With isopropyl alcohol, basic conditions. -- Reaction of the cyclopropanone with 1-PrOK, 2-PrONa rapidly afforded isopropyl *tert*-butyl-neopentyl-acetate: ir (CCl_4) 2960 (s), 1720 (s), 1480 (m), 1370 (s), 1190 (m), 1150 (s), 1105 (m) cm^{-1}; nmr (CCl_4) 0.82 (9H, s), 0.92 (9H, s), 1.20 (6H, d), 1.3–2.2 (3H, m), 4.95 (1H, septet) ppm.

Anal. Calcd for $C_{14}H_{28}O_2$: C, 73.63; H, 12.36. Found: C, 73.51; H, 12.66.

With isopropyl alcohol, neutral conditions. -- Cyclopropanone 1 in isopropyl alcohol, degassed and sealed, heated at 80° for 5 days afforded α-isopropoxydineopentyl ketone (30%), isopropyl *tert*-butyl-neopentyl acetate (30%) and 8 minor products.

With Methanol. -- Cyclopropanone 1 in CH_3OH, degassed, sealed, heated at 80° for 60 hr afforded a single product α-methoxydineopentyl ketone: ir (CCl_4) 2960 (s), 1725 (s), 1480 (s), 1370 (s), 1105 (s) cm^{-1}; nmr (CCl_4) 0.90 (9H, s), 1.01 (9H, s), 2.40 (2H, ABqdv = 10 Hz, J = 15 Hz), 2.93 (1H, s), 3.33 (3H, s) ppm; uv (dioxane) λ_{max} = 316 nm (ε = 44.0).

Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.07. Found: C, 71.91; H, 12.14.

When the methanol hemiketal of cyclopropanone was pre-formed in flame-dried glassware, washed with pentane, dissolved in neutral methanol and heated at 80°, less than 2% formation of the methoxy ketone was observed by uv after 10 days. This observation implies a maximum rate of methoxy ketone formation of 2×10^{-8} sec^{-1}, *i.e.*, the preparation of the methoxy ketone described above is catalyzed by some extraneous acid. The preparation was repeated several times with the same results.

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Methanolysis of α-Bromodineopentyl Ketone. -- α-Bromodineopentyl ketone (0.90 g, 2.4 mmol) and 0.75 g of $AgNO_3$ (4.4 mmol) in 3 ml of methanol was degassed and sealed in a Pyrex tube and heated at 100° for 48 hr. The methanol was evaporated and the organic products were obtained by trituration with pentane. Analysis (glc) showed bromo ketone (70%) and three products in the ratio of 23:32:44. Samples of each of these peaks were collected for spectral analysis. The first peak was assigned as 2,3,6,6-tetramethyl-2-hepten-4-one on the basis of its spectral properties: ir (CCl_4) 2960 (s), 1710 (s), 1640 (m), 1485 (m), 1366 (m), 930 (s) cm^{-1}; nmr (CCl_4) 0.90 (9H, s), 1.15 (3H, s), 1.60 (3H, s), 2.10 (2H, s), 2.20 (3H, s) ppm.

The second peak was found to be identical to α-methoxydineopentyl ketone by ir and nmr. The third peak was identified as 2,3,6,6-tetramethyl-2-methoxy-4-heptanone: ir (CCl_4) 2960 (s), 1715 (s), 1465 (m), 1360 (s), 1190 (s), 1070 cm^{-1}; nmr (CCl_4) 0.95 (9H, s), 1.05 (3H, d, J = 7 Hz), 1.10 (6H, s), 2.33 (2H, s), 2.66 (1H, q, J = 7 Hz), 3.05 (3H, s) ppm.

Anal. Calcd for $C_{12}H_{24}O_2$: C, 71.95; H, 12.07. Found: C, 71.72; H, 12.26.

Nmr Study of the Formation of α-Methoxydineopentyl Ketone. -- Cyclopropanone 1 (50 mg, 0.36 mmol) and toluenesulfonic acid monohydrate (5 mg, 0.03 mmol) were dissolved in 1 ml of methanol in an nmr tube. The formation of α-methoxydineopentyl ketone was followed at room temperature by nmr ($t_{1/2}$ was about 95 hr). After mixing, only the methanol hemiketal (singlets at 0.95 and 1.00 ppm) was visible in the nmr spectrum; no cyclopropanone remained. As the reaction proceeded the spectrum of the methoxy ketone appeared (singlets at 0.90 and 1.01 ppm). At no time were any peaks other than those of the solvent, the hemiketal, and the methoxy ketone observed in the nmr spectrum.

Kinetics of Hemiketal Formation at 25° from Cyclopropanone 1. -- trans-2,3-Di-tert-butylcyclopropanone (approximately 50 mg) was placed in a dry uv cell. Approximately 3 ml of the anhydrous alcohol was added at 25° and the disappearance of the cyclopropanone was followed by uv at 320 nm. The solutions were not degassed and were sealed only with rubber serum caps. The results are summarized in Table III.

Exchange of Deuterated Methanol Hemiketal of Cyclopropanone 1. -- Cyclopropanone 1 (108 mg, 0.64 mmol) was allowed to react with 1 g of methanol-d_4 for 1 hr at 25° in a flame-dried flask. The excess alcohol was evaporated and 3 ml of pentane was added. The white solid hemiketal was allowed to stand under the pentane at 0° for 16 hr. The pentane was drawn off with a canula and the resulting solid dissolved in 5 ml of anhydrous methanol. This solution was degassed and sealed in five tubes and placed in a 25° oil bath. The tubes were removed from the bath at various times and the methanol evaporated. The hemiketal thus obtained was dissolved in CCl_4 and examined by nmr: time in nmr, fraction of label present, $k \times 10^5$ sec^{-1} (0, 1.0; 73, 0.68, 4.86; 167, 0.74, 3.00; 353, 0.537, 4.81; 573, 0.324, 5.62) $k_{av} = 5.5 \times 10^{-5}$ sec^{-1}. A similar experiment at 80° had a k_{av} = 9.6×10^{-5} sec^{-1}.[21]

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Kinetics of Hydration of Cyclopropanone 1 in Dioxane at 30°. -- Stock solutions of cyclopropanone 1 in dioxane and H_2O in dioxane were made up by weight in flame-dried flasks stoppered with serum caps. In calculating the molarity the volumes are assumed to be additive. Equal aliquots (1.5 ml) of each solution were transferred by syringe to oven-dried Pyrex uv cells, degassed, and sealed. The solutions were allowed to warm to room temperature and the initial absorbance was read. The cells were heated in an oil bath at 79.6° for predetermined time intervals (30 seconds allowed for warm-up time) and then quenched by cooling in an ice bath. The absorbance was read quickly and the cell returned to the oil bath. Absorbance values at infinite time were taken after at least 10 half lives. The results are summarized in Table I.

The equilibrium constants for the hydration reaction were calculated by the following formula: $K' = \frac{A_0 - A_\infty}{A_\infty - A_t}$, $K = K'/[H_2O]$. Where A_0 is the initial absorbance, A_∞ is the absorbance after 10 half-lives and A_t is the absorbance of the cell filled with pure dioxane. This procedure avoids the need to determine the extinction coefficient for the cyclopropanone at each aqueous dioxane mixture used.

Kinetics of Methanol Hemiketal Formation from Cyclopropanone 1 in Dioxane at 80°. -- The procedure given above for the hydration was used here with freshly distilled methanol (from magnesium methoxide) replacing the distilled water. In this case equilibrium constants could not be obtained directly since the cyclopropanone concentration at equilibrium was too small.

Deuterium Exchange of trans-Di-tert-butylcyclopropanone with Potassium tert-Butoxide in tert-Butanol-O-d. -- A solution of potassium *tert*-butoxide (0.07 N by titration) was prepared by reaction of 12 mg of potassium metal with 6 ml of *tert*-butanol-O-d, 98% deuterated by nmr. Cyclopropanone 1 (43.8 mg, 0.28 mmol) was added to 2 ml of this solution and allowed to react for 20 min at room temperature. The alcohol was then evaporated and the residue triturated with pentane. The *tert*-butyl

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tert-butyl-neopentylacetate was collected from gc and analyzed for deuterium content by mass spectroscopy. Since the ester had no molecular ion in the mass spectrum, fragment ions had to be used to determine deuterium content. Ions at 171 and 130 m/e in the undeuterated compound were used since these are rather intense peaks formed by fragmentations involving only the tert-butyl groups which show relatively small M + 1 peaks (less than 13%): 3% d_0, 24% d_1, 30% d_2, and 16% d_3 at the 130 fragment, and 5% d_0, 48% d_1, 31% d_2, and 16% d_3 at the (less reliable, large M-2) 171 fragment. A sample of the ester prepared from undeuterated reactants showed no deuterium incorporation when subjected to this same procedure.

Oxidation of Di-tert-butylcyclopropanone in Hexane in the Presence of Water. -- A solution of 0.760 g (4.45 mmole) of di-2-butylcyclopropanone in 4.00 ml of freshly distilled hexane in a 10.0 ml flask was attached to a manometer for measuring uptake of oxygen. The system was flushed with oxygen and equilibrated followed by the addition of 40 µl (2.2 mmol) of water. Time in minutes, volume of O_2 absorbed in ml [0,0; 13,0; 25, 9.8; 35, 14.8; 45, 21.4; 56, 26.0; 72, 29.0;

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130, 34.0; 186, 36.5; 216, 39.5; 1000, 39.5 ml (1.61 mmol)]. A solution containing 0.830 g (4.98 mmole) of cyclopropanone to which no water had been added absorbed only a trace of oxygen in 6 hr.] During the oxidation a white crystalline solid precipitated, tentatively assigned the structure 2-tert-butyl-3-hydroxy-4,4-dimethylpentanoic acid, 0.030 g, mp 222-223.5°, ir bands at 1675 cm^{-1} and a broad band between 2500 and 3200 cm^{-1}.

Anal. Calcd for $C_{11}H_{22}O_3$: C, 65.30; H, 10.96. Found: C, 64.98; H, 10.98.

Analysis of the hexane solution (gle, SE 30 on Chromosorb W, 120°, 65 cc/min) showed five components with retention times 1.60 (pivaldehyde), 2.25 (unknown), 4.40 (di-tert-butylacetaldehyde), 5.0 (tert-butyl neopentyl ketone), 24.2 min (tert-butyl-neopentylacetic acid), identified by comparison of retention times and infrared spectra with authentic samples. A second solution of 0.775 g (4.645 mmole) of the cyclopropanone, 0.10 g (5.6 mmole) of water, 0.0225 g decane (internal standard) in 4.0 ml of pentane was exposed to O_2 atmosphere for 24 hr: analysis (glc)

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showed pivaldehyde (0.192 mmole), di-tert-butylacetaldehyde (0.038 mmol), tert-butyl- neopentyl ketone (0.050 mmol), tert-butylneopentylacetic acid (0.485 mmol).

tert-Butyl Neopentyl Ketone was prepared in 37% yield by the reaction of tert-butyllithium with tert-butylacetyl chloride: ir (CCl_4) 1708, 1475, 1462, 1367, 1362, 1338 cm^{-1}; nmr (CCl_4) 1.01 (s, 9H), 1.10 (s, 9H), 2.37 (s, 2H).

Anal. Calcd for $C_{10}H_{20}O$: C, 72.65; H, 12.90

Found: C, 72.66; H, 12.90

tert-Butylneopentylacetic Acid was prepared by hydrolysis of 2 g of the corresponding tert-butyl ester in 25 ml of conc. H_2SO_4 at 25° for 1 hr. Addition to 200 ml of ice-water, collection of the precipitate, washing and recrystallization from methanol-water afforded the acid in 45% yield, mp 62-64°, further purified by sublimation, mp 66.5-67°: ir 1700 (s); nmr ($CDCl_3$) 0.89 (s, 9H), 0.97 (s, 9H), 1.1-2.3 (multt, 3H), 11.6 (s, 1H).

Anal. Calcd for $C_{11}H_{22}O_2$: C, 70.91; H, 11.91

Found: C, 71.16; H, 11.81.

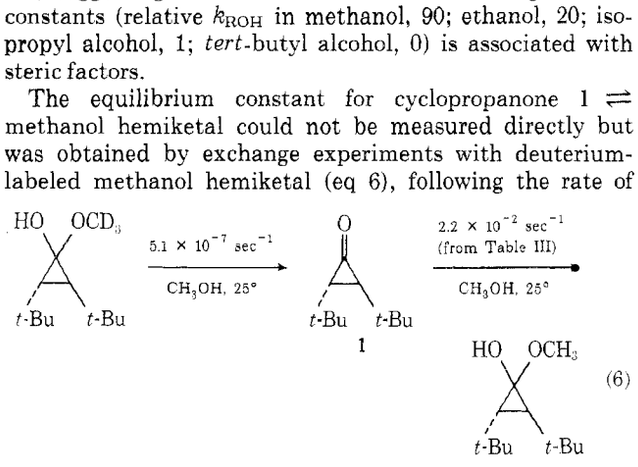
Table II
Formation of Methanol Hemiketal from Cyclopropanone 1 in Dioxane at 80°

$[CH_3OH]$, M	$k \times 10^5$, sec^{-1}
1.08	7.06
1.60	21.3
1.89	36.2

in dioxane at low methanol concentration to give the hemiketal are reported in Table II. The rate constants for both methanol addition (Table II) and water addition (Table I) are markedly dependent on the concentration of the nucleophile; rough interpolation indicates a several-fold faster rate of addition for the methanol. The amount of free cyclopropanone at equilibrium is too low for direct measurement in the methanol–dioxane studies.

Rates of addition of a few simple alcohols to the cyclopropanone in alcohol solution are summarized in Table III. In order to obtain an indication of the relative importance of changes in medium *vs.* changes in steric effects, the cyclopropanone was subjected to methanol–isopropyl alcohol mixtures (last two entries, Table III), following both the rate of disappearance of the cyclopropanone and analyzing for the relative amounts of the two hemiketals. The resulting rate constant for the methanol addition in isopropyl alcohol, $\sim 4 \times 10^{-4}$ M^{-1} sec^{-1}, is within a factor of 2 of the corresponding rate constant in pure methanol, suggesting that much of the observed change in rate constants (relative k_{ROH} in methanol, 90; ethanol, 20; isopropyl alcohol, 1; *tert*-butyl alcohol, 0) is associated with steric factors.

The equilibrium constant for cyclopropanone 1 ⇌ methanol hemiketal could not be measured directly but was obtained by exchange experiments with deuterium-labeled methanol hemiketal (eq 6), following the rate of



(6)

appearance of the undeuterated methoxyl group by nmr analysis of the hemiketal isolated at various times. The equilibrium constant for methanol hemiketal formation from the cyclopropanone 1 in methanol solution at 25° is thus 4.3×10^4 (or 1.7×10^3 M^{-1} if methanol concentration is included in the expression).

Attempted Removal of α Hydrogen of Cyclopropanone 1. Exchangeability of the α hydrogens was of interest both with regard to the acidity of these hydrogens and to the possible use of the enolate anion in subsequent synthetic reactions. In general, attack at α hydrogen and attack at a carbonyl carbon are competitive reactions, markedly dependent on the nature of the attacking base.

Table III
Hemiketal Formation from Cyclopropanone 1 in Neat Alcohols at 25°

ROH	$k_{obsd} \times 10^4$, sec^{-1}	[ROH], M	$k_{obsd} \times 10^4$/ROH, M^{-1} sec^{-1}
CH_3OH	219	25.4	8.62[d]
C_2H_5OH	35.3	17.1	2.06
i-PrOH	1.24×10^{-4}	13.1	0.095
t-BuOH	0[a]	10.6	
CH_3OH, *i*-PrOH	7.33	1.41[b]	4.37[e]
CH_3OH, *i*-PrOH	3.58	0.60[c]	3.95[f]

[a] No observable reaction at 25° or at 80°. [b] 1.41 M CH_3OH, 12.3 M *i*-PrOH. [c] 0.60 M CH_3OH, 12.8 M *i*-PrOH. [d] k'_{CH_3OH} (calculated from $k_{obsd} = k'_{CH_3OH}[CH_3OH] + k_{i\text{-}PrOH}[i\text{-PrOH}]$ and assuming that $k_{i\text{-}PrOH}$ is the same as the value in pure *i*-PrOH. [e] (methyl hemiketal/isopropyl hemiketal) observed by nmr = 5:1; calculated on assumption in footnote *d*, 5.3:1. [f] (methyl hemiketal/isopropyl hemiketal) observed = 2:1; calculated on assumption in footnote *d*, 1.95:1.

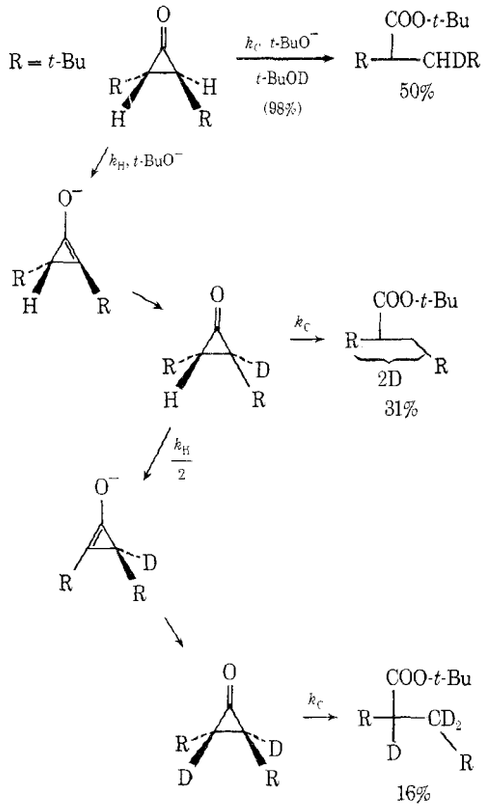
An immediate difficulty in the study of these reactions with a cyclopropanone is the irreversible conversion to ring-opened products—Favorskii ester or α-alkoxy ketone —under basic or acidic conditions. We have nevertheless attempted the removal of the α hydrogens under a variety of conditions. No exchange was observed upon exposure of the cyclopropanone to triethylamine (which does not add to the cyclopropanone) and deuterium oxide, to deuterium oxide in DMF, or to *tert*-butyl alcohol-*O*-*d*. Triphenylmethyllithium in dimethoxyethane rapidly destroyed the cyclopropanone but no volatile products were obtained on quenching with acetic anhydride. Lithium diisopropylamide in dimethoxyethane effected the reduction of the cyclopropanone to the cyclopropanol rather than α-hydrogen exchange.

Evidence for Exchange of α Hydrogens of Cyclopropanone 1 by *tert*-Butoxide in *tert*-Butyl Alcohol. In view of the difficulties described above, we examined the question of exchangeability of the α hydrogens in the overall process of conversion of 1 to the Favorskii ester. The extent of attack on α hydrogen should be reflected in the extent of deuteration of the ester. Subjection of the cyclopropanone to *tert*-butoxide in *tert*-butyl alcohol-*O*-*d* afforded ester with the deuterium content d_0 3%, d_1 50%, d_2 31%, d_3 16%. Samples of undeuterated ester subjected to the reaction conditions for a time period several-fold longer than the reaction were shown not to undergo exchange. Thus the di- and trideuterated ester *must have come from cyclopropanone molecules which had undergone exchange.*

It is of interest to see what the results imply about the relative rates of attack at carbonyl carbon with ring opening and attack at α hydrogen. The finding that the ester product contains approximately equal amounts of monodeuterated material (the result of attack at carbonyl carbon followed by ring opening, k_C) and of higher deuterated material (the result of initial attack at α hydrogen, k_H) indicates that k_C and k_H are approximately equal. The observed values of dideuterated ester (31%) and trideuter-

ated ester (16%) are also consistent with a value of $k_C \cong k_H$. The results and interpretation are summarized in Chart III.[19] Chart III and the brief derivations assume either noninvolvement of *cis*-di-*tert*-butylcyclopropanone[19] or $(k'_C/k'_H)_{cis\text{-cyclopropanone}} \cong (k_C/k_H)_{trans\text{-cyclopropanone}}$.

Chart III



$$\%d_1 = \frac{k_C}{k_C + k_H} \times 100 \cong 50 \quad \therefore \quad \frac{k_C}{k_H} = 1$$

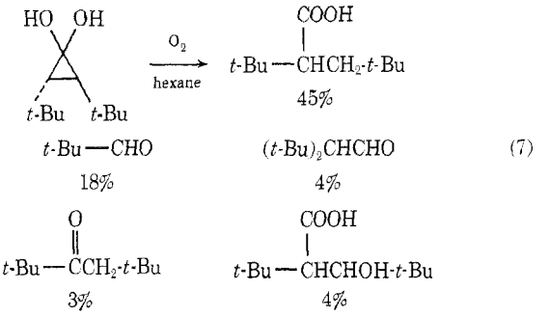
$$\%d_2 = \left(\frac{k_H}{k_C + k_H}\right)\left(\frac{k_C}{k_{H/2} + k_H}\right) \times 100$$

$$\%d_3 = \left(\frac{k_H}{k_C + k_H}\right)\left(\frac{k_{H/2}}{k_C + k_{H/2}}\right) \times 100$$

	Obsd	Calcd for $k_C/k_H = 1$
$\%d_2$	31	33
$\%d_3$	16	17

In a study of the stereochemistry of ring opening of cyclopropanols and hemiketals,[16] the cyclopropanone 1 was subjected to sodium methoxide in methanol-*O*-*d* and to sodium ethylene glycolate in ethylene glycol-*O*-d_2. Only monodeuterated esters were observed in contrast to the di- and trideuterated esters in the present study. Apparently the ratio of k_C/k_H increases with decreasing size of R in the attacking RO^-, ROH.

Reaction of the Cyclopropanone Hydrate with Oxygen. Because of the instability of the cyclopropanone 1 in air, the effect of oxygen was briefly examined in the presence and absence of water. Under anhydrous conditions the cyclopropanone is stable to oxygen.[20] Shaking of a hexane solution of the cyclopropanone with water in the presence of oxygen resulted in the absorption of ~0.3 mol of oxygen per mole of 1 in 3.5 hr. Subjection of the reaction solution to glc analysis afforded a complex mixture (eq 7). The major product was the ring-opened isomer of the hydrate, 2-*tert*-butyl-4,4-dimethylpentanoic acid.



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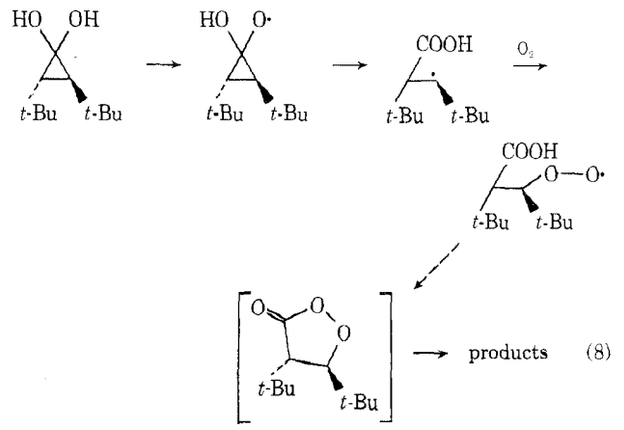
The products of oxidation are derivable by hydrogen atom abstraction from hydrate with ring opening and reaction of the carbon radical with oxygen, followed by various routes, possibly including a peroxylactone (eq 8).



(8)

The presence of such a species was suggested by ir absorption at 1790 cm^{-1} in the crude reaction mixture. Good analogy for the products *tert*-butyl neopentyl ketone and di-*tert*-butylacetaldehyde is found in studies of decomposition of peroxy lactones.[21] Reaction of the methanol hemiketal of tetramethylcyclopropanone with oxygen has been reported to yield the ring-opened β-hydroperoxy ester, which was cyclized to a peroxy lactone in a subsequent step.[22] Lability of cyclopropanone hemiketals to oxygen also has been reported by de Boer.[2d] The major product from oxygen and 2,2-dimethylcyclopropanone methylhemiketal is the hydroperoxy ester, methyl 3-hydroperoxy-3-methylbutyrate. Under radical initiation but insufficient oxygen, the major products are the ring-opened esters, methyl 3-methylbutyrate and methyl pivaloate, isomers of the starting hemiketal.[2d]

Registry No.—1, 14743-58-9; 3,3-dimethylbutyric acid, 1070-83-3; methyl neopentyl ketone, 590-50-1; dineopentyl ketone, 4436-99-1; 2-*tert*-butyl-5-neopentylfuran, 51392-18-8; α-bromodineopentyl ketone, 33712-48-0; *trans*-2,3-di-*tert*-butyl-*N*-(1-methyl-2-phenylethyl)cyclopropanimine, 51392-19-9; *trans*-2,3-di-*tert*-butylcyclopropanol, 51392-20-2; *trans*-2,3-di-*tert*-butylcyclopropyl α-methoxy-α-trifluoromethylphenylacetate, 51392-21-3 (*R* isomer), 51547-28-5 (*S* isomer); diisopinocampheylborane, 1091-56-1; α-hydroxydineopentyl ketone, 51392-23-5; *trans*-di-*tert*-butylcyclopropanone methanol hemiketal, 51392-24-6; *trans*-2,3-di-*tert*-butylcyclopropanone benzyl alcohol hemiketal, 51392-25-7; potassium *tert*-butoxide, 865-47-4; *tert*-butyl 2-*tert*-butyl-4,4-dimethylpentanoate, 51392-26-8; *tert*-butyl alcohol, 75-65-0; α-*tert*-butoxydineopentyl ketone, 51392-27-9; ethanol, 64-17-5; α-ethoxydineopentyl ketone, 51392-28-0; isopropyl alcohol, 67-63-0; α-isopropoxydineopentyl ketone, 51392-29-1; isopropyl *tert*-butylneopentyl acetate, 51392-30-4; methanol, 67-56-1; α-methoxydineopentyl ketone, 51392-31-5; 2,3,6,6-tetramethyl-2-hepten-4-one, 51392-32-6;

2,3,6,6-tetramethyl-2-methoxy-4-heptanone, 51392-33-7; *tert*-butyl neopentyl ketone, 868-91-7; *tert*-butyllithium, 594-19-4; *tert*-butylacetyl chloride, 7065-46-5; *tert*-butylneopentylacetic acid, 51392-34-8.

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(18) The question of ring opening to oxyallyl is taken up in detail in a forthcoming publication (ref 5).
(19) It is not possible from these results to determine whether reprotonation of the enolate anion affords *cis*- or *trans*-cyclopropanone. Generation of the *cis*-cyclopropanone might be expected to lead to rapid attack at the greatly deshielded carbonyl, but by the same token the hydrogens are also more exposed. In a somewhat related case, reprotonation of the enolate from *trans*-di-*tert*-butylcyclobutanedione (ref 5) affords only the trans compound. On this basis, one might expect the di-*tert*-butylcyclopropanone enolate to be reprotonated with regeneration of the *trans*-cyclopropanone.
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Reactions of 2,3-Dibromoindole Derivatives with Bromine and Other Oxidizing Agents. 2,3-Dibromoindole → 3,3-Dibromooxindole Transformation

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When an excess of bromine was allowed to react with 2,3-dibrominated polybromoindoles in acetic acid, the corresponding 3,3-dibrominated oxindoles were isolated. Only in one case, both oxidation and substitution took place. 2,3-Dibrominated polybromoindoles were the main reaction products when the bromination was carried out in anhydrous carbon tetrachloride. Present results confirm a previously proposed pathway according to which a 3,3-dibrominated indolenine (6) is the possible intermediate in the formation of 3,3-dibrominated oxindoles by reaction of some indoles with excess bromine. When 2,3-dibrominated polybromoindoles were treated with chromic anhydride or with peracetic acid the corresponding 3,3-dibrominated oxindoles were isolated in fairly good yields. This method could be used as a diagnostic tool in the structure determination of 2,3-dibromoindoles.

Halogenation of the indole nucleus has been extensively studied. Several halogenating agents, in aqueous and nonaqueous media, have been employed, and beside substitution products oxindole derivatives were almost always found.[1,2] It is known that an aqueous medium favors oxidation and an anhydrous one bromination, and that the two reactions are always competitive, neither one being completely excluded. However, more than one pathway has been proposed to explain the formation of 3-halooxindoles from indoles.[1b,2a,b,d] We have now investigated the behavior of some 2,3-dibrominated polybromoindoles with bromine in aqueous (acetic acid) and in nonaqueous media (carbon tetrachloride).

When excess bromine was added to an acetic acid suspension of 2,3,5,6-tetrabromoindole (**1a**),[1a] 3,3,5,6-tetrabromooxindole (**2a**, 67% yield) was formed. Compound **2a** was hydrolyzed with alkali to 5,6-dibromoisatin (**3a**)[1a] and led, with phenylhydrazine, to a β-phenylhydrazone identical with an authentic sample prepared from **3a**; these facts indicate that two bromine atoms in compound **2a** are in the 3 position.[1b] The infrared spectrum of **2a** shows strong N–H and C=O peaks at 3200 and 1730 cm^{-1}, respectively, in good agreement with those found for other 3,3-dibrominated oxindoles.[1b,3]

The main product of the reaction of **1a**[1a] with excess bromine in anhydrous CCl_4 was a nonoxindolic material