The Stereochemistry of Enolate Alkylation of 4a-Methyl-*trans*-2-decalone Systems

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Summary The stereochemistry of enolate alkylation observed in two simple decalones is discussed in terms of the n.m.r. solvent shifts.

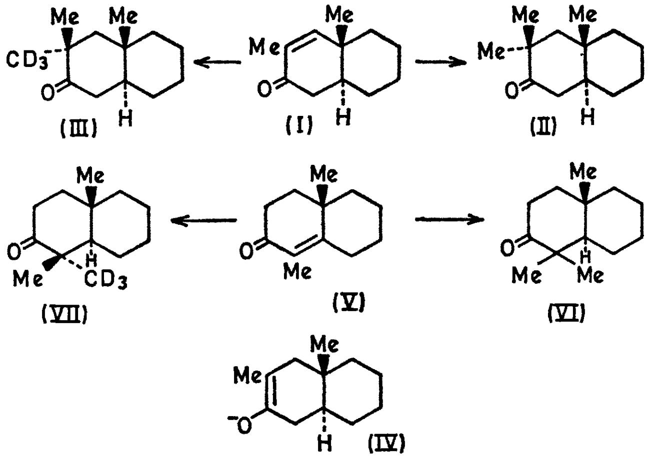
THE problem of predicting the stereochemical outcome of enolate alkylations in which quaternary carbon atoms are generated is of crucial importance in the synthesis of polycyclic natural products. We report the first alkylation data on the β-decalone system.[1]

Ketone (I) was synthesized[2] by the usual bromination–dehydrobromination sequence and then reductively alkylated[3] with methyl iodide. The resulting mixture of products could be separated by preparative g.l.p.c. (SE 30, 10 ft., 120°) to provide pure (II) [i.r. (film) 5·85 μm].

The 60 MHz n.m.r.[3] spectrum of (II) in $CHCl_3$ displayed 3 singlets at 61 (3H), 64 (3H), and 71 (3H) Hz: and in C_6H_6, 2 singlets, at 44 Hz (3H) and 64 Hz (6H).

Bhacca and Williams[4] have studied such solvent shifts and have shown them to be related to stereochemical environment. The data given above can be interpreted to mean that the two methyl signals at 61 Hz and 71 Hz ($CHCl_3$) represent axial methyl groups while the signal at 64 Hz which did not shift can be assigned to the equatorial methyl.†

A repetition of the above experiment using CD_3I in place of CH_3I produced a similar mixture from which could be isolated the ketone (III):‡ n.m.r. identical to that of (II) but without the 64 Hz singlet. Since this peak corresponded to the equatorial methyl we have demonstrated that alkylation of enolate (IV) takes place from the α-side exclusively.§ In order to determine the possible position dependence of this result the same type of experiment was tried on the known ketone[5] (V). Reductive alkylation¶ of (V) with CH_3I gave after extensive chromatography the pure ketone (VI) (n.m.r. data in Table). By the argument given above the equatorial methyl signal can be assigned. The repetition of this experiment with CD_3I in place of CH_3I gave a mixture from which could be isolated the ketone (VII) whose n.m.r. spectrum showed the almost complete absence of the signal at 64 Hz. Integration of the spectrum indicated the presence of *ca.* 7%[6] of the α-equatorial Me remaining. These results are mutually consistent and are



60MHz *N.m.r. data*

	Chloroform			Benzene solvent shift in Hz [$\delta(CHCl_3)$ − $\delta(C_6H_6)$]		
Ketone	Angular Methyl	C-4 Methyl	C-2 Methyl	Angular Methyl	C-4 Methyl	C-2 Methyl
(II)	67	*ax* 61 *eq* 64		17	*ax* 11 *eq* −1	
(III)	67	*ax* 61 *eq* —		17	*ax* 11 *eq* —	
(VI)	61		*ax* 71 *eq* 64	17		*ax* 7 *eq* 0
(VII)	61		*ax* 71 *eq* —	17		*ax* 7 *eq* 0

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† An investigation of the solvent shifts in variously substituted decalones containing 1,3-diaxial methyl–methyl interaction has been conducted in our laboratories. It has been shown that the distortion thus introduced into the ring system does not invalidate the solvent shift results in such cases.

‡ The i.r. spectra of (VI) and (VII) were very much the same; the most striking difference was the presence in (VII) of a strong band at 4·5 μm (CCl_4). The C=O frequencies were the same in both cases, *i.e.* 5·85 μm:(VI)*m*/*e* = 194, (VII)*m*/*e* = 197.

§ The precision of the integration of 60 MHz spectra is in our hands only accurate to about 5%. Therefore all ratios reported are understood to be ±5% in accuracy.

¶ The reduction of (V) as described in ref. 3 in our hands produced a complex mixture of products from which could be isolated in poor yield and pure (VI). The n.m.r. of (VI) is not the same as published in ref. 3, since our spectra are taken in $CHCl_3$ whereas those for (VI) in ref. 3 were taken neat. We thank Professor G. Stork for his help in clearing up this problem and providing advice on the reductive alkylation. We have noticed that the spectra of (VI) are very solvent dependent. Thus a CCl_4 spectrum of (VI) shows singlets (3H) at 58, 61, 67 Hz: i.r. (CCl_4) 5·85 μm; *m*/*e* 194; (VII) i.r. (CCl_4) 4·5, 5·85 μm; *m*/*e* 197.

in agreement with certain non-reductive alkylations of Δ^4-3-oxo-steroids.[6]

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[1] For alkylation of some simple related systems see: W. S. Johnson, *J. Amer. Chem. Soc.*, 1962, **84**, 2182, and references cited therein; H. O. House, B. A. Tefertiller, and H. D. Olmstead, *J. Org. Chem.*, 1968, **33**, 935; H. O. House and W. F. Fischer, jun., *ibid.*, p. 949; F. J. McQuillen and R. B. Yeats, *J.Chem. Soc.*, 1965, 4273.

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