CHEMISTRY LETTERS, pp. 713-716, 1978. Published by the Chemical Society of Japan

AN ENANTIOMER DIFFERENTIATING REACTION OF p-TOLYLSULFINYLCARBANION WITH (-)-MENTHYL CARBOXYLATES

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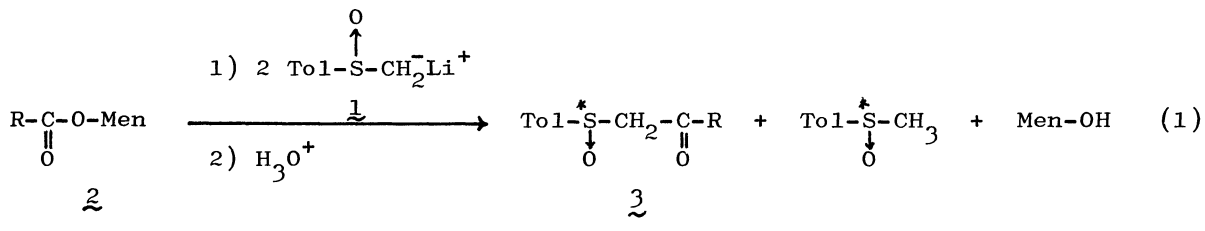
Treatment of (-)-menthyl carboxylates(2) with 2 equiv of p-tolylsulfinylcarbanion(1) afforded the corresponding optically active β-keto sulfoxides(3) together with optically active methyl p-tolyl sulfoxide. The enantiomeric purity and the predominant configuration of the products were discussed.

In connection with our interest in asymmetric induction by chiral sulfinyl group,[1] recently, we reported that 2 equiv of (±)-α-sulfinylcarbanions reacted with (-)-menthyl-(S)-arenesulfinates to yield a diastereomeric mixture of (R,S)- and (R,R)-β-disulfoxides in the ratio of about 6 : 4.[1b] We have now found that the reaction of (±)-p-tolylsulfinylcarbanion(1) toward (-)-menthyl carboxylates(2) also displays the feature of a similar type of enantiomer differentiating reaction. Namely, when 2 equiv of 1, derived from (±)-methyl p-tolyl sulfoxide and lithium diethylamide, was allowed to react with 2 in tetrahydrofuran(THF), the corresponding optically active β-keto sulfoxide(3) was produced together with optically active methyl p-tolyl sulfoxide which has the opposite configuration to 3 (eq 1).



(1)

2 3

Tol = p-$CH_3C_6H_4$, Men = (-)-Menthyl

(2a): R = CH_3, (2b): R = C_2H_5, (2c): R = n-C_3H_7, (2d): R = n-C_9H_{19},
(2e): R = iso-C_3H_7, (2f): R = t-C_4H_9, (2g): R = C_6H_{11}, (2h): R = C_6H_5,
(2i): R = o-$CH_3C_6H_4$

Table 1. Reaction of p-Tolylsulfinylcarbanion(1) with (-)-Menthyl Carboxylates(2)[a]

Run	RCOOMen R:	Reaction time (hr)	β-Keto sulfoxides Yield(%)[b]	Specific rotation[c]	Config.	%e.e.[e]	Recovered Tol-SO-CH_3 Yield(%)[b]	Specific rotation[c]	Config.	%e.e.[g]
1	CH_3 (2a)	3	(3a) 89	$[\alpha]_D^{20}$ +23.5°[d]	R	11.9[f]				
2	C_2H_5 (2b)	3	(3b) 93	$[\alpha]_D^{16}$ +3.5°	R	1.3	90	$[\alpha]_D^{18}$ -2.1°	S	1.4
3	n-C_3H_7 (2c)	3	(3c) 86	$[\alpha]_D^{16}$ -13.5°	S	5.3	93	$[\alpha]_D^{18}$ +6.3°	R	4.3
4	n-C_9H_{19} (2d)	3	(3d) 90	$[\alpha]_D^{16}$ -12.0°	S	6.4	93	$[\alpha]_D^{16}$ +7.0°	R	4.8
5	iso-C_3H_7 (2e)	3	(3e) 78	$[\alpha]_D^{18}$ -17.5°	S	6.8	98	$[\alpha]_D^{18}$ +7.9°	R	5.4
6	t-C_4H_9 (2f)	5	(3f) 75	$[\alpha]_D^{20}$ -188°	S	71.5				
7	C_6H_{11} (2g)	5	(3g) 63	$[\alpha]_D^{18}$ -56.6°	S	23.6	120	$[\alpha]_D^{18}$ +13.7°	R	9.4
8	C_6H_5 (2h)	3	(3h) 91	$[\alpha]_D^{20}$ +35.0°	R	13.2	89	$[\alpha]_D^{20}$ -19.5°	S	13.4
9	o-$CH_3C_6H_4$ (2i)	3.5	(3i) 70	$[\alpha]_D^{20}$ +20.3°	R	7.6	108	$[\alpha]_D^{20}$ -9.8°	S	6.7

a) In THF at -78°C. b) Yields are based on the starting carboxylic esters(2). c) Determined in acetone. d) Determined in methanol. e) Calculated on the basis of the specific rotations for the corresponding authentic (+)-(R)-β-keto sulfoxides. See ref. 3. f) This value was calculated using the reported specific rotation of (+)-(R)-α(p-tolylsulfinyl)acetone, $[\alpha]_D^{29}$ +197°(MeOH). See ref. 4. g) Calculated on the basis of the specific rotation of (+)-(R)-methyl p-tolyl sulfoxide, $[\alpha]_D^{20}$ +146°(c = 0.490, acetone)(lit,[5] $[\alpha]_D$ +145.5°(acetone)).

In this communication we report an approach to the asymmetric synthesis of β-keto sulfoxides by this finding, using nine (-)-menthyl carboxylates(2a~i)[2] possessing a variety of groups(R).

In a typical reaction, a solution of 651 mg(2.5 mmol) of (-)-menthyl benzoate (2h) in 5 ml of dry THF was added to a solution of 1 (derived from 771 mg(5 mmol) of (±)-methyl p-tolyl sulfoxide, 3.2 ml of 100 mg/ml solution of n-butyl lithium in hexane, and 370 mg of diethylamine in 10 ml of dry THF at 0°C) at -78°C under nitrogen. After 3 hr stirring at -78°C, water(10 ml) was added, acidified(ca. pH 3) with 10% hydrochloric acid, and extracted with chloroform(3 x 30 ml). The combined extracts were then washed with brine, dried(Na_2SO_4), and evaporated under vacuum. Preparative TLC of the residue on silica gel(elution with ethyl ether) afforded dextrorotatory α(p-tolylsulfinyl)acetophenone(3h)(588 mg, 91%, $[\alpha]_D^{20}$ +35.0° (c = 0.622, acetone), 13.2% e.e., (R)-rich) and levorotatory methyl p-tolyl sulfoxide(343 mg, 89%, $[\alpha]_D^{20}$ -19.5°(c = 0.955, acetone), 13.4% e.e., (S)-rich).

The enantiomeric purity and the predominant configuration of the β-keto sulfoxides(3) obtained, listed in Table 1, were confirmed by comparison with specific rotations for the corresponding (+)-(R)-β-keto sulfoxides prepared from (+)-(R)-methyl p-tolyl sulfoxide.[3]

Table 1 reveals that the degree of enantioselectivity of this reaction is affected by the nature of the ester moiety R, indicating a dramatic increase in optical yields, from 1.3% where R is ethyl(3b) to 71.5% where R is t-butyl(3f). Incidentally, in the case of 3f, two recrystallizations(ethyl ether) after TLC gave a 99% e.e. of (-)-(S)-3f, $[\alpha]_D^{20}$ -261°(c = 0.273, acetone). The reversal in configuration with the variation in the ester moiety R is also observed. The ester 2a(R = methyl), 2b(R = ethyl), 2h(R = phenyl), and 2i(R = o-tolyl) preferentially react with (R)-1 to yield an excess of (R)-β-keto sulfoxides, while the ester 2c(R = n-propyl), 2d(R = n-nonyl), 2e(R = iso-propyl), 2f(R = t-butyl), and 2g(R = cyclohexyl) preferentially react with (S)-1 affording (S)-β-keto sulfoxides in excess. Especially, the reversal in configuration from (R) to (S) in going from 3b(R = ethyl, see Run 2) to 3c(R = n-propyl, see Run 3) is significant. Further investigations are in progress, in order to elucidate stereochemical implications for this reaction.

References and Notes

1) a) N. Kunieda, J. Nokami, and M. Kinoshita, Chem. Lett., 1973, 871; b) idem, Bull. Chem. Soc. Jpn., 49, 256 (1976); c) idem, Chem. Lett., 1974, 369; d) idem, Chem. Lett., 1977, 289.

2) (-)-Menthyl carboxylates(2a~i) were prepared by the reaction of (-)-menthol with the corresponding acid chlorides in the presence of pyridine.

3) We synthesized the authentic (+)-(R)-β-keto sulfoxides(3a~i) by the reaction of p-tolylsulfinylcarbanion derived from (+)-(R)-methyl p-tolyl sulfoxide, mp 74°C, $[\alpha]_D^{20}$ +146°(c = 0.490, acetone), with the corresponding ethyl carboxylates, according to the method described above. Satisfactory NMR and elemental analytical data were obtained for all the (+)-(R)-β-keto sulfoxides Their specific rotations were compiled in Table 2.

Table 2. Specific rotations of (+)-(R)-β-keto sulfoxides, Tol-$\overset{*}{S}$O-CH_2-CO-R.

R:	Specific rotation in acetone (c)
C_2H_5	$[\alpha]_D^{23}$ +265°(0.194)
n-C_3H_7	$[\alpha]_D^{22}$ +257°(0.266)
iso-C_3H_7	$[\alpha]_D^{22}$ +258°(0.196)
t-C_4H_9	$[\alpha]_D^{25}$ +263°(0.275)
n-C_9H_{19}	$[\alpha]_D^{15}$ +186.5°(0.222)
C_6H_{11}	$[\alpha]_D^{14}$ +240°(0.224)
C_6H_5	$[\alpha]_D^{25}$ +265.5°(0.264)
o-$CH_3C_6H_4$	$[\alpha]_D^{20}$ +268°(0.320)

4) S. Iriuchijima and N. Kojima, Agric. Biol. Chem., 42, 451 (1978).

5) K. Mislow, M. M. Green, P. Laur, J. T. Melillo, T. Simmons, and A. L. Ternay, Jr., J. Am. Chem. Soc., 87, 1958 (1965).

(Received May 9, 1978)