Preparation of *trans,trans,trans,cis*- and *trans,trans,trans,trans*-Tricyclo[7.3.1.0^{5,13}]tridecan-3-ols and Acetolysis of the corresponding Toluene-*p*-sulphonates

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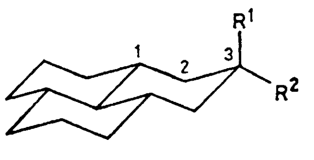
The epimeric *trans,trans,trans*-tricyclo[7.3.1.0^{5,13}]tridecan-3-ols and their corresponding toluene-*p*-sulphonates have been produced in the first stereospecific general synthesis of this all-*trans*-carbocyclic system of fused cyclohexane rings; both toluene-*p*-sulphonates are less reactive than the t-butylcyclohexyl and *trans*-β-decalyl analogues (but not by large factors), but their epimeric rate ratio is the same and the rates and the axial:equatorial epimeric rate ratios of these cyclohexyl toluene-*p*-sulphonates which are undistorted in their conformational ground states are much lower than for bridged cyclohexyl analogues.

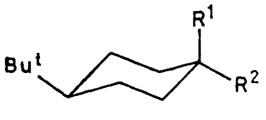
Remote bulky substituents have been used as conformational locks for cyclohexane derivatives,[1] and this device was successful for elucidating the relationship between the equatorial or axial disposition of an amino-group and the product distribution from deamination.[2] Product ratios,[3,4] rates of reaction,[1,5,6] and secondary deuterium kinetic isotope effect measurements,[5,6,7] for several cyclohexane systems, however, appear to require mechanisms which involve reactions *via* non-chair (*i.e.* non-ground state) conformers if the leaving group is equatorial in the conformational ground state. Consequently, virtually nothing is known with any certainty of the reactivity of unambiguously equatorial leaving groups in solvolytic reactions of simple cyclohexyl halides and arenesulphonates.

Provisional molecular mechanics calculations[8] indicated that the ground-state conformer of all-*trans*-tricyclo[7.3.1.0^{5,13}]tridecane[9] (**1a**) is not significantly more strained than cyclohexane itself, nor is the carbocyclic system distorted from regular cyclohexane geometry. In contrast, the conformer with a single boat form (**1a′**) is appreciably more strained than

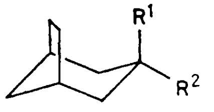


(1) a, $R^1 = R^2 = H$
b, $R^1 = OTs, R^2 = H$
c, $R^1 = H, R^2 = OTs$
d, $R^1 = OH, R^2 = H$
e, $R^1 = H, R^2 = OH$

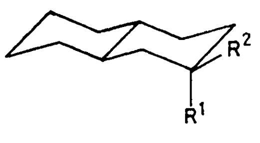
(1a')



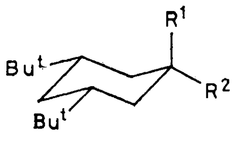
(2) a, $R^1 = OTs, R^2 = H$
b, $R^1 = H, R^2 = OTs$



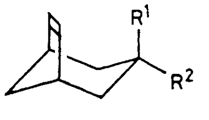
(3) a, $R^1 = OTs, R^2 = H$
b, $R^1 = H, R^2 = OTs$



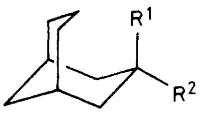
(6) a, $R^1 = OTs, R^2 = H$
b, $R^1 = H, R^2 = OTs$



(7) a, $R^1 = OTs, R^2 = H$
b, $R^1 = H, R^2 = OTs$



(8) a, $R^1 = OTs, R^2 = H$
b, $R^1 = H, R^2 = OTs$



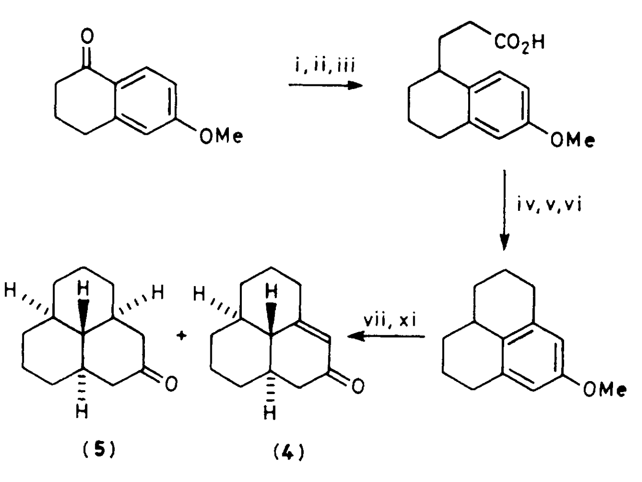
(9) a, $R^1 = OTs, R^2 = H$
b, $R^1 = H, R^2 = OTs$

OTs = $OSO_2C_6H_4Me$-*p*

its simple cyclohexane analogue. Moreover, molecular models suggest that single twist conformers in this tricyclic system, as in bicyclo[3.2.1]octanes, do not appear to correspond to local energy minima. The position is the other way round for monocyclic cyclohexanes: twist conformers correspond to minima whereas boat forms do not. It appeared, therefore, that the all-*trans*-tricyclo[7.3.1.$0^{5,13}$]tridecane system with epimeric leaving groups at position 3 provides a better model for axial *vs.* equatorial leaving groups than any system previously used. And if non-chair conformers are less accessible in this system, the solvolytic rate ratio for the compound with an axial toluene-*p*-sulphonate group (**1b**) and its equatorial epimer (**1c**) should be larger than that for the t-butylcyclohexyl toluene-*p*-sulphonates, (**2a**):(**2b**). The beginnings of such a trend appeared evident from the epimeric-rate ratio for (**3a**):(**3b**) compared with that for (**2a**):(**2b**).

The parent hydrocarbon (**1a**) and various substituted and unsaturated derivatives are known[10] but no versatile general synthesis, particularly of 3-substituted compounds, has been reported. We have developed such a procedure as shown in Scheme 1; compounds (**1b**)—(**1e**), (**4**), and (**5**) gave sharp melting points unchanged by further recrystallization or sublimation. Structural assignments are based upon the crystal structure of (**4**),[11] the ^{13}C n.m.r. spectra of compounds (**5**), (**1d**), and (**1e**), the ^1H n.m.r. spectra of (**1b**)—(**1e**), high resolution mass spectra of (**1d**), (**1e**), (**4**), and (**5**), and chemical interconversion of (**1d**), (**5**), and (**1e**).

Rate constants and activation parameters for the acetolysis of (**1b**) and (**1c**) are shown in Table 1 and compared with results for related compounds in Table 2. Two features are immediately evident. First, (**1c**) is less reactive than the unbridged cyclohexyl toluene-*p*-sulphonates (**2b**), (**6b**), and (**7b**) with ground state equatorial leaving groups, but not by a large factor. Surprisingly, however, (**1b**) is also less reactive than axial toluene-*p*-sulphonates (**2a**), (**6a**), and (**7a**) with the consequence that the epimeric reactivity ratio of (**1b**):(**1c**) is virtually the same as the values for (**2a**):(**2b**), (**6a**):(**6b**), and (**7a**):(**7b**). The anticipated divergence in rate ratio along the series (**2a**):(**2b**), (**3a**):(**3b**), and (**1b**):(**1c**) has not, therefore, been found. Secondly, the reactivities and the common epimeric axial:equatorial rate ratios of the unbridged compounds (**1b,c,**) (**2a,b**), (**6a,b**), and (**7a,b**) are significantly different from corresponding results for the bridged systems (**3a,b**), (**8a,b**),



$$(4) \xrightarrow{\text{x, v}} (5) + (1e)$$
$$(5) \xrightarrow{\text{viii, v}} (1d) + (1e), (85:15)$$
$$(5) \xrightarrow{\text{iv, v}} (1d) + (1e), (18:82)$$
$$(1e) \xrightarrow{\text{ix}} (1c)$$
$$(1d) \xrightarrow{\text{ix}} (1b)$$

Scheme 1. i, diethyl succinate, $KOBu^t$, $HOBu^t$, N_2; ii, H_3O^+, $MeCO_2H$, reflux; iii, H_2 (4 atm.), 10% Pd–charcoal; iv, $LiAlH_4$, Et_2O; v, H_3O^+, 25 °C; vi, Amberlyst 15, petroleum (b.p. 90—100 °C), reflux; vii, Li, NH_3, EtOH; viii, L-Selectride; ix, *p*-$MeC_6H_4SO_2Cl$, pyridine; x, Li, NH_3, NH_4Cl; xi, H_3O^+, tetrahydrofuran.

Table 1. Rate constants[a] and activation parameters for the buffered acetolysis[b] of (**1b**) and (**1c**).

Compound	$10^6\,k/s^{-1}$	(T/°C)	$\Delta H^\ddagger$/kJ mol^{-1}	$\Delta S^\ddagger$/J K^{-1} mol^{-1}
(**1c**)	78.9 ∓ 1.4	(91.28)	118[d]	−1[e]
	13.7 ∓ 0.1	(75.93)		
	4.08 ∓ 0.03	(66.14)		
	0.0111[c]	(25.00)		
(**1b**)	209 ∓ 1	(91.25)	112[d]	−8[e]
	64.3 ∓ 0.3	(80.30)		
	15.4 ∓ 0.1	(67.91)		
	0.0447[c]	(25.00)		

[a] Rate constants quoted are mean values of duplicate parallel runs and quoted errors are equal to, or greater than, the difference between the mean and the upper and lower measured values. Standard deviations on individual rate constants measured by our previously described method[5,6,12] were always less than 0.5%; the standard deviation on the temperature measured throughout each run was 0.016—0.078 °C depending upon the length of the run. [b] $MeCO_2H$, 0.05 M in $MeCO_2Na$. [c] Estimated from the results at higher temperatures. [d] Estimated error, ≤ ∓3 kJ mol^{-1}. [e] Estimated error, ≤ ∓7 J K^{-1} mol^{-1}.

Table 2. Relative rate constants for the acetolysis of modified cyclohexyl toluene-*p*-sulphonates at 50 °C ($C_6H_{11}OSO_2C_6H_4Me$ = 1.00)[1]

Axial ground state leaving group	**(1b)** 0.891	**(6a)** 1.34[a]	**(2a)** 2.62[b]	**(7a)** 3.71[c]	**(3a)** 61.2[d]	**(8a)** 66.0[e]	**(9a)** 5400[f]
Equatorial ground state leaving group	**(1c)** 0.263	**(6b)** 0.412[a]	**(2b)** 0.809[b]	**(7b)** 1.03[c]	**(3b)** 5.31[d]	**(8b)** 4.43[e]	**(9b)** 620[f]
Axial : equatorial rate ratio	3.4	3.3	3.2	3.6	12	15	8.7

[a] Ref. 13. [b] Ref. 1. [c] Ref. 14. [d] Ref. 15. [e] Ref. 16. [f] Ref. 17.

and (**9a,b**). (The exceptional reactivity of the bicyclo[3.3.1]-nonan-3-yl toluene-*p*-sulphonates in particular requires explanation.)

We have considered but rejected the most obvious explanation of our results, *i.e.* that non-rigid cyclohexyl toluene-*p*-sulphonates with ground-state equatorial leaving groups react *via* their ground-state conformations. Such a mechanism cannot satisfactorily account for either the product distributions or the secondary deuterium kinetic isotope effects which have been established in the 4-t-butylcyclohexyl and bicyclo-[3.2.1]octan-3-yl systems.[3–7]

Our detailed interpretation of these solvolysis results in terms of (i) reactions of (**1b**) from its ground-state conformation *via* reversible ionization and rate-determining subsequent reaction of the intimate ion-pair, and (ii) rate-determining ionization of (**1c**) *via* a non-chair conformation followed by (parallel) rapid product-determining steps will be discussed in a later report.

Received, 3rd November 1982; Com. 1256

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