Stereochemical Aspects of Michael-type Additions to 5-t-Butylcyclohex-2-enone

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5-t-Butylcyclohex-2-enone undergoes Michael-type addition of methanol in the presence of 0·01M-sodium methoxide at 25°. At equilibrium the mixture comprises: 5-t-butylcyclohex-2-enone (57%), *trans*-3-methoxy-5-t-butylcyclohexanone (28%), and *cis*-3-methoxy-5-t-butylcyclohexanone (15%). From a kinetic study it is found that axial attack is favoured over equatorial attack by a factor (k_a/k_e) of 9. The axial adduct predominates over the equatorial adduct in the equilibrium mixture by a factor of 1·9. This is discussed in the light of related examples where relatively electronegative substituents show apparently anomalous axial preferences.

The base-catalysed addition of thiophenol to 5-t-butylcyclohex-2-enone has also been briefly investigated.

THE Michael reaction has been known for many years,[1] but few studies relevant to stereochemical aspects have been reported. In most cases where stereochemistry is considered,[2] and the configuration of the adduct has been determined, the mode of initial attack of the nucleophile cannot be deduced. One exception to this statement is the paper by Allinger and Riew [3] on the 1,4-addition of a methyl Grignard reagent to 5-methylcyclohex-2-enone, where the predominant product is *trans*-3,5-dimethylcyclohexanone considered to be formed by *anti*-parallel attack on the predominant (methyl equatorial) conformation of the conjugated ketone.

We have recently described our investigations on the base-catalysed addition of methanol to cycloalk-2-

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[1] E. D. Bergmann, D. Ginsburg, and R. Pappo, *Org. Reactions*, 1959, **10**, 179.

[2] *E.g.*, D. Ginsburg and R. Pappo, *J. Chem. Soc.*, 1951, 938; W. E. Bachmann and E. J. Fornefeld, *J. Amer. Chem. Soc.*, 1950, **72**, 5529; H. Pleininger and K. Schneider, *Chem. Ber.*, 1959, **92**, 1594; K. Alder and H. Wirtz, *Annalen*, 1956, **601**, 143; W. E. Truce and A. J. Levy, *J. Amer. Chem. Soc.*, 1950, **72**, 5529; R. A. Abramovitch and D. L. Struble, *Tetrahedron*, 1968, **24**, 357.

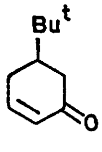
[3] N. L. Allinger and C. K. Riew, *Tetrahedron Letters*, 1966, 1269.

enones,[4] in the course of which it emerged that the equilibrium constant [3-methoxycyclohexanone]/[cyclohex-2-enone] for addition to cyclohex-2-enone was close to 1. It seemed therefore that a scrutiny of methanol addition to a conformationally biassed cyclohex-2-enone would be worthwhile, since both kinetic and thermodynamic stereochemical preferences should be determinable. The present paper deals with conjugate addition to 5-t-butylcyclohex-2-enone for which a kinetic *and* thermodynamic preference for axial adduct is found.

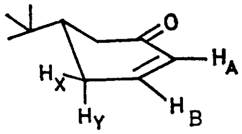
RESULTS

Preparation of 5-t-*Butylcyclohex*-2-*enone* (I).—Although the 2,4-dinitrophenylhydrazone of the ketone (I) had been obtained by Djerassi *et al.*[5] from the reaction of 2-bromo-5-t-butylcyclohexanone with 2,4-dinitrophenylhydrazine, this method did not appear convenient as a route to useful quantities of the ketone itself. We utilised the following sequence: allylic bromination of 4-t-butylcyclohexene[6] followed by hydrolysis of the mixed allylic bromides in aqueous acetone gave a mixture of allylic alcohols containing *trans*-5-t-butylcyclohex-2-enol[7] (60%) and *cis*-5-t-butylcyclohex-2-enol[8] (20%). Oxidation of the mixed allylic alcohols with chromic acid gave a mixture of two ketones in the ratio 4 : 1. The major component, 5-t-butylcyclohex-2-enone, was isolated and purified as its crystalline semicarbazone, followed by regeneration using pyruvic acid.

In the n.m.r. spectrum of 5-t-butylcyclohex-2-enone, the signal attributable to the proton at C-3 is an octuplet which is consistent with it being the B proton of an ABXY system. Of the three first-order coupling constants, the largest, 10·1 Hz, may be assigned to J_{AB}, while the remaining two, J_{BX} 5·9 and J_{BY} 2·2 Hz, correspond to vicinal vinyl-allylic dihedral angles[9] of *ca.* 25 and 90° respectively. Although these values are only approximate, they are most readily compatible with a ' sofa ' conformation for the molecule, *cf.* (II).



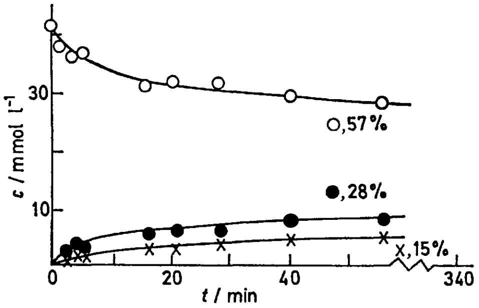
(I)



(II)

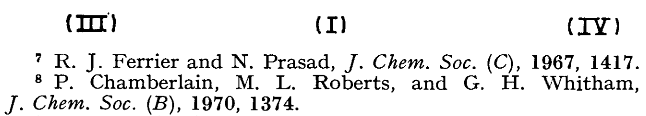
Addition of Methanol to 5-t-*Butylcyclohex*-2-*enone*.—Under conditions previously used for addition of methanol to cycloalk-2-enones (0·01M-sodium methoxide in MeOH at 25°)[4] the u.v. absorption maximum of ketone (I) at 226 nm diminished to an intensity 57% of the original value in the course of a few hours. Under preparative conditions, the reaction products were isolated, after acidification, and shown by t.l.c. to contain two new materials in addition to starting ketone. Chromatography on silica gel gave samples of each of the new products which had i.r. and n.m.r. spectra consistent with their expected structures as 5-t-butyl-3-methoxycyclohexanones. In the n.m.r. spectrum of the methoxy-ketone eluted second, absorption at τ 6·15 attributable to the proton α- to methoxy had band width, W 12·5 Hz typical of an equatorial proton.[10] Unfortunately the corresponding n.m.r. band in the other methoxy-ketone fell directly under the signal of the methoxy-group at τ 6·75 in CCl_4 solution, and no separation was achieved in benzene or pyridine as solvents. Since configurational assignments by n.m.r. band widths are unsatisfactory in the absence of comparable data for each diastereoisomer, we decided to confirm stereochemistry by direct correlation with compounds of known configuration. The method chosen was conversion of the methoxy-ketones in turn to the corresponding dithioacetals with ethanedithiol–BF_3, conditions which did not result in loss of methanol, followed by desulphurisation with Raney nickel. The methyl ethers obtained were identified by comparison with authentic samples of *cis*- and *trans*-3-t-butylcyclohexyl methyl ethers. In this way the methoxy-ketone eluted first on chromatography was identified as the equatorial methoxy-ketone (IV) the other being the axial isomer (III) as indicated previously by n.m.r. spectroscopy. With the configurational identity of the two methoxy-ketones now assured we could turn to a more quantitative study of methanol addition.

The course of the methanol addition to 5-t-butylcyclohex-2-enone could be followed by gas chromatography, giving the results shown in the Figure. The surprising feature thus emerges that not only is the *trans*-3-methoxy-5-t-butylcyclohexanone (axial methoxy) kinetically favoured but it also predominates at equilibrium. That a true equilibrium is in fact achieved was shown by establishment of the same equilibrium mixture from treatment of the *trans*-methoxy-ketone under the same conditions.



Addition of MeOH (0·053M in NaOMe) to 5-t-butylcyclohex-2-enone: ○, 5-t-butylcyclohex-2-enone; ●, *trans*-; ×, *cis*-3-methoxy-5-t-butylcyclohexanone

The following simplified kinetic scheme may be written for the system:



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[4] P. Chamberlain and G. H. Whitham, *J. Chem. Soc.* (*B*), 1969, 1131.

[5] C. Djerassi, E. Warawa, R. E. Wolff, and E. J. Eisenbraun, *J. Org. Chem.*, 1960, **25**, 917.

[6] J. Sicher, F. Sipos, and M. Tichy, *Coll. Czech. Chem. Comm.*, 1961, **26**, 847.

[7] R. J. Ferrier and N. Prasad, *J. Chem. Soc.* (*C*), 1967, 1417.

[8] P. Chamberlain, M. L. Roberts, and G. H. Whitham, *J. Chem. Soc.* (*B*), 1970, 1374.

[9] E. W. Garbisch, *J. Amer. Chem. Soc.*, 1964, **86**, 5561.

[10] N. C. Franklin and H. Feltkamp, *Angew. Chem. Internat. Edn.*, 1965, **4**, 774.

where k_e is the second-order rate constant for formation of the equatorial adduct from 5-t-butylcyclohex-2-enone, *etc.* These rate constants will apply irrespective of whether the addition is concerted, or, as is likely, involves an enolate ion as intermediate.[4] Values for k_{-a} and k_{-e} could be estimated by determining the initial rates of formation of the cyclohexenone starting from axial methoxy-ketone (III) and equatorial methoxy-ketone (IV) respectively. Hence knowing the respective equilibrium constants from the position of the overall equilibrium, the rate constants k_a and k_e for addition could be found. The following values were obtained: k_{-a}, 9·76 (±0·61); k_{e-}, 2·04 (±0·12); k_a, 4·79 (±0·29); k_e, 0·53 (±0·04) l mol^{-1} min^{-1}. The initial rate of disappearance of (I) should be given by:

$$-\mathrm{d}I/\mathrm{d}t = (k_a + k_e)[\mathrm{MeO}^-][\mathrm{I}]$$

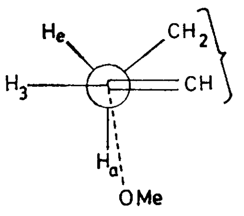
the rate constant $(k_a + k_e)$ determined in this was 5·53 (±0·02) which agrees well with the sum of the above values: 5·32 (±0·33).

Some preliminary experiments were also done on the sodium methoxide-catalysed addition of thiophenol to cyclohex-2-enone and 5-t-butylcyclohex-2-enone in methanol (see Experimental section). In the conformationally biassed system the two expected adducts were obtained in the ratio 4 : 1 and shown by n.m.r. to be respectively the isomers with axial and equatorial phenylthio-groups. A control experiment showed that a pure sample of the major adduct was unaffected by the conditions of the reaction. The product ratio in this case thus reflects directly the kinetic preference for axial *versus* equatorial attack of thiophenoxide ion and corresponds to $\Delta\Delta G^\ddagger$ of 0·8 kcal mol^{-1} compared to 1·3 kcal mol^{-1} found for addition of methoxide ion.

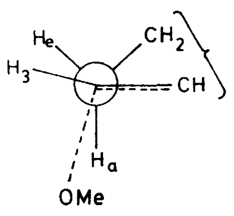
DISCUSSION

The two main points which emerge from the study of methoxide ion-catalysed addition of methanol to 5-t-butylcyclohex-2-enone at 25° are: (*a*) the ratio of rate constants for axial to equatorial attack (k_a/k_e) is 9·0 corresponding to $\Delta\Delta G^\ddagger = 1{\cdot}31$ kcal mol^{-1}, and (*b*) at equilibrium the axial adduct/equatorial adduct ratio is 1·9 corresponding to $\Delta G^\circ = 0{\cdot}38$ kcal mol^{-1}.

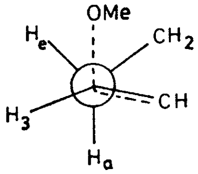
At least three factors *may* contribute to the preference for axial entry of the nucleophile. Firstly along the lines of the considerations of Allinger and Riew,[3] to the extent that the transition state is product-like, only axial attack *via* a chair transition state or boat axial attack in a twist-boat transition state maintain maximum orbital overlap. The former would be preferred on energetic grounds. Secondly, and this is analogous to Chérest and Felkin's [11] treatment for the preferred direction of attack at carbonyl for simple cyclohexanones, there will be torsional strain involving the partially formed C-3 · · · OMe bond and the C-4–H$_a$ bond which would destabilise a (reactant-like) transition state leading to the equatorial adduct [see (V)]. Thirdly, in so far as rehybridisation at C-3 has occurred at the transition state, an unfavourable 3-H, 4-H$_e$ torsional interaction will develop for equatorial attack [see (VI)] in contrast to relief of such torsional strain for axial attack (VII). The viewpoint here is similar to that of Garbisch [12] and Schleyer.[13] The relative importance of the above three factors in this system is insufficiently clear to warrant further discussion here.



(V)



(VI)



(VII)

On the basis of steric considerations alone, one would expect the axial β-methoxy-ketone (III) to be less stable than the equatorial isomer (IV). For methoxycyclohexanes the conformational free-energy difference ($-\Delta G^\circ$, $ax \longrightarrow eq$) is 0·6 kcal mol^{-1},[14] and although this might be reduced by *ca.* 0·14 kcal mol^{-1} (0·4 × 0·6/1·7) due to a ' 3-alkyl ketone effect ' for a β-methoxycyclohexanone [15] the equatorial preference, on steric grounds, should still be 0·46 kcal mol^{-1}. The axial preference found thus corresponds to an overriding factor of *ca.* 0·46 + 0·38 ≈ 0·85 kcal mol^{-1}.

A number of instances have been reported recently of 4-substituted cyclohexanones with a polar substituent where an apparently anomalous preference for the axial isomer (or conformer) is found.[16] A related steroid example has also been described.[17] In these examples it is postulated that dipole–dipole interactions between the polar substituent and the carbonyl group favour the axial form, and semiquantitative calculations suggest that these interactions are of roughly the right magnitude to explain the observations. Our results suggest that analogous polar interactions can stabilise an axial 3-methoxycyclohexanone. Owing to the conformational complexity of the methoxy-substituent however [different

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[11] M. Chérest and H. Felkin, *Tetrahedron Letters*, 1968, 2205.

[12] E. W. Garbisch, S. Schildcrout, D. B. Patterson, and C. M. Sprecher, *J. Amer. Chem. Soc.*, 1965, **87**, 2932.

[13] P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1967, **89**, 699, 701.

[14] J. A. Hirsch, *Topics Stereochem.*, 1967, **1**, 199.

[15] E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, ' Conformational Analysis,' Interscience, London, 1965, p. 114.

[16] R. D. Stolow and T. Groom, *Tetrahedron Letters*, 1968, 4069; R. D. Stolow, T. W. Giants, and P. D. McMaster, *Tetrahedron Letters*, 1968, 5781; R. D. Stolow and T. W. Giants, *Chem. Comm.*, 1971, 528; D. N. Kirk, *Tetrahedron Letters*, 1969, 1727; F. Loustalot, M. Loudet, S. Gromb, F. Metras, and J. Petrissans, *Tetrahedron Letters*, 1970, 4195.

[17] D. N. Jones, R. Grayshaw, and E. Kime, *J. Chem. Soc.* (*C*), 1969, 48.

rotameric arrangements about the C–O(Me) bond] it is difficult to make a plausible estimate of the magnitude expected for such an effect. In a recent discussion of a related phenomenon—the anomeric effect[18]—Wolfe *et al.* have emphasised that in conformational equilibria involving polar substituents, *syn*- and *anti*-periplanar orientations between adjacent polar bonds are disfavoured relative to *gauche*-interactions. If C-1, C-2 is considered to be a polar bond due to the effect of the C=O group, then our observations fit into this generalisation.

We have attempted to demonstrate a preference for the axial conformation of 3-methoxycyclohexanone itself from the n.m.r. spectrum. Although we were unsuccessful in observing signals due to two conformers in low-temperature spectra, the signal for the proton at C-3 had τ 6·4; *W* 18 Hz. Now the C-3-H for axial-3-methoxy-5-t-butylcyclohexanone (III) at τ 6·15 has *W* 12·5 Hz while *W* for the equatorial isomer (IV) can be estimated as 30 Hz. Using these figures as models for the two conformers of 3-methoxycyclohexanone, the averaged spectrum corresponds to an equilibrium comprising 69% axial methoxy and 31% equatorial. Again the preference for axial methoxy is demonstrated and the magnitude of the effect is closely similar to that derived above from direct equilibration in the biassed system.

Similar considerations of the n.m.r. spectrum of 3-phenylthiocyclohexanone and the two conformationally biassed 5-t-butyl analogues led to an estimate of 67% for the contribution of the conformer with the *equatorial* phenylthio-group. This corresponds to a conformational free-energy difference of 0·5 kcal mol^{-1} and may be compared with the value of 0·8 kcal mol^{-1} quoted for the phenylthio-group in the saturated cyclohexane system.[14] Clearly the 3-phenylthiocyclohexanone does not show the marked conformational anomaly which characterises the 3-methoxycyclohexanone, in line with the lower electronegativity of sulphur *versus* oxygen.

EXPERIMENTAL

G.l.c. columns of polyethylene glycol adipate, silicone oil, or G.E.O. 100 were employed and are designated in the text as (A), (B), or (C) respectively. N.m.r. spectra are for solutions in carbon tetrachloride unless otherwise stated (Perkin-Elmer R10, 60 MHz or R14, 100 Hz).

5-t-*Butylcyclohex*-2-*enone*.—*N*-Bromosuccinimide (162 g, 0·9 mol. equiv.) and 4-t-butylcyclohexene[6] (138 g, 1 mol. equiv.) were added to carbon tetrachloride (700 ml). Benzoyl peroxide (0·5 g) was added to the mixture which was then brought rapidly to reflux point on a water-bath. A vigorous exothermic reaction occurred (after *ca.* 5 min) which was completed by heating the mixture under reflux for 40 min by which time the *N*-bromosuccinimide had been converted into succinimide. The cooled reaction mixture was filtered and the carbon tetrachloride was evaporated to yield a crude mixture of allylic bromides.

The bromo-compounds were hydrolysed in water (150 ml) and acetone (500 ml) containing sodium hydrogen carbonate[19] (150 g) by heating them under reflux for 1 h with vigorous stirring. The precipitated salts were filtered off from the cooled mixture; the acetone was removed by evaporation from the filtrate and the product was isolated with ether. Evaporation of the dried ethereal solution followed by distillation gave unchanged olefin (13·5 g, 10%) and then alcohol mixture (106 g, 65% based on olefin), b.p. 100—123°/20 mmHg (lit.,[7] b.p. 100—110°/20 mmHg). G.l.c. (A) showed the presence of 20% *cis*- and 60% *trans*-5-t-butylcyclohex-2-enol. Three minor products of similar retention time were also present.

To the stirred mixture of t-butylcyclohex-2-enols (90 g) in acetone (700 ml) was added chromic acid (6N; 208 ml, 1·1 equiv.) during 1 h the temperature being maintained at 10—15° by cooling. After a further 15 min the upper layer was decanted and the acetone was evaporated. The residual solid was dissolved in water and the combined aqueous residues were extracted with ether. Evaporation of the dried ethereal layer gave a crude ketone mixture which was added to semicarbazide hydrochloride (90 g), sodium acetate (135 g), water (450 ml), and ethanol (600 ml). After being shaken vigorously for 15 min the reaction mixture was cooled in ice and the solid was filtered off. Recrystallisation from water–ethanol (3 : 7) gave 5-t-*butylcyclohex*-2-*enone semicarbazone* (29·1 g, 23%) as plates, m.p. 194—195° (Found: C, 63·0; H, 9·2; N, 20·2. $C_{11}H_{19}N_3O$ requires C, 63·1; H, 9·2; N, 20·0%).

The semicarbazone (13 g, 1 mol) was added to a mixture of sodium acetate (32 g), 57% pyruvic acid (24 g, 1 mol. equiv.), acetic acid (400 ml), and water (40 ml). The reaction mixture was heated on a water-bath for 1 h. It was then poured into water (1·5 l) and extracted with dichloromethane (3 × 200 ml). The organic phase was washed with sodium hydrogen carbonate and water and then dried ($MgSO_4$) and evaporated. Distillation yielded 5-*t-butylcyclohex*-2-*enone* (8·4 g, 86%), b.p. 62—65°/0·4 mmHg, n_D^{20} 1·4791 (Found: C, 78·9; H, 10·0. $C_{10}H_{16}O$ requires C, 78·75; H, 10·7%), $\nu_{max.}$ (liq. film) 2950 (C–H), 1665 (C=O), 1400, 1385 (Me_3C), 1260, 1240, 880, and 740 cm^{-1}; $\lambda_{max.}$ (EtOH) 226 nm (ε 9850); $\lambda_{max.}$ (cyclohexane) 219 nm (ε 8800); τ 9·05 (s, 9H, Me_3C) 7·5—8·3 (complex multiplet, 5H), 4·12 (doublet with fine splitting, 1H, 2-H), and 3·11 (eight-line multiplet, 1H, 3-H).

The 2,4-dinitrophenylhydrazone, recrystallised from ethanol, had m.p. 156—157°, $\lambda_{max.}$ ($CHCl_3$) 381 nm (ε 33,000) [lit.,[5] m.p. 155·5—156·5°, $\lambda_{max.}$ ($CHCl_3$) 383 nm (ε 23,000)].

cis- *and* trans-3-*Methoxy*-5-*t-butylcyclohexanones*.—5-t-Butylcyclohex-2-enone (8·3 g) was set aside overnight in 0·01M-sodium methoxide in methanol (900 ml). Dilute sulphuric acid was added to the mixture until the solution was pH 4·5. The bulk of the methanol was evaporated, water was added to the residue, and the product was isolated by ether extraction. The extract was dried ($MgSO_4$) and evaporated to dryness; the crude product was adsorbed on silica gel (500 g) from light petroleum and was then eluted with graded mixtures of light petroleum and ether. Evaporation of the fractions yielded successively starting material (2·6 g, 31%), *cis*-isomer (1·2 g, 13%), and *trans*-isomer (1·3 g, 14%), together with some mixed fractions (4%).

The crude *cis*-isomer was distilled under reduced pressure, b.p. 78—82°/0·25 mm. The product slowly crystallised with time. Recrystallisation at low temperature from

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[18] S. Wolfe, A. Rauk, L. M. Tel, and I. G. Csizmadia, *J. Chem. Soc.* (*B*), 1971, 136.

[19] N. Heap and G. H. Whitham, *J. Chem. Soc.* (*B*), 1966, 164.

light petroleum yielded plates of cis-3-*methoxy-5-t-butylcyclohexanone*, m.p. 36—37° (Found: C, 71·9; H, 11·0. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·95%), $\nu_{max.}$ (CCl_4) 2985 (C–H), 1720 (C=O), 1375 (Me_3C), 1125, 1105, and 1095 (C–O) cm^{-1}; τ 9·05 (s, 9H, Me_3C), 7·6—8·7 (complex multiplet, 6H), 7·4 (doublet with fine splitting, 1H), and 6·78 (s, 4H, CH_3OC-*H*).

A portion of the crude *trans*-isomer (0·28 g) was adsorbed on silica gel (25 g) from light petroleum. Elution with graded mixtures of light petroleum and ether yielded material (0·26 g) which was distilled under reduced pressure to give trans-3-*methoxy-5-t-butylcyclohexanone*, b.p. 76—80°/0·2 mmHg; one peak on g.l.c. (A) (Found: C, 71·2; H, 10·9. $C_{11}H_{20}O_2$ requires C, 71·7; H, 10·95%), $\nu_{max.}$ (CCl_4) 2980 (C–H), 1720 (C=O), 1375 (Me_3C), 1135, 1100, and 1080 (C–O) cm^{-1}; τ 9·05 (s, 9H, Me_3C), 7·4—8·2 (complex multiplet, 7H), 6·75 (s, 3H, CH_3O–), and 6·14 (m, 1H, CH_3OC-*H*).

cis-3-*t-Butylmethoxycyclohexane*.—To a stirred solution of *cis*-3-t-butylcyclohexanol[20] (0·39 g, 1 mol. equiv.) in dimethyl sulphoxide (30 ml; dried by distillation from calcium hydride) under nitrogen was added a 10% solution of butyl-lithium in hexane (2·0 ml, 1·2 mol. equiv.) followed by methyl iodide (1·5 ml). Stirring was continued until all the precipitated lithium alkoxide had dissolved to give a clear solution (*ca.* 2 h). The reaction mixture was then added to brine and the product was extracted with light petroleum. The extract was dried ($MgSO_4$) and the solvent was evaporated; distillation of the residue under reduced pressure yielded the product (0·21 g), b.p. 82—85°/12 mmHg, contaminated with some starting material.

A pure sample of cis-3-*t-butylmethoxycyclohexane* (Found: C, 77·05; H, 12·7. $C_{11}H_{22}O$ requires C, 77·55; H, 13·05%) was obtained by adsorption on silica gel (15 g.) from light petroleum and elution with graded mixtures of light petroleum and ether, $\nu_{max.}$ (liq. film) 2950 (C–H), 1475, 1375 (Me_3C), and 1100 (C–O) cm^{-1}; τ 9·07 (s, 9H, Me_3C), 7·9—9·0 (complex multiplet, 9H), 7·02 (m, 1H, *H*–C–OMe), and 6·75 (s, 3H, CH_3O–).

trans-3-*t-Butylmethoxycyclohexane*.—*trans*-3-t-Butylcyclohexanol (0·33 g), prepared by reduction of 3-t-butylcyclohexanone using the method of Henbest *et al.*,[21] was methylated under conditions identical to those used for the *cis*-isomer. The crude product was purified in an analogous manner to yield trans-3-*t-butylmethoxycyclohexane* (0·16 g), one peak on g.l.c. (B), b.p. 74—79°/11 mmHg (Found: C, 77·9; H, 12·8. $C_{11}H_{22}O$ requires C, 77·55; H, 13·05%), $\nu_{max.}$ (liq. film) 2950 (C–H), 1490, 1470, 1375 (Me_3C), 1120, and 1095 (C–O) cm^{-1}; τ 9·07 (s, 9H, Me_3C), 7·9—9·0 (m, 9H), 6·90 (s, 3H, CH_3O), and 6·36 (m, 1H, *H*–C–OCH_3).

3-*Methoxycyclohexanone Dithioacetal*.—3-Methoxycyclohexanone[4] (0·5 g) was dissolved in ethanedithiol (0·8 ml) and boron trifluoride–ether (0·4 ml) was added dropwise to it.[22] After 1 h the reaction mixture was adsorbed on silica gel (20 g) from light petroleum. Elution with 1% ether in light petroleum yielded a crude product (0·48 g). Distillation under reduced pressure yielded 3-*methoxycyclohexanone dithioacetal*, b.p. 150°/20 mmHg, homogeneous to t.l.c. (Found: C, 52·4; H, 8·4; S, 31·6. $C_9H_{16}S_2O$ requires C, 52·9; H, 7·9; S, 31·4%), $\nu_{max.}$ (liq. film) 2900 (C–H), 1450, and 1190 (C–O) cm^{-1}; τ 7·9—9·1 (m, 6H), 7·61 (m, 2H at C-2), 7·85 (m, 1H, CH_3OC-*H*), 6·76 (s, 3H, CH_3O–), and 6·72 (s, 4H, S–CH_2–CH_2–S).

cis-5-*t-Butyl*-3-*methoxycyclohexanone Dithioacetal*.—*cis*-3-Methoxy-5-t-butylcyclohexanone (0·52 g) was treated with ethanedithiol (0·7 ml) and boron trifluoride–ether (0·3 ml), and the product was isolated under conditions identical to those used for 3-methoxycyclohexanone dithioacetal. Distillation under reduced pressure yielded *cis*-3-methoxy-5-t-butylcyclohexanone dithioacetal (0·44 g, 54%) as a colourless viscous liquid, b.p. 124—129°/0·5 mmHg; $\nu_{max.}$ (liq. film) 2950 (C–H), 1470, 1375 (Me_3C), 1130, and 1095 (C–O) cm^{-1}; τ 9·07 (s, 9H, Me_3C), 7·3—9·0 (complex multiplet, 7H), 6·75—7·0 (m, 1H, MeOC-*H*), 6·76 (s, 3H, CH_3O), and 6·72 (s, 4H, S·CH_2CH_2·S).

trans-3-*Methoxy-5-t-butylcyclohexanone Dithioacetal*.—*trans*-3-Methoxy-5-t-butylcyclohexanone (0·51 g) was treated in a manner identical to that used for 3-methoxycyclohexanone dithioacetal. Trituration of the crude product from the column with methanol and recrystallisation from aqueous ethanol yielded *trans*-3-methoxy-5-t-butylcyclohexanone dithioacetal (0·61 g, 79%) as white crystalline plates, m.p. 74—75·5°, $\nu_{max.}$ (CCl_4) 2950 (C–H), 1370 (Me_3C), 1115, and 1085 (C–O) cm^{-1}; τ 9·07 (s, 9H, Me_3C), 7·1—9·0 (complex multiplet, 7H), 6·85 (s, 3H, CH_3O), 6·76 (s, 4H, S·CH_2CH_2·S), 6·5 (m, 1H, MeOC–H).

Desulphurisation of cis-3-*Methoxy-5-t-butylcyclohexanone Dithioacetal*.—*cis*-3-Methoxy-5-t-butylcyclohexanone dithioacetal (0·43 g) was heated under reflux with W.2. Raney nickel (*ca.* 5 g) in acetone (25 ml) for 3 h. Filtration of the mixture and evaporation of the solvent from the filtrate yielded a crude product which was shown by g.l.c. to contain one major product with a R_t value identical to that of *cis*-3-t-butylmethoxycyclohexane and two minor products (*ca.* 15% each) each with R_t values different from those of the two ethers.

The product was adsorbed on silica gel (18 g) from light petroleum. Elution with graded mixtures of light petroleum and ether yielded a pure sample of the major component which had an i.r. spectrum identical in all respects with that of *cis*-3-methoxy-t-butylcyclohexane. The identity of the compound was confirmed by peak enhancement of the product by authentic *cis*-isomer on g.l.c. (B) under conditions where a mixture of *cis*- and *trans*-isomers may be separated.

Desulphurisation of trans-3-*Methoxy-5-t-butylcyclohexanone Dithioacetal*.—*trans*-3-Methoxy-5-t-butylcyclohexanone dithioacetal (0·31 g) was treated under conditions identical to those used for the *cis*-isomer, to yield a crude product (0·17 g) which was shown by g.l.c. to contain two components in the ratio 5 : 1. The minor component had a R_t value different from those of the two authentic ethers.

Adsorption of the product on silica gel (26 g) from light petroleum and elution with graded mixtures of light petroleum and ether yielded a pure sample of the major product whose i.r. spectrum was identical in all respects with that of authentic *trans*-3-methoxy-t-butylcyclohexane. Peak enhancement on g.l.c. under conditions identical to those used for the *cis*-isomer confirmed the identity of the material as *trans*-methyl-3-t-butylcyclohexyl ether.

Monitoring of the Reaction of Methoxide Ion with 5-*t-Butylcyclohex*-2-*enone*.—The reaction was followed by g.l.c. (A). The relative response of the detector to the reactant and the two products was calibrated by injecting weighed mixtures of each with 2-methylnaphthalene which was used throughout the experiments as internal standard.

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[21] H. B. Henbest and T. R. B. Mitchell, *J. Chem. Soc.* (*C*), 1970, 785.

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Under the conditions used (100° for 15 min followed by an increase of 6°/min to 160°) the following data were obtained:

Compound	Relative R_t	Relative response/mol
2-Methylnaphthalene	1·07	1·00
5-t-Butylcyclohex-2-enone	1·00	0·79
cis-3-Methoxy-5-t-butyl-cyclohexanone	1·23	0·74
trans-3-Methoxy-5-t-butyl-cyclohexanone	1·29	0·74

(a) 5-t-Butylcyclohex-2-enone (1·448 g) and 2-methylnaphthalene (0·377 g) were dissolved in dry methanol and the volume made up to 250 ml. The flask was placed in a water-bath maintained at 25·0 ± 0·1°. When temperature equilibrium had been achieved, 25·0 ml of the solution was withdrawn and 25·0 ml of 0·106M-sodium methoxide in dry methanol was added as timing was commenced. At known intervals of time, 10-ml samples were withdrawn and added to dilute sulphuric acid, the solution being adjusted to pH 5. The solutions were filtered and the samples were analysed directly by g.l.c. The results (average of at least two injections) are plotted in the Figure.

Composition of equilibrium mixture; 5-t-butylcyclohex-2-enone: *cis*-3-methoxy-5-t-butylcyclohexanone: *trans*-3-methoxy-5-t-butylcyclohexanone: 57 : 15 : 28%.

(b) *trans*-3-Methoxy-5-t-butylcyclohexanone (21·8 mg) and 2-methylnaphthalene (12·2 mg) were dissolved in dry methanol (5·0 ml) and 0·106M-sodium methoxide (0·50 ml) was added to the solution. The reaction mixture was set aside in a water-bath at 25° for 48 h. Treatment with sulphuric acid and analysis by g.l.c. as before gave the results shown:

	Molar composition			
	Enone	*cis* Isomer	*trans* Isomer	Total
Initially	0	0	0·0217	0·0217
At equilibrium	0·0124	0·0030	0·0059	0·0213

Composition of equilibrium mixture; 5-t-butylcyclohex-2-enone : *cis*-3-methoxy-5-t-butylcyclohexanone : *trans*-3-methoxy-5-t-butylcyclohexanone: 58 : 14 : 28%.

Thus the reversibility of the reaction is established.

(c) 5-t-Butylcyclohex-2-enone (40·9 mg) and 2-methylnaphthalene (26·2 mg) were dissolved in dry methanol (10 ml) and the mixture was set aside in a water-bath at 25° for 60 h. After this time, analysis was carried out as before:

	Molar composition			
	Enone	*cis*-Isomer	*trans*-Isomer	Total
Initially	0·0269	0	0	0·0269
At equilibrium	0·00273	0	0	0·0273

Hence there is no uncatalysed reaction.

Rate Measurements.—The spectrometer was set at the wavelength of maximum absorption of 5-t-butylcyclohex-2-enone (226 nm) and read zero absorption when both cells (1 cm, stoppered to keep out moisture) contained methoxide ion solution of the concentration used in the experiment.

An aliquot (2·00 ml) of the standard solution of *cis*-3-methoxy-5-t-butylcyclohexanone in dry methanol was placed in the solution cell. The solvent cell contained 2·00 ml of dry methanol. The cells were set aside in the cell-compartment for 30 min to attain temperature-equilibrium and equal volumes of 0·116M-sodium methoxide (previously stored in a flask in the water-bath) were added to both cells. Timing was commenced on addition of the methoxide ion to the solution cell and the change in absorbance was measured on the recorder chart which moved at the uniform speed of 15 in/h. The initial slope of the resultant curve was measured by drawing a tangent. The experiment was repeated using different volumes of the sodium methoxide solution.

Similar experiments were carried out using *trans*-3-methoxy-5-t-butylcyclohexanone and 5-t-butylcyclohex-2-enone as substrates. The initial rate constants derived are given in the Results section.

Addition of Thiophenol to Cyclohex-2-enone.—To cyclohex-2-enone (0·54 g, 1 mol. equiv.) and thiophenol (0·65 ml, 1·1 mol. equiv.) in dry methanol (150 ml) was added 0·1M-sodium methoxide (2·5 ml). After 2 h at room temperature, the solution was neutralised with hydrochloric acid and the volume of methanol was reduced by evaporation. The concentrated solution was added to water and the product was isolated by extraction with ether. The ethereal layer was washed with M-sodium hydroxide and water, dried ($MgSO_4$), and evaporated to yield the crude product (1·05 g, 91%).

Distillation of a sample of product yielded 3-phenylthiocyclohexanone, b.p. 152—154°/0·4 mmHg, homogeneous to t.l.c.; $\nu_{max.}$ (liq. film) 3040 (C–H aromatic), 2950 (C–H), 1710 (C=O), 1580 (aromatic), 1485, 1450, 1320, 1220, 750, and 700 (monosubstituted aromatic) cm^{-1}; τ 7·2—8·5 (complex multiplet, 8H), 6·6 (m, *W* 28 Hz, 1H at C-3), 2·7 (m, 5H, aromatic).

Addition of Thiophenol to 5-t-Butylcyclohex-2-enone.—5-t-Butylcyclohex-2-enone (1 g) was treated with thiophenol under conditions identical to those used for cyclohex-2-enone to yield a crude mixture of *cis*- and *trans*-phenylthiocyclohexanones (1·33 g, 78%).

Recrystallisation from light petroleum ether yielded a sample of trans-5-*t-butyl*-3-*phenylthiocyclohexanone* (0·32 g), m.p. 57—58°, homogeneous to t.l.c. (Found: C, 73·25; H, 8·45; S, 12·2. $C_{16}H_{22}SO$ requires C, 73·45; H, 8·5; S, 12·6%), $\nu_{max.}$ (CCl_4) 3080 (C–H aromatic), 2960 (C–H), 1725 (C=O), 1485, 1445, 1375 (Me_3C) and 1020 cm^{-1}; τ 9·1 (s, 9H, Me_3C), 7·4—8·9 (complex multiplet, 7H) 6·15 (m, *W* 12·5 Hz, 1H at C-3), 2·7 (m, 5H, aromatic).

The mother-liquor was adsorbed on silica gel (30 g) from light petroleum. Elution with graded mixtures of light petroleum and ether yielded *cis*-5-t-butyl-3-phenylthiocyclohexanone (105 mg) (followed by *trans*-isomer), homogeneous to t.l.c. $\nu_{max.}$ (CCl_4) 3080 (C–H aromatic), 2960 (C–H), 1725 (C=O), 1480, 1440, 1375 (Me_3C), and 1310 cm^{-1}; τ 9·1 (s, 9H, Me_3C), 7·3—8·9 (complex multiplet, 7H), 6·7 (m, *W* 30 Hz, 1H at C-3), and 2·7 (m, 5H, aromatic).

Integration of the signals of the proton α to the phenylthio-group showed that the original mixture contains 20% *cis*- and 80% *trans*-isomer.

trans-5-t-Butyl-3-phenylthiocyclohexanone was recovered unchanged after 3 h in the reaction mixture, showing that the reaction is irreversible.

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