Pure & Appl. Chem., Vol. 68, No. 3, pp. 711–714, 1996.
Printed in Great Britain.

Diastereofacial control in the radical addition to chiral α-sulfinyl enones

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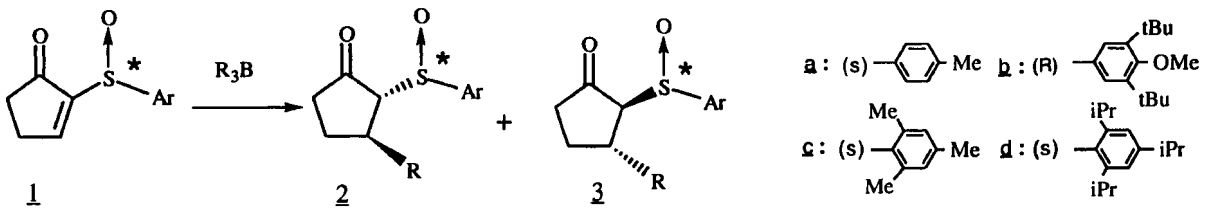
Abstract: The β-addition of alkyl radicals to chiral 2-(arylsulfinyl)-2-cyclopentenones 1 gives 3-alkyl-2-(arylsulfinyl)-1-cyclopentanones 2 with stereoselectivities depending on the bulkiness of alkyl radicals as well as the aryl sulfoxides. The X-ray analysis of the single crystal as well as the NOE experiment of 2,4,6-triisopropylphenyl sulfoxides 1d showed the effective shielding at the β position by the triisopropylphenyl group. The reaction of a diastereomeric mixture of 4-methyl-2-sulfinyl-cyclopentenones 4(S) and 4(R) gives the kinetically resolved addition product. Radical reaction of acyclic sulfinylpentenones gives abnormal Pummerer-type reaction products.

Recently numerous new free-radical synthetic methods have emerged (1). Especially, interests have been focused on the stereoselective radical reactions. Intermolecular radical addition to C-2 chiral amide-substituted alkenes gives addition products α to the amide with significant stereoselectivity, whereas little or no selectivities are observed in the radical addition at the position β to the auxiliary (2). Curran and his coworkers have shown a successful diastereoselective β-addition to the alkene having a sterically bulky imide to give the β-addition product with high diastereoselectivity (3). We envisaged the diastereofacial control of the alkene face β to the carbonyl by the chiral sulfoxide auxiliary (4). Such sulfinyl auxiliary has some characteristic features. The sulfoxide has a trigonal pyramidal structure and the bulky substituent on the sulfinyl group is expected to shield a face of the alkene at the β position and to control the β-stereoselectivity of the radical attack. The S-O and C=O bonds would be arranged either in the antiperiplanar orientation without Lewis acid or in the synperiplanar by chelating with bidentate Lewis acid (5). Furthermore, the sulfinyl group is chemically versatile and can be removed under mild conditions. These features render the sulfoxide group attractive as a chiral auxiliary in the stereoselective radical addition (6).

A CH_2Cl_2 solution of α-sulfinylcyclopentenones 1 was treated with trialkylboranes (7) in the presence of $TiCl_2(Oi\text{-}Pr)_2$ (8) or without Lewis acid at 0°C. The results are summarized in Table 1. The reaction of (*R*)-2-((3,5-di-*tert*-butyl-4-methoxyphenyl)sulfinyl)-2-cyclopentenone 1b in the presence of $TiCl_2(Oi\text{-}Pr)_2$ gave the addition product with higher diastereoselectivity in comparison with p-tolylsulfinylcyclopentenone 1a (entries 1 and 3). The reaction without $TiCl_2(Oi\text{-}Pr)_2$ led to reversed-face selection (entry 2). Stereoselectivities depended on the bulkiness of the alkyl radicals, bulkier alkyl radical showing higher stereoselection (entries 3-6).



Scheme 1

TABLE 1. Reaction of sulfinylcyclopentenones 1 with trialkylboranes

entry	sulfinylcyclo-pentenone	R	Lewis acid	time, h	yield, %	ratio 2 : 3
1	1a	t-Bu	$TiCl_2(Oi\text{-}Pr)_2$	8	60	28 : 72
2	1b	t-Bu	-	8	91	38 : 62
3	1b	t-Bu	$TiCl_2(Oi\text{-}Pr)_2$	8	94	98 : 2
4	1b	c-C_6H_{11}	$TiCl_2(Oi\text{-}Pr)_2$	3	90	89 : 11
5	1b	i-Pr	$TiCl_2(Oi\text{-}Pr)_2$	10	61	84 : 16
6	1b	Et	$TiCl_2(Oi\text{-}Pr)_2$	12	72	77 : 23
7	1c	t-Bu [a)]	-	1	99	>98 : 2
8	1c	c-C_6H_{11} [a)]	-	1	89	>98 : 2
9	1c	i-Pr	-	1	99	>98 : 2
10	1c	Et	-	1	94	94 : 6
11	1d	t-Bu	-	8	66	>98 : 2
12	1d	c-C_6H_{11}	-	3	71	>98 : 2
13	1d	i-Pr	-	2	94	>98 : 2
14	1d	Et	-	6	95	>98 : 2

[a)] t-BuI and Et_3B were used.

The sulfoxides having an o-substituted aryl group showed high diastereoselection without Lewis acid. The reaction of (*S*)-2-((2,4,6-trimethylphenyl)sulfinyl)-2-cyclopentenone 1c (9) as well as (*S*)-2-((2,4,6-triisopropylphenyl)sulfinyl)-2-cyclopentenone 1d without Lewis acid afforded only a single diastereomer (entries 7-14). The stereochemistry of the addition product was the one expected from the transition state in which the S-O and C=O bonds were in an antiperiplanar orientation. The early transition state is important in the addition of nucleophilic radicals to electron deficient olefins (2, 10). Single-crystal X-ray analysis of 1d showed the antiperiplanar orientation of the S-O and C=O bonds, and the distinct face-shielding effect of the o-isopropyl group on the phenyl ring as shown in Fig. 1. One of the isopropyl group is located below β position of the olefin, allowing radicals to attack the face opposite the triisopropylphenyl group (see top view in Fig. 1). The distance between the β- and isopropyl methine protons is 2.74 Å as shown in side view. Appreciable NOE was observed between these protons in the nmr study of 1d, supporting this conformation in solution.

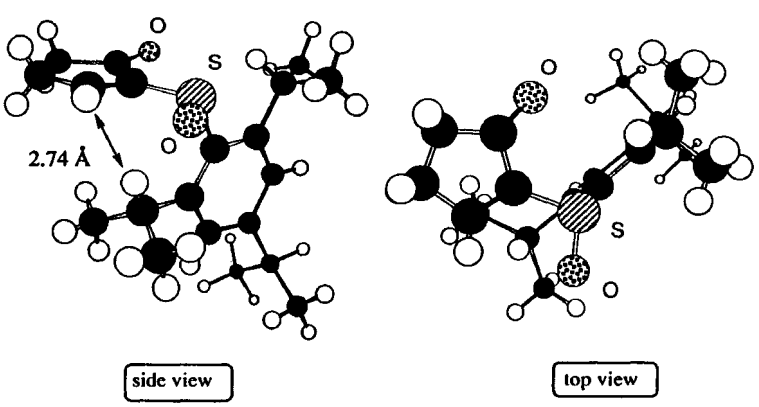
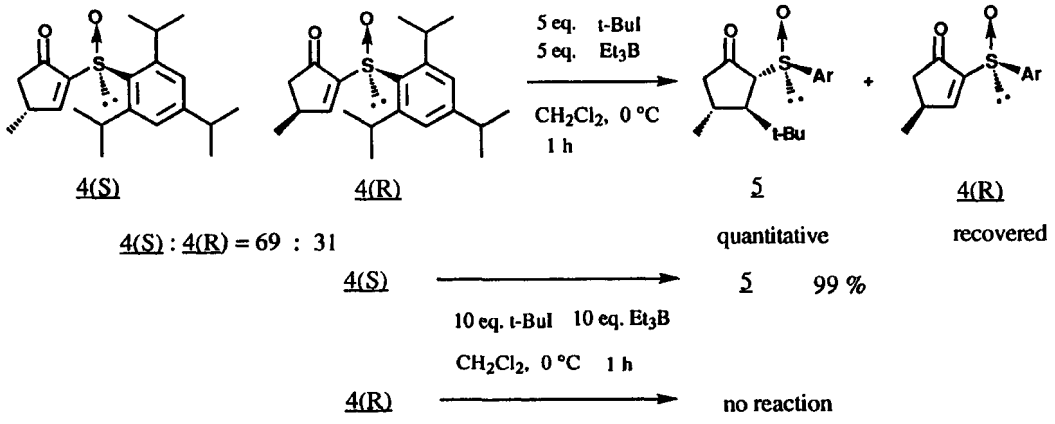


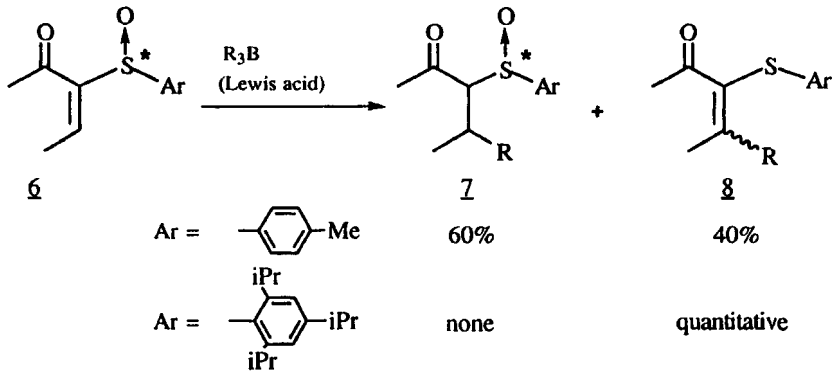
Fig. 1 Solid-state conformation of 1d

A 69/31 mixture of 4-methyl-2-((2,4,6-triisopropylphenyl)sulfinyl)--2-cyclopentenones 4(S) and 4(R) was reacted with tert-butyl iodide and triethylborane in CH_2Cl_2 at 0°C for 1 h to give a single stereoisomer of *tert*-butyl addition product 5 quantitatively, the enone 4(R) being completely recovered (Scheme 2). Indeed, the reaction of the isolated isomer 4(S) afforded 5 in 99% yield, whereas 4(R) did not react at all under the same conditions. Thus, this reaction, followed by removal of the sulfinyl moiety, would provide a convenient pathway for the preparation of chiral 3,4-dialkyl-substituted cyclopentanones starting with a mixture of two diastereomers such as 4(S) and 4(R).

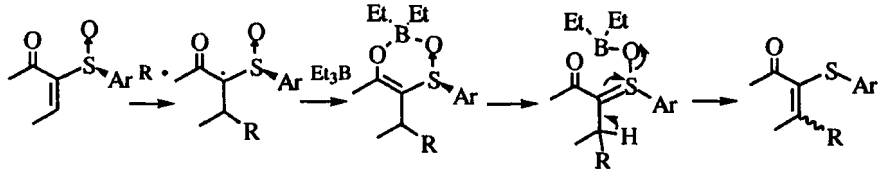


Scheme 2

We next examined the intermolecular radical addition to acyclic sulfinyl enones. Reaction of (*E*)-3-(p-tolylsulfinyl)-3-penten-2-one 6a with trialkylboranes gave addition products 7a as a mixture of 4 diastereomers. In addition, an appreciable amount of unexpected p-tolylthiopentenone 8a (a mixture of E and Z isomers) was isolated (Scheme 3). Unfortunately, the reaction of 3-(2,4,6-triisopropylphenyl)sulfinyl-3-penten-2-one 6b in the presence of Lewis acid or without Lewis acid gave the undesired product 8b quantitatively, no sulfoxide 7b being isolated. The plausible mechanism for the formation of 8 is shown in Scheme 4, following the abnormal Pummerer-type reaction (11).



Scheme 3. Radical addition to acyclic sulfynylpentenones 6.



Scheme 4. Abnormal Pummerer-type reaction.

REFERENCES

1. (a) B. Giese, *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*, Pergamon, New York (1986); (b) C. P. Jasperse, D. P. Curran, and T. L. Fevig, *Chem. Rev.* **91**, 1237 (1991); (c) B. Giese, *Angew. Chem., Int. Ed. Engl.* **28**, 969 (1989) (d) D. Crich and L. Quintero, *Chem. Rev.* **89**, 1413 (1989) (e) W. B. Motherwill and D. Crich, *Free Radical Chain Reactions in Organic Synthesis*, Academic, London (1992)
2. N. Porter, B. Giese, and D. P. Curran, *Acc. Chem. Res.* **24**, 296 (1991)
3. J. G. Stack, D. P. Curran, J. Rebek, Jr., and P. Ballester, *J. Am. Chem. Soc.* **113**, 5981 (1991)
4. T. Toru, Y. Watanabe, M. Tsusaka, and Y. Ueno, *J. Am. Chem. Soc.* **115**, 10464 (1993)
5. G. H. Posner, M. Hulce, J. P. Mallmo, S. A. Drexler, and J. Clardy, *J. Org. Chem.* **46**, 5244 (1981)
6. M. Zahouily, M. Journet, and M. Malacria, *Synlett* 366 (1994)
7. H. C. Brown andM. M. Midland, *Angew. Chem., Int. Ed. Engl.* **11**, 692 (1972)
8. K. Mikami, M. Terada, and T. Nakai, *J. Am. Chem. Soc.* **112**, 3949 (1990)
9. For the preparation of chiral 2,4,6-trimethylphenylsulfinate, see F. Rabiere, O. Samuel, L. Ricard, and H. B. Kagan, *J. Org. Chem.* **56**, 5991 (1991)
10. (a) M. J. S. Dewar and S. Olivella, *J. Am. Chem. Soc.* **100**, 5290 (1978) (b) D. C. Spellmeyer and K. N. Houk, *J. Org. Chem.* **52**, 959 (1987)
11. M. Kennedy and M. A. McKervey, *Comprehensive Organic Synthesis*, Vol. 7, pp.196-206, B. M. Trost, I. Fleming, Eds., Pergamon, Oxford (1991)