

Highly Diastereoselective Addition Reactions of a Radical Derived from a β -Ethoxycarbonyl Sulphoxide

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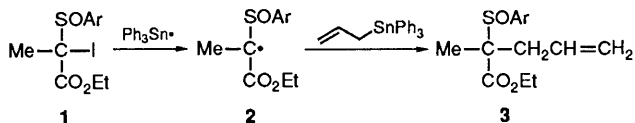
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The 1-ethoxycarbonyl-1-*p*-tolylsulphinylethyl radical **2**, generated by iodine abstraction from **1**, adds to the alkenic bond in allyltriphenylstannane or in hex-1-ene with very high diastereoselectivity (>98%).

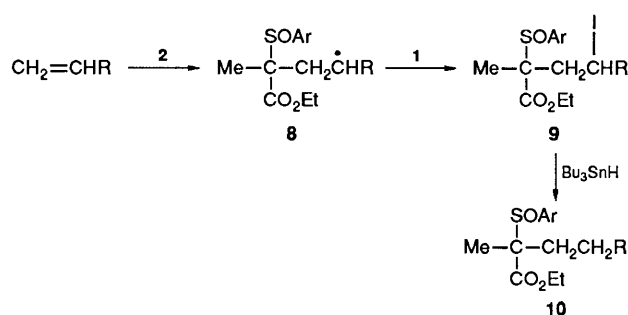
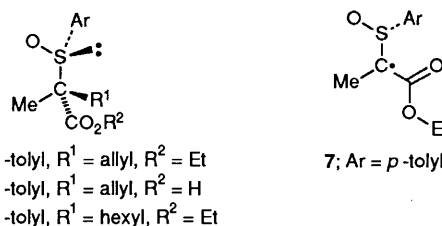
The recognition¹ that radical reactions can be conducted with high chemo- and regio-selectivity has stimulated the development of a variety of useful new synthetic methods.² Recently, attention has focused on the stereochemistry of radical reactions³ with the aim of identifying highly enantioselective processes. Examples include the use of chiral auxiliaries,⁴ and of sequences⁵ involving 'chirality transfer'.⁶ An example of stereospecific homolytic substitution at the sulphoxide group has been reported,⁷ while very recently radicals derived from β -keto sulphoxides have been shown to undergo highly diastereoselective intramolecular addition.⁸ We now report that the radical **2** bearing an arylsulphinyl group and an ester group undergoes intermolecular addition with remarkably high diastereoselectivity (>98%).

The radical precursor **1**[†] was obtained in an overall yield of 65% by sequential treatment of ethyl 2-bromopropionate with (i) *p*-thiocresol/triethylamine in diethyl ether under reflux, (ii) *m*-chloroperoxybenzoic acid in dichloromethane at -77 °C, and (iii) lithium diisopropylamide in THF at -77 °C to give the enolate, which was added to an iodine solution at -77 °C. When a solution of **1** (0.5 mmol) and allyltriphenylstannane (1.0 mmol) in benzene (1.0 ml) was irradiated with UV light (254 nm) at ambient temperature for 30 min, it afforded one diastereoisomer **4** of the addition product **3** in 87% yield after chromatography on silica gel. Careful NMR spectroscopy of the crude product revealed very weak signals for the other diastereoisomer of **3**, an authentic sample of which was prepared by sequential treatment of **4** with trifluoroacetic anhydride and water. Integration of the NMR spectrum showed the diastereoisomeric ratio to be >98:2. Although **4** slowly decomposed on storage by elimination of *p*-toluenesulphonic acid, it was converted by mild hydrolysis (NaOH/MeOH) into a stable crystalline acid **5**, m.p. 96–100 °C. The relative configurations of the chiral centres of **5** were determined by X-ray crystallography (Fig. 1).[‡]

When a solution of 0.4 mmol of **1**, hex-1-ene (12 mmol), and hexabutylditin (0.04 mmol) in benzene (0.5 ml) was irradiated



with UV light for 30 min, a chain reaction involving the atom-transfer mechanism⁹ ensued to afford a mixture (ca. 1 : 1) of the diastereoisomeric iodides **9**, treatment of which *in situ* with tributylstannane gave one diastereoisomer **6** of the reaction product **10** in 37% yield after chromatography. Once again, NMR spectroscopy of the crude product detected only a trace amount (<2%) of the other diastereoisomer of **10**. The relative configurations of the chiral centres of **6** are assigned by analogy with **4** on the basis of similarities between the NMR spectra and chromatographic behaviour of the two compounds.



[†] All new compounds were characterised by ¹H NMR, ¹³C NMR, and mass spectroscopy.

[‡] C₁₃H₁₆O₅S: M_r = 252.33, monoclinic, P2₁/n, a = 13.2742(9), b = 13.7121(7), c = 14.919(2) Å, β = 100.880(8)°, V = 2667.5 Å³, Z = 8, D_x = 1.25 g cm⁻³, λ(Cu-Kα) = 1.5418 Å, μ = 1.88 mm⁻¹, F(000) = 1072, T = 298 K, R = 0.0530 for 2675 observed reflections. The structure contains two independent molecules in the asymmetric unit. The crystal packing of **1** is held together by hydrogen bonds between the carboxy groups of one molecule and the sulphoxide oxygen of the other independent molecule forming chains extending parallel to the a axis, [O(1) ··· H(22') 1.82(6), O(1) ··· O(2') 2.596(4) Å, O(1) ··· H(22')-O(2') 149(3)°; O(1') ··· H(22) 1.73(9) Å; O(1') ··· O(2) 2.603 Å; O(1') ··· H(22)-O(2) 170(3)°]. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

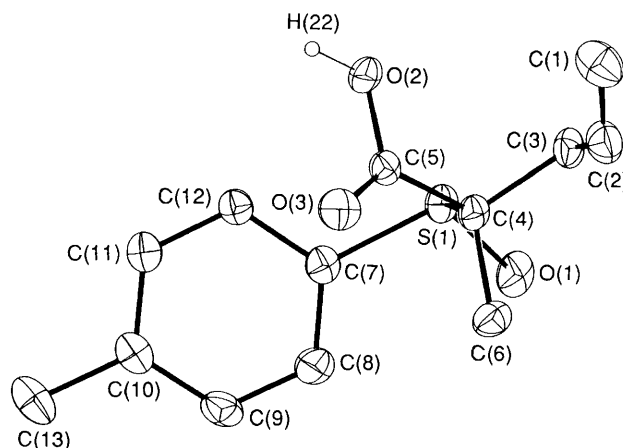


Fig. 1 View (ORTEP) of the acid **6**.[‡]

The results indicate that the addition of the radical **2** to the alkenic bond in allyltriphenylstannane or in hex-1-ene proceeds with very high diastereoselectivity (>98:2). This is, to our knowledge, the first report of a homolytic *intermolecular* addition reaction that proceeds with essentially absolute stereocontrol. Although the underlying basis of the stereoselectivity will be explored further, it seems significant that *intramolecular* reactions of radicals containing the β -keto sulphoxide moiety show similarly high diastereoselectivity,⁸ whereas radicals containing the sulphoxide group but no carbonyl substituent show much less selectivity.¹⁰ To rationalise these observations we suggest that **2** is a captodative radical (the sulphur atom acting as the donor group) and that it preferentially adopts a relatively stable configuration **7** in which the C=O and S-O groups are anti because of dipole-dipole interactions. Examination of models shows that approach to alkenes on the face remote from the bulky aryl group to yield, eventually, products such as **4** and **6** is less hindered than the alternative pathway leading to their diastereoisomers.

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