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

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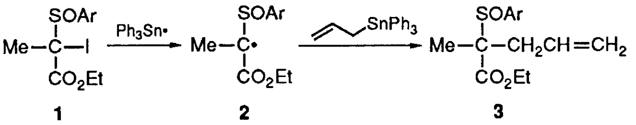
The 1-ethoxycarbonyl-1-*p*-tolylsulphinylethyl radical **2**, generated by iodine abstraction from **1**, adds to the alkenic bond in allyltriphenylstannane or in hex-1-ene with very high diastereoselectivity (>98%).

The recognition[1] 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 reactions[3] with the aim of identifying highly enantioselective processes. Examples include the use of chiral auxiliaries,[4] and of sequences[5] 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%).

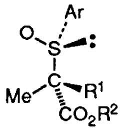
The radical precursor **1**† was obtained in an overall yield of 65% by sequential treatment of ethyl 2-bromoproprionate with (*i*) *p*-thiocresol/triethylamine in diethyl ether under reflux, (*ii*) *m*-chloroperoxybenzoic acid in dichloromethane at −77 °C, and (*iii*) lithium diisopropylamide in THF 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*-toluenesulphenic 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 mechanism[9] 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.

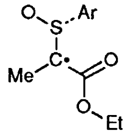


$$\mathrm{Me{-}\overset{SOAr}{\underset{CO_2Et}{C}}{-}I}\ \xrightarrow{Ph_3Sn\cdot}\ \mathrm{Me{-}\overset{SOAr}{\underset{CO_2Et}{C}}\cdot}\ \xrightarrow{CH_2=CHCH_2SnPh_3}\ \mathrm{Me{-}\overset{SOAr}{\underset{CO_2Et}{C}}{-}CH_2CH{=}CH_2}$$

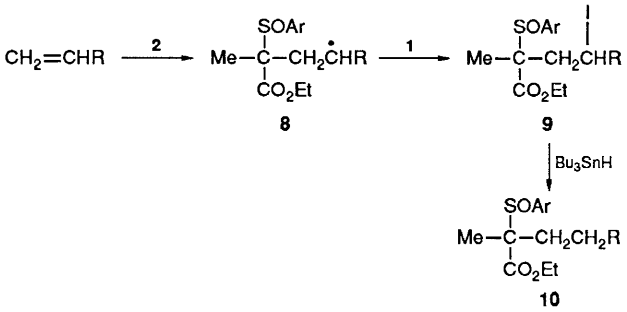
Scheme 1 R = *p*-tolyl



4; Ar = *p*-tolyl, R^1 = allyl, R^2 = Et
5; Ar = *p*-tolyl, R^1 = allyl, R^2 = H
6; Ar = *p*-tolyl, R^1 = hexyl, R^2 = Et



7; Ar = *p*-tolyl



$$\mathrm{CH_2{=}CHR}\ \xrightarrow{\mathbf{2}}\ \mathrm{Me{-}\overset{SOAr}{\underset{CO_2Et}{C}}{-}CH_2\dot{C}HR}\ (\mathbf{8})\ \xrightarrow{\mathbf{1}}\ \mathrm{Me{-}\overset{SOAr}{\underset{CO_2Et}{C}}{-}CH_2\overset{I}{C}HR}\ (\mathbf{9})\ \xrightarrow{Bu_3SnH}\ \mathrm{Me{-}\overset{SOAr}{\underset{CO_2Et}{C}}{-}CH_2CH_2R}\ (\mathbf{10})$$

Scheme 2 Ar = *p*-tolyl, R = Bu

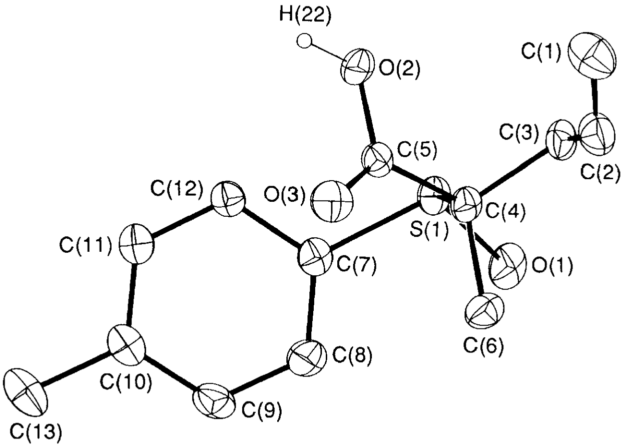


Fig. 1 View (ORTEP) of the acid **6**.‡

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† All new compounds were characterised by ^{1}H NMR, ^{13}C NMR, and mass spectroscopy.

‡ $C_{13}H_{16}O_3S$: M_r = 252.33, monoclinic, $P2_1/n$, a = 13.2742(9), b = 13.7121(7), c = 14.919(2) Å, β = 100.880(8)°, V = 2667.5 Å^3, 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.

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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References

1 A. L. J. Beckwith, *Tetrahedron*, 1981, **37**, 3037; B. Giese, *Radicals in Organic Synthesis: Formation of Carbon–Carbon Bonds*, Pergamon, Oxford, 1986.

2 D. P. Curran, *Synthesis*, 1988, **417**, 489; A. Ghosez, B. Giese, W. Mehl, J. O. Metzger and H. Zipse, in *Methoden der organischen Chemie* (Houben-Weyl), eds. M. Regitz and B. Giese, Thieme, Stuttgart, 1989, vol. E 19a, p. 2.

3 B. Giese, *Angew. Chem., Int. Ed. Engl.*, 1989, **28**, 969.

4 For recent examples see D. P. Curran, W. Shen, J. Zhang and T. A. Heffner, *J. Am. Chem. Soc.*, 1990, **112**, 6738; N. A. Porter, E. Swann, J. Nally and A. T. McPhail, *J. Am. Chem. Soc.*, 1990, **112**, 6740; B. Giese, M. Zehnder, M. Rosh and H.-G. Zietz, *J. Am. Chem. Soc.*, 1990, **112**, 6741.

5 A. L. J. Beckwith and C. L. L. Chai, *J. Chem. Soc., Chem. Commun.*, 1990, 1087.

6 D. Seebach, R. Nef and G. Calderari, *Tetrahedron*, 1984, **110**, 1313.

7 A. L. J. Beckwith and D. R. Boate, *J. Chem. Soc., Chem. Commun.*, 1986, 189.

8 B. B. Snider, B. Y.-F. Wan, B. O. Buckman and B. M. Foxman, *J. Org. Chem.*, 1991, **56**, 328.

9 D. P. Curran, M.-H. Chen and D. Kim, *J. Am. Chem. Soc.*, 1986, **108**, 2489; D. P. Curran and D. Kim, *Tetrahedron Lett.*, 1986, **27**, 5821.

10 Y.-M. Tsai, B.-N. Ke and C.-H. Lin, *Tetrahedron Lett.*, 1990, **31**, 6047.