methyl-d_3-4-*t*-butylcyclohexanone) were prepared and then were equilibrated and analyzed under identical conditions. The method of synthesis was similar to that used by Allinger and co-workers[8a,b] and involved alkylation of 2-carboethoxy-4-*t*-butylcyclohexanone with either methyl iodide or methyl-d_3 iodide followed by hydrolysis and decarboxylation. The two ketones were purified by gas chromatography prior to equilibration. The results of the equilibration studies are shown in Table I. Our results for 2-methyl-4-*t*-butylcyclohexanone do not differ materially from those of Allinger and Blatter.[8a]

TABLE I
EQUILIBRIUM DATA FOR 2-ALKYL-4-*t*-BUTYLCYCLOHEXANONE IN METHANOL WITH METHOXIDE

2-Alkyl group	Temp, °C	% *cis*[a]
Methyl	25	93.04 ± 0.26
	64	91.68 ± 0.28
Methyl-d_3	25	93.15 ± 0.34
	64	91.15 ± 0.47

[a] Each of these values represents the average of three separate equilibrations. Each equilibration was analyzed five times.

If the methyl-d_3 group is smaller than the methyl group, then the 2-methyl-d_3 ketone should show a smaller amount of *cis* isomer at equilibrium since the *cis* isomer has the 2-alkyl group in an equatorial configuration. While this appears to actually occur at 64°, the difference appears to be at the limits of experimental error. From the observed precision a difference of greater than ±0.5% in the *cis* and *trans* isomers at equilibrium in going from the 2-methyl to the 2-methyl-d_3 ketone would have been required in order to be reliably observed. In order to set the limits of error in thermodynamic quantities which our method could observe, it can be calculated that an error of ±0.5% in the *cis* and *trans* isomers at equilibrium corresponds to an error of approximately ±0.05 kcal/mole in ΔF, and an error of ±1.0% in the *cis* and *trans* isomers corresponds to an error of approximately ±0.10 kcal/mole in ΔF.

It appears that in the degree of steric crowding in the axial position of a cyclohexanone ring the methyl and methyl-d_3 groups do not show a difference in steric size of greater than about 0.05 kcal/mole relative to the equatorial position. It is not clear whether the method used here is simply not sensitive enough to detect a difference in size of a methyl and methyl-d_3 groups or whether as Mislow has suggested[5] a more sterically crowded situation is required before a difference in size can be detected.

Experimental Section

Methyl-d_3 Iodide.—The methyl-d_3 iodide was prepared by thermal decomposition of trimethyl-d_9-sulfoxonium iodide according to the procedure of Cotton and co-workers[9] and had bp 41° (760 mm) (lit.[9] bp 41°).

2-Alkyl-4-*t*-butylcyclohexanones.—Since reduction using a hydrogenation catalyst was not feasible with a methyl-d_3 compound the method of Allinger and co-workers[8a,b] involving alkylation of 2-carbethoxy-4-*t*-butylcyclohexanone (bp 125–128° (6 mm); $n^{25}\text{D}$ 1.4781) with methyl iodide or methyl-d_3 iodide followed by hydrolysis and decarboxylation was used. The 2-methyl-4-*t*-butylcyclohexanone had bp 77° (3.5 mm) and the 2-methyl-d_3-4-*t*-butylcyclohexanone had bp 80–81° (4 mm). In each case the products appeared to be contaminated with 4-*t*-butylcyclohexanone. They were therefore purified by gas chromatography on a 2-m column of 25% tricyanoethylation product of glycerine on firebrick prior to equilibration. The purified 2-methyl-d_3-4-*t*-butylcyclohexanone was analyzed by combustion[10] and showed 14.5 atom % excess deuterium, or 2.9 deuteriums per molecule. This indicates the compound is about 90% d_3 and 10% d_2.

Equilibrations.—Both sets of ketones, the 2-methyl and 2-methyl-d_3, were equilibrated and analyzed under identical conditions. Equilibration was carried out by dissolving 170 mg of sodium in 30 ml of dry methanol and then adding 200 mg of purified ketone. The resulting solution was then maintained at 64° for 30 hr or 25° for 72 hr. The equilibrated ketones were isolated by pouring the methanol solutions onto ice, and extraction with benzene. After drying the benzene solutions and removal of most of the solvent under reduced pressure the resulting ketone mixture was analyzed on a 2-m column of 25% tricyanoethylation product of glycerine on firebrick using an F & M Model 500 gas chromatograph. Each ketone was equilibrated three times at each temperature and each equilibration was analyzed five times. Analysis of the gas chromatograms was carried out by cutting out each peak and weighing it. The results are shown in Table I. It was assumed that the two isomers of the 2-methyl ketone would show the same relative thermal response as the two isomers of the 2-methyl-d_3 ketone. This was necessary because difficulty of isolating a sufficient quantity of the pure *trans* ketones precluded the possibility of preparation of standards. The assumption made appears to be a safe one and should not affect the validity of the results.

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[9] F. A. Cotton, J. H. Fassnacht, W. D. Horrocks, Jr., and N. A. Nelson, *J. Chem. Soc.*, 4138 (1959).

[10] Deuterium analysis was performed by J. Nemeth, University of Illinois, Urbana, Ill.

Alkylation of 2-Carbethoxycyclopentanone in Dimethyl Sulfoxide[1]

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In the course of other work we had occasion to alkylate 2-carbethoxycyclopentanone. In general, alkylations of this β-keto ester are carried out in refluxing benzene or toluene,[2] solvents in which high molecular weight ion pair aggregates of the metal enolate are formed.[3] The reactivity of such aggregates is considerably less than that of the "free" enolate ion.[3] We have found that interaction of the potassium salt of 2-carbethoxycyclopentanone with an appropriate alkyl halide in dimethyl sulfoxide at room temperature (25–30°) provides good yields of alkylated keto ester and probably constitutes the best method of alkylating this β-keto ester.[2,4] Our results are summarized in Table I.

Rhoads[5] has found that alkylation of the sodium salt of 2-carbethoxycyclopentanone in dimethyl sulfoxide with isopropyl iodide led to appreciable O-alkylation. Our repetition of this work gave identical results. On the other hand we were unable to detect

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[1] We thank the donors of the Petroleum Research Fund administered by the American Chemical Society and the National Science Foundation for support of this research.

[2] H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, Inc., New York, N. Y., p 172; see also p 170, footnote 20.

[3] H. E. Zaugg, B. W. Horrom, and S. Borgwardt, *J. Am. Chem. Soc.*, **82**, 2895 (1960).

[4] See D. Martin, A. Weise, and H. J. Niclas, *Angew. Chem. Intern. Ed. Engl.*, **6**, 318 (1967), for leading references.

[5] S. J. Rhoads and R. W. Hasbrouck, *Tetrahedron*, **22**, 3557 (1966).

TABLE I
ALKYLATION OF METAL ENOLATE OF 2-CARBETHOXYCYCLOPENTANONE

Metal	Halide	Time, hr	Yield, %[a]	O-Alkylation, %[b]
K	$(CH_3)_2CHBr$	5	61	7
K	$(CH_3)_2CHI$	12	77	0
Na	$(CH_3)_2CHI$	3	78	15
K	$CH_3(CH_2)_2CH_2Br$	5	82	0
Na	$CH_3(CH_2)_2CH_2Br$	15	90	14
K	c-$C_6H_{11}Br$	11	40	~40
K	$BrCH_2CO_2Et$	1	94	0
K	$PhCH_2CH_2Br$	6	79	0

[a] Total yield of alkylated keto ester. [b] As per cent of total yield determined by glpc. Limit of detection <1%.

any O-alkylated product when the potassium salt was alkylated with isopropyl iodide. Use of isopropyl bromide, however, did result in some O-alkylation (see Table I).

Experimental Section[6]

The typical alkylation reaction is exemplified by the reaction described below.

2-(2-Phenylethyl)-2-carbethoxycyclopentanone.[7]—To 6.27 g (0.0268 mole) of the potassium salt of carbethoxycyclopentanone[8] in 50 ml of dry dimethyl sulfoxide was added dropwise 8.70 g (0.0536 mole) of freshly distilled 1-bromo-2-phenylethane. The resulting solution was allowed to stir at room temperature under a nitrogen atmosphere. After 6 hr, the reaction mixture was poured into water and extracted with pentane. The pentane extract was washed with water and dried over magnesium sulfate. Distillation afforded 5.27 g (78.8%) of 2-(2-phenylethyl)-2-carbethoxycyclopentanone, bp 90° (oil bath) at 0.1 torr.

2-(2-Phenylethyl)cyclopentanone.—A solution of 2.604 g (0.0103 mole) of 2-(2-phenylethyl)-2-carbethoxycyclopentanone in 100 ml of 3 *N* hydrochloric acid was refluxed for 24 hr. The reaction mixture was then poured into water and extracted several times with pentane. The pentane extracts were combined, washed with 10% sodium bicarbonate solution and then with water, and dried over magnesium sulfate. Distillation afforded 1.52 g (78.5%) of 2-(2-phenylethyl)cyclopentanone, bp 125° (oil bath) at 0.2 torr.

Registry No.—2-Carbethoxycyclopentanone, 611-10-9; dimethyl sulfoxide, 67-68-5; 2-(2-phenylethyl)-2-carbethoxycyclopentanone, 14721-43-8; 2-(2-phenylethyl)cyclopentanone, 14721-44-9.

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[6] The dimethyl sulfoxide was distilled from calcium hydride. Identification of products was based upon comparison of nuclear magnetic resonance and infrared spectra with those of the known 2-alkylcyclopentanones obtained by hydrolysis and decarboxylation, and, in appropriate cases, of the alkylated esters. We wish to thank the National Science Foundation for funds toward the purchase of a Varian A-60 nmr spectrometer and Crown Zellerbach Corp., Camas, Wash., for a generous gift of dimethyl sulfoxide.

[7] H. Adkins and G. F. Hager, *J. Am. Chem. Soc.*, **71**, 2965 (1949).

[8] R. Mayer, G. Wenschuh, and W. Topfelmann, *Chem. Ber.*, **91**, 1616 (1958). The commercial mixture of methyl and ethyl esters was used.

Transannular Aldol Condensation of Cyclododecane-1,6-dione and Cyclododecane-1,7-dione

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Cyclododecane-1,6-dione[1] and cyclododecane-1,7-dione have become readily available from the microbiological oxygenation of cyclododecanol.[2] Both diketones undergo ready transannular aldol condensation comparable to that reported for cyclodecane-1,6-dione.[3] Treatment of cyclododecane-1,7-dione with aqueous methanolic potassium carbonate at room temperature gave a 66% yield of 8-hydroxybicyclo[6.4.0]dodecan-2-one. The same condensation carried out under more vigorous conditions with sodium methoxide gave less pure product contaminated with a conjugated keto compound, presumably bicyclo[6.4.0]dodec-1(8)-en-2-one.

Treatment of cyclododecane-1,6-dione with methanolic sodium methoxide gave a mixture of three unsaturated ketones, one of which was nonconjugated and the others conjugated. Wolff–Kishner reduction of the mixture, followed by ozonolysis, afforded cyclododecane-1,7-dione and cyclododecane-1,5-dione,[2] suggesting that the structures of the two conjugated ketones are probably bicyclo[5.5.0]dodec-1(7)-en-2-one and bicyclo[7.3.0]dodec-1(9)-en-2-one. The third (nonconjugated) ketone is assumed to be a β,γ-unsaturated isomer of one of the conjugated ketones.

Experimental Section[4]

8-Hydroxybicyclo[6.4.0]dodecan-2-one.—Two grams of cyclododecane-1,7-dione dissolved in 100 ml of methanol and 20 ml of 10% potassium carbonate solution was allowed to stand in a covered beaker for 44 hr. The mixture was adjusted to pH 6–7 with 1 *N* hydrochloric acid and solvent was allowed to evaporate at room temperature to a final volume of 25–30 ml. After chilling at 0–5° the product was recovered and washed with cold water; yield 1.32 g, mp 70–71°. The infrared spectrum showed an extremely sharp hydroxyl absorption at 3500 and carbonyl absorption at 1685 cm^{-1}. Recrystallization from pentane did not change the melting point.

Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.56; H, 10.33.

When a solution of 0.30 g of cyclododecane-1,7-dione in 6 ml of methanol was heated on a steam bath for 10 to 135 min with 0.15 g of sodium methoxide, approximately 0.25 g of crude crystalline 8-hydroxy-bicyclo[6.4.0]dodecan-2-one, mp 52–58°, was obtained which showed a trace of ultraviolet absorption at 250 mμ and a weak infrared absorption (shoulder) at 1675 cm^{-1}, perhaps due to a trace of dehydration product.

Attempts to prepare the dehydration product by treating the 8-hydroxybicyclo[6.4.0]dodecan-2-one with *p*-toluenesulfonic acid resulted, even after a 3.5-hr reflux in benzene through a Dean–Stark trap, only in low conversions (λ_{max} 251 mμ (ϵ 4720)) to conjugated ketone.

Aldol Condensation of Cyclododecane-1,6-dione.—This condensation was conducted with sodium methoxide as described above for the 1,7-dione to give a mixture of (probably) bicyclo-[5.5.0]dodec-1(7)-en-2-one, bicyclo[7.3.0]dodec-1(9)-en-2-one, and a nonconjugated ketone. The infrared spectrum had maxima at 1710 (nonconjugated C=O), 1665, 1648 (conjugated C=O), and 1628 cm^{-1} (C=C).

The semicarbazone of the mixed ketones was prepared in the usual manner by heating the mixture at reflux with semicarbazide hydrochloride and sodium acetate in aqueous methanol. The twice recrystallized product melted at 192–195°; λ_{max}^{EtOH} 269 mμ (ϵ 19,850).

Anal. Calcd for $C_{13}H_{21}N_3O$: C, 66.35; H, 9.00; N, 17.86. Found: C, 66.29; H, 8.87; N, 17.52.

Hydrolysis of this semicarbazone with aqueous methanolic sulfuric acid gave a ketonic mixture with an infrared spectrum as described above.

Wolff–Kishner Reduction.—The aldol condensation product obtained from 1.88 g of 1,6-cyclododecanedione was refluxed for 1 hr with 15.0 ml of triethylene glycol, 1.5 ml of 99% hydra-

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[1] E. T. Niles and H. R. Snyder, *J. Org. Chem.*, **26**, 330 (1961).

[2] G. S. Fonken, M. E. Herr, H. C. Murray, and L. M. Reineke, *J. Am. Chem. Soc.*, **89**, 672 (1967).

[3] W. Hückel, R. Danneel, A. Schwartz, and A. Gercke, *Ann.*, **474**, 121 (1930); W. Hückel, A. Gercke, and A. Gross, *Ber.*, **66**, 563 (1933).

[4] Melting points were determined using a Fisher-Johns block. Florisil is a synthetic magnesium silicate product of the Floridin Co., Warren, Pa.