Stereochemistry of the S_N2' Reaction with Acyclic Allylic Esters

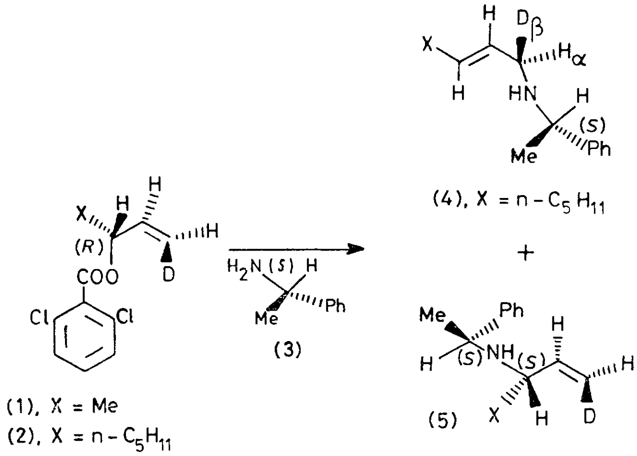
By TAKAYUKI ORITANI and KARL H. OVERTON*

(*Department of Chemistry, The University of Glasgow, Glasgow* G12 8QQ)

Summary Aminolysis of (*R*)- or (*S*)-α-methyl[γ-^{2}H]allyl (**1**) or α-n-pentyl[γ-^{2}H]allyl (**2**) 2,6-dichlorobenzoates with (*R*)- or (*S*)-α-methylbenzylamine (**3**) favours *syn* over *anti* displacement by a factor of 1·4—1·8.

WE and others have recently reported on the stereochemistry of the S_N2' reaction with cyclohex-2-enyl esters.[1,2] Lest the results obtained reflect special constraints operating in cyclohexenyl systems, we have investigated and now report our findings with acyclic allylic esters.[3]

We have subjected the deuteriated optically pure (*R*)- and (*S*)-esters (**1**)† and (**2**)† to aminolysis by (*R*)- or (*S*)-α-methylbenzylamine (**3**).† Only two major products were formed: (**4**) (S_N2') and (**5**) (S_N2). The case of *syn* attack by the (*S*)-amine upon the (*R*)-ester is illustrated; the epimeric D configuration would result from either *anti* displacement of the (*R*)-ester or *syn* displacement of the (*S*)-ester. Decisively, the ratio of $\mathrm{CD}_\beta H_\alpha : \mathrm{CD}_\alpha H_\beta$ in (**4**) and hence of *syn* : *anti* displacement (if both were to operate in the S_N2' reaction could be directly determined by n.m.r. spectroscopy.



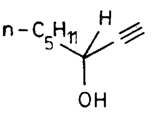
(1), X = Me

(2), X = n-C_5H_{11}

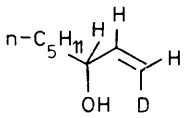
(3)

(4), X = n-C_5H_{11}

(5)



(6)



(7)

(*R*)- and (*S*)-Oct-1-yn-3-ols (**6**), $[\alpha]_D$ ($CHCl_3$): (*R*), +8·4°; (*S*), −8·6° {resolved *via* the phthalate half ester salts with (*R*)- or (*S*)-(**3**), m.p. and $[\alpha]_D$ (C_6H_6) : (*RR*)-salt, 52—53 °C, +33·5°; (*SS*)-salt, 53—53·5 °C, −34°} were reduced ($LiAlH_4$-tetrahydrofuran, then D_2O[4]) to the (*R*)- and (*S*)-[1-^{2}H]oct-1-en-3-ols (**7**), oils, $[\alpha]_D$ ($CHCl_3$): (*R*), +10·3°; (*S*), −10·0° (Lit.[5] −5·5°), and converted (Bu^nLi–pentane, ArCOCl) into the (*R*)- and (*S*)-2,6-dichlorobenzoates (**2**),† oils, $[\alpha]_D$ (C_6H_6): (*R*), +6·8°; (*S*), −6·9°, which were shown by n.m.r. spectroscopy {$CDCl_3$, $Eu(hfc)_3$ shift reagent: tris-[3-heptafluoropropylhydroxymethylene)-(+)-camphorato]europium} to be optically pure (>98%) with D exclusively *cis* to the hexanol chain.

Aminolysis of (*R*)-(**2**) with (*S*)-(**3**) (130—140 °C, 72 h, sealed tube) afforded an amine mixture (46% theory) consisting (g.l.c., 5% Carbowax 20M + 1% KOH, 140 °C) of (**4**) (S_N2' product, mixture of D_α and D_β, see below) (77%), (**5**)‡ (S_N2 product, 19%), 3-*epi*-(**5**)‡ (S_N1 product, 1%) and the *cis*-isomer of (**4**)‡ (3%). Recovered ester (*R*)-(**2**) (37%) was free (<1%) from (*S*)-(**2**) (n.m.r., $CDCl_3$ + 0·4M THFC-Eu). Allylically rearranged ester was not formed in excess of 3% (g.l.c., n.m.r. comparison with authentic samples) under the reaction conditions or when (*R*)-(**2**) was heated to reflux in xylene or xylene containing CF_3CH_2OH (3 equiv.) for 48 h. Furthermore, the amine (**4**) was not aminolysed by (**3**) under the reaction conditions [(*S*)-α-methylbenzylamino-(**4**) was unchanged (n.m.r.) when heated at reflux with (*R*)-(**3**)]. The n.m.r. spectrum [100 MHz; $CDCl_3$ + 0·1M $Eu(dpm)_3$] of (**4**) had δ4·42 (0·38H, $CH_\beta D_\alpha$) and 4·58 (0·62H, $CH_\alpha D_\beta$), showing a 3 : 2 preference for *syn* displacement (see below). Analogous aminolyses led to comparable results as follows: (*S*)-(**2**) + (*S*)-(**3**): δ4·16 (0·62H, $CH_\beta D_\alpha$) and 4·50 (0·38H, $CH_\alpha D_\beta$); (*S*)-(**2**) + (*R*)-(**3**): δ 4·28 (0·41H, $CH_\alpha D_\beta$) and 4·70 (0·59H, $CH_\beta D_\alpha$); (*R*)-(**1**) + (*R*)-(**3**): δ4·17 (0·64H, $CH_\alpha D_\beta$) and 4·57 (0·36H, $CH_\beta D_\alpha$).

A reference sample of (**4**) containing an excess of $CH_\alpha D_\beta$ was prepared *via* asymmetric reduction of crotonaldehyde with deuteriated isobornyloxymagnesium bromide.[6] The tosylate of the resulting (*R*)-[1-^{2}H]but-2-en-1-ol was aminolysed with (*R*)- or (*S*)-(**3**). The amines (**4**) produced showed in the n.m.r. spectrum [*ca.* 0·1M $Eu(dpm)_3$]: from (*R*)-(**3**) δ4·32 (0·63 $CH_\alpha D_\beta$) and 4·77 (0·37 $CH_\beta D_\alpha$) and from (*S*)-(**3**) δ4·40 (0·35 $CH_\beta D_\alpha$) and 4·81 (0·65 $CH_\alpha D_\beta$).

In five experiments, changing the chirality of (**1**) and (**2**) and the X group of (**1**), the S_N2' product (**4**) was the result of preferred *syn* displacement by a factor of *ca.* 1·4—1·8. The difference in the activation energies for *syn* and *anti* displacement in this system cannot therefore be in excess of 500 cal mol^{-1}. It is reasonable on this basis to assume that the recently established[7] *syn* geometry for the S_N' reaction of α-methylallyl chloride with diethylamine reflects the more effective hydrogen bonding between the amine and the allylic chlorine, resulting in the appropriate orientation for *syn* attack, as suggested long ago by Winstein and Young.[8] In contrast, an intramolecular variant (S_N2') of the systems reported in this paper and in ref.7, but employing a charged nucleophile (RS^-), reacts as in (**8**) → (**9**) and entirely with *anti* geometry.[9]

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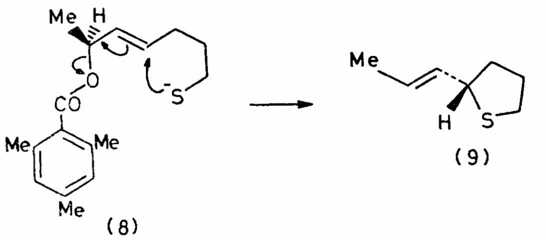
† One antipode is shown.

‡ G.l.c. comparison with authentic samples.



(8) (9)

It becomes apparent that, contrary to the long-held view that $\mathrm{S_N}2'$ reactions proceed with *syn*-stereochemistry, the whole spectrum spanned by the *syn* and *anti* extremes is to be expected depending, in any particular case, on the nature of the displacing and displaced groups, counterions, and solvent.

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