Tetrahedron Letters, Vol. 33, No. 52, pp. 8051-8054, 1992
Printed in Great Britain

0040-4039/92 $5.00 + .00
Pergamon Press Ltd

Asymmetric Radical Additions Using Chiral 1,3-Dioxolane-4-ones

Georg Kneer[1] and Jochen Mattay *

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität,
Orléansring 23, D-(W)-4400 Münster, Germany

Abstract: Moderate facial selectivities are observed in additions of alkyl radicals to the chiral (c,d) olefin (2*S*)-2-*tert*-butyl-5-ethoxycarbonylmethylene-1,3-dioxolane-4-one **1**. The following hydrogen abstraction from tributylstannane proceeds with excellent asymmetric stereocontrol, leading to two of four possible diastereoisomers with high diastereomeric excesses. Additions of chiral radicals obtained from (2*R*,5*R*)-5-alkyl-5-bromo-1,3-dioxolane-4-ones to ethyl acrylate show high asymmetric 1,3-induction.

Part A: Radical Additions to the Chiral Alkene 1

The formation of C-C-bonds by radical additions to alkenes is one of the most useful synthetical reactions in organic synthesis[2]. In recent years stereochemical control has played a dominant role in this field of investigations.[3] Chiral 5-alkyl-2-*tert*-butyl-1,3-dioxolane-4-ones which are easily prepared from malic and lactic acid give high facial selectivities in cycloadditions.[4] BECKWITH described significant stereoselectivity of (2*S*)-2-*tert*-butyl-5-methylene-1,3-dioxolane-4-one in radical additions.[5] We now report on the addition of free radicals to (2*S*)-2-*tert*-butyl-5-ethoxycarbonylmethylene-1,3-dioxolane-4-one **1**.

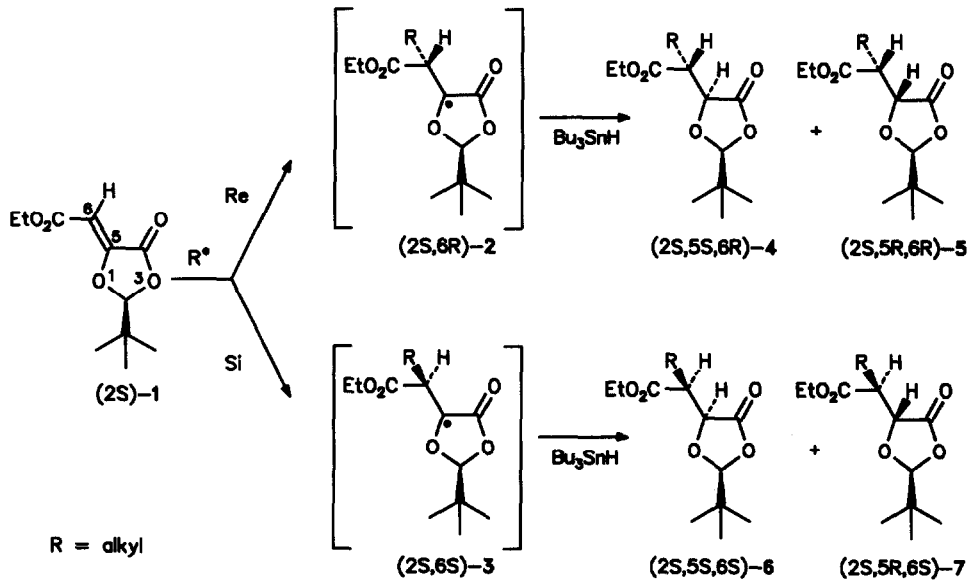
The chiral olefin **1** shows some interesting features: a) The C-5 atom is bearing both an electron donor and an electron acceptor as geminal substituents. Olefins like this are defined as (c,d) olefins and radicals should be stabilized at this site according to VIEHE's concept of captodative (c,d) substitution of alkenes.[6] Thus, the addition of an alkyl radical should occur at the C-6 atom with high regioselectivity generating a stabilized radical. b) The *Si*-face of the olefin is sterically hindered by the bulky *tert*-butyl group. Therefore the attack of the alkyl radical should take place at the *Re*-side preferably. c) Both C-atoms of the double bond are prochiral centres. Consequently, addition of free radicals to the olefin followed by abstraction of hydrogen using the tin hydride method leads to four possible products as shown in scheme 1.

Table 1. Additions of Alkyl Radicals to Olefin **1**.

entry	R•	product ratio				yield	conversion
		4	**5**	**6**	**7**	%	%
1	C_6H_{11}	1.00	0.10	0.94	0.09	84	100
2	*tert*-C_4H_9	1.00	0.19	0.64	0.05	66	80
3	*n*-C_4H_9	1.00	0.10	0.90	0.04	79	90
4	C_2H_5	1.00	0.06	1.00	0.06	90	100
5	CH_3	1.00	0.22	0.77	0.11	66	70

We investigated the addition of various alkyl radicals and in fact we obtained the four diastereoisomers **4**, **5**, **6** and **7** in all cases.[7] The detailed results of the reactions are listed in table 1.

The formation of the intermediates **2** and **3** by addition of alkyl radicals at C-6 takes place with low facial selectivity (1,4-induction). Consequently the radical intermediates are formed in nearly equal ratio.[8]



Scheme 1. Addition of alkyl radicals to olefin **1** with following hydrogen abstraction

Following hydrogen abstraction from tributylstannane leads to the diastereoisomers **4**, **5**, **6**, and **7**. The stereochemistry concerning 2-H and 5-H is *cis* for compound **4** and **6** and *trans* for **5** and **7**. The relative configurations were assigned by NOE measurements.[9] However, it was impossible to distinguish between compound **4** and **6** respectively **5** and **7** by NMR data.

Assuming the mechanism shown in scheme 1 the diastereomeric excesses for alkyl addition and hydrogen abstraction are calculated (table 2).

Table 2. Diastereomeric Excesses of Radical Additions and Hydrogen Abstractions.

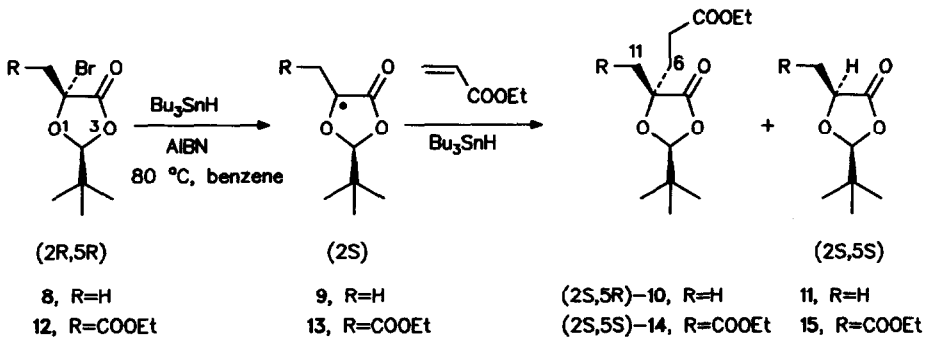
entry	alkyladdition	hydrogen abstraction	
		2 → 4+5	**3 → 6+7**
1	3	82	83
2	22	68	86
3	5	82	92
4	0	89	89
5	13	64	75

The hydrogen abstraction from tributylstannane at C-5 proceeds with high stereochemical control, which is caused by the conformation of the radical intermediate. It is likely that the radical intermediate adopts a preferred conformation which directs the hydrogen abstraction from the *Re*-side of the radical centre. The high facial selectivity is not only controlled by a simple 1,2-asymmetric induction of the alkyl and the ester group. Furthermore the interaction of these substituents with the *tert*-butyl group and the *endo*cyclic carbonyl function generates a conformation which shields the *Si*-side. Therefore the hydrogen abstraction takes place from the *Re*-side. This conclusion is based on semiempirical calculations.

Part B: Additions of Chiral Radicals to Ethyl Acrylate

The addition of alkenes to chiral five-membered ring radicals has been intensively studied concerning 1,2 induction.[10] We now describe this kind of reaction with respect to 1,3 induction. The syntheses of the bromides **8** and **12** have already been reported earlier[4a,4c,11] These bromides are yielded as crystalline

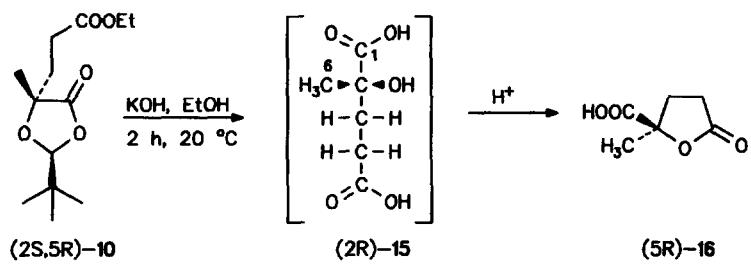
solids with excellent diastereoisomeric excesses (> 96%).[12,13] Both are useful precursors for the chiral radicals **9** and **13**, which are generated by bromine abstraction using the tin hydride method (scheme 2).



Scheme 2. Addition of chiral radicals to ethyl acrylate

The addition of **9** to ethyl acrylate gave the adduct **10** in 55% yield after hydrogen abstraction.[7] The by-product **11** is formed in 45% yield by hydrogen addition to **9**.[14] The adduct **14** is yielded under the same conditions in 27%.[7,15] Again 6% of the hydrogen substituted product **15** was found.[16] In both cases only one diastereoisomer was isolated. The configuration determined by NOE experiments is (2*S*,5*R*) for **10** and (2*S*,5*S*) for **14**.[17]

Saponification of **10** leads to the hydroxydicarboxylic acid **15**. By treatment with acid we obtained the corresponding lactone **16** in 90% yield (ee = 97.6%)[18] of which the optical rotation is almost identical with (*R*)-**16** described by PARTRIDGE.[19] Consequently, the absolute configuration of **10** must be (5*R*). In this manner we determined the absolute configuration of **10** and therefore the facial selectivity of **8**.



Scheme 3. Formation of (5*R*)-γ-butyrolactone-γ-carboxylic acid **16**

Acknowledgements: We gratefully acknowledge the financial support by the *Deutsche Forschungsgemeinschaft*, the *Fonds der Chemischen Industrie*, the *Ministerium für Wissenschaft und Forschung NRW* and the *Gesellschaft zur Förderung der Westf. Wilhelms-Universität Münster e. V.* We are indebted to Prof. B. Krebs, M. Läge, A. Heidbreder for X-ray analysis of **8**. We further thank the Bayer AG and Wacker Chemie GmbH for generous contributions of materials and experimental equipment as well as the BASF and Ruhrchemie AG (Oberhausen) for providing pivalaldehyde.

References and Notes:

1 Part of the projected dissertation of G. K., Westfälische Wilhelms-Universität Münster.

2 a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon Press, Oxford, **1986**; b) Curran, D. P. *Synthesis* **1988**, 417-439 and 489-513; c) Hart, D. J. *Science (Washington D. C.)* **1984**, *223*, 883-887.

3 Giese, B. *Angew. Chem.* **1989**, *101*, 993-1004; *ibid. Int. Ed.* **1989**, *28*, 969; Porter, N. A.; Giese, B.; Curran, D. P. *Acc. Chem. Res.* **1991**, *24*, 296-304.

4 a) Mattay, J.; Mertes, J.; Maas, G. *Chem. Ber.* **1989**, *122*, 327-330; b) Mattay, J.; Kneer, G.; Mertes, J. *Synlett* **1990**, 145-147; c) Kneer, G.; Mattay, J.; Raabe, G.; Krüger, C.; Lauterwein, J. *Synthesis*, **1990**, 599-603; d) Roush, W. R.; Essenfeld, A. P.; Warmus, J. S.; Brown, B. B. *Tetrahedron Lett.* **1989**, *30*, 7305-7308; e) Roush, W. R.; Brown, B. B. *J. Org. Chem.* **1992**, *57*, 3380-3387.

5 Beckwith, A. L. J.; Chai, C. L. L. *J. Chem. Soc., Chem. Commun.* **1990**, 1087-1088.

6 a) Viehe, H. G.; Merenyi, R.; Stella, L.; Janousek, Z. *Angew. Chem.* **1979**, *91*, 982-997; *ibid. Int. Ed.* **1979**, *18*, 917; b) Viehe, H. G.; Janousek, Z.; Merenyi, R.; Stella, L. *Acc. Chem. Res.* **1985**, *18*, 148-154; c) Sustmann, R.; Korth, H.-G. *Adv. Phys. Org. Chem.* **1990**, *26*, 131-178.

7 Typical procedure: A solution of the alkyl halide and the olefin in benzene is heated under reflux while a solution of tributylstannane and azobisisobutyronitrile (AIBN) in benzene is added during 2 h. After evaporation of the solvent the residue is solved in cyclohexane and extracted with acetonitrile. The diastereoisomers are isolated from the acetonitrile layer and separated by HPLC if possible.

8 The attack of the radical should proceed preferably from the sterically less hindered *Re*-face, analogous to previous results in Diels-Alder reactions (ref. 4). Consequently we assume that **2** is the major and **3** the minor radical isomer.

9 Irradiation with the ^{1}H-NMR frequency of 2-H caused an intensity increase of the signal from 5-H and vice versa for **4** and **6**, and no change for **5** and **7**.

10 For a review see ref. 3.

11 For the synthesis of **8** see also: Zimmermann, J.; Seebach, D. *Helv. Chim. Acta* **1987**, *70*, 1104-1114.

12 The diastereomeric excess is determined by ^{1}H-NMR spectroscopy (the second diastereoisomer is not detectable). The absolute configuration of **8** is determined by X-ray analysis as (*R*) at C-5 (see also ref. 13).

13 Lists of structure factors, anisotropic thermal parameters and table of bond distances and angles of **8** may be obtained through Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-(W)-7514 Eggenstein-Leopoldshafen 2, Germany, referring CSD 56643, the authors and the bibliographical data.

14 The NMR data are the same as for **11** prepared by the method of SEEBACH: Seebach, D.; Naef, R.; Calderari, G. *Tetrahedron* **1984**, *40*, 1313-1324.

15 The moderate yield is caused in the formation of polymeric by-products. There is no indication for the formation of the other distereoisomer on the basis of chromatographic and NMR spectroscopic measurements after usual workup.

16 The NMR data are the same as for **15** described in ref. 4c.

17 We have observed an NOE between 2-H and 6-H, however the experiments reveal no NOE between 2-H and 11-H.

18 A solution of ethanol, KOH and **10** is stirred for 2 h at ambient temperature. After evaporation of the solvent the residue is acidified with HCl and extracted with diethyl ether. The product (5*R*)-**16** is isolated from the organic layer.

19 Optical rotation of **16**: $[\alpha]_D^{20} = 16.8$ (c = 2.6); Lit.: $[\alpha]_D^{20} = 17$ (c = 2), Partridge, J. J.; Shiuey, S.-J.; Chadha, N. K.; Baggiolini, E. G.; Blount, J. F.; Uskokovic M. R. *J. Am. Chem. Soc.* **1981**, *103*, 1253-1255.

(Received in Germany 6 July 1992)