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Asymmetric hetero Diels–Alder reaction of homochiral thiabutadienes, 3-(arylmethylene)thiocamphors

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Abstract

The highly diastereoselective hetero Diels–Alder reactions of homochiral camphor-derived thiabutadienes to afford novel, optically active bornene ring-fused dihydrothiopyrans are described.

Keywords: asymmetric synthesis; Diels–Alder reactions; thiocarbonyl compounds; thiopyrans.

A wide range of camphor derivatives have been extensively exploited as chiral intermediates, reagents, and chiral auxiliaries in asymmetric organic chemistry.[1,2] Merits of these camphor derivatives for utilization in asymmetric chemistry are due mainly to the easy availability of inexpensive natural camphor and its antipode, facile and potent transformation ability, and to resulting, efficient and attractive asymmetric induction owing to predictable topological differentiation by virtue of the conformationally rigid bornane framework.[1,2] On the other hand, in the course of our investigation on α,β-unsaturated thiocarbonyl compounds, we have reported asymmetric hetero Diels–Alder reactions of thiabutadienes to afford optically active dihydrothiopyrans.[3]

In spite of the rich chemistry with camphor derivatives, it is surprising that there is no report, to the best of our knowledge, of the use of α,β-unsaturated camphorthiones that take part as 4π-components as well as homochiral templates in asymmetric hetero Diels–Alder reaction. In this communication we report highly diastereoselective hetero Diels–Alder cycloaddition of homochiral camphor-derived thiabutadienes and unequivocal determination of the stereochemistry of a resulting Diels–Alder cycloadduct by X-ray crystallographic analysis.

(Arylmethylene)thiocamphors **1** were prepared in good yield (70–86%) by thionation of the corresponding ketones with Lawesson's reagent (LR) in refluxing benzene (Scheme 1).[4–6] The thioketones **1**, after isolation, exist stably as monomers even in solution for a long time, adopting the *E*-configuration

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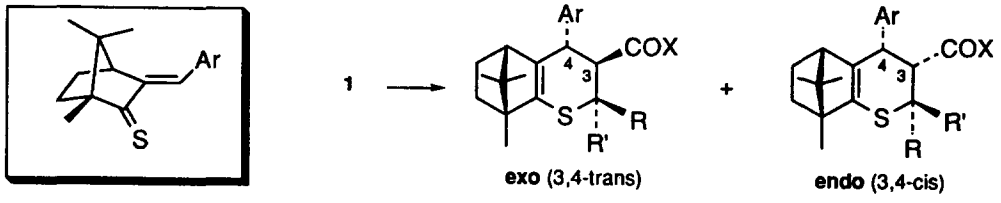
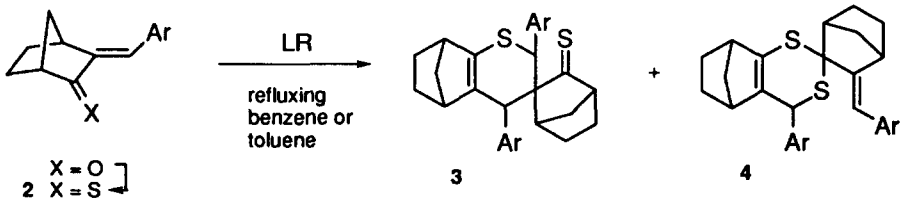
with respect to the carbon–carbon double bond.[4–6] In contrast, 3-(arylmethylene)norbornane-2-thiones **2**, generated from the corresponding ketones by thionation with LR, were not stable enough to allow isolation, and in the case of (*p*-chlorophenylmethylene)norbornane-2-thione (**2**, Ar=*p*-Cl-phenyl), the formation of two types of [4+2]dimers, **3** and **4**, was confirmed (Scheme 2). These observations and the facts described below suggest that the methyl groups at the 1- and 7-positions play an important role not only in permitting kinetic stabilization of the thiocamphors (**1**), thus preventing self-dimerization, but also in controlling the stereoselectivity of the cycloaddition.



1 **a** Ar = *p*-Tol
b Ar = Ph
c Ar = *p*-MeOphenyl

5 X = OMe, R = R' = H
6 X = 2-oxo-1,3-oxazolidin-3-yl, R = R' = H
7 X = OMe, R = CO_2Me, R' = H
8 X = OMe, R = H, R' = CO_2Me

Scheme 1.



2 X = O, X = S

3 **4**

Scheme 2.

First, the reactions of **1a–c** with methyl acrylate were conducted under either uncatalyzed (thermal) or Lewis acid-promoted conditions (Table 1). The reactions at room temperature (Runs 1, 9 and 12) indeed proceeded slowly to afford cycloadducts **5a**, **5b** and **5c** in excellent yield and in good to fair *exo:endo* ratios with complete π-isofacial selectivity in all cases. At 80°C in refluxing benzene (Runs 2, 10 and 13), the reaction time was shortened to 5–6 h without any reduction of the π-facial selectivity. Several common Lewis acids selected greatly accelerated the reaction to show again the perfect facial selectivity (Runs 3–6, 11 and 14). The catalyzed and uncatalyzed reactions of **1a** with 3-acryl-1,3-oxazolidin-2-one also gave similar results, viz., quantitative yield, perfect asymmetric induction and preferential formation of the *exo* isomer of **6a** (Runs 7 and 8). It should be noted that this dienophile enhanced the reactivity and the exo selectivity more than methyl acrylate in the cycloaddition (Run 1 versus Run 7 and Run 5 versus Run 8).

The reactions of **1** with dimethyl maleate and dimethyl fumarate revealed that in all former cases, single stereoisomers were formed, whereas both *exo* and *endo* isomers were produced in the latter (Table 2). Thus, the reaction is completely isoface-selective, but occasionally diastereoface(*exo*)-selective depending on the dienophiles and the reaction conditions used.

The stereochemical determination of the *exo* and *endo* cycloadducts (**5–8**) was based on ^{1}H NMR spectroscopy. The nuclear Overhauser effects (NOE) enhancement was observed between the methyl group hydrogens and proton H-4 in both *exo* and *endo* isomers, which suggests that the dienophile cycloadds preferentially from the bottom side (C_4-*Si*) of the thiadiene **1**. The assignment of *exo/endo* isomers was not easy to make from ^{1}H NMR spectroscopic analysis only, as the *J* values between protons

Table 1
Asymmetric hetero Diels–Alder reaction of thiabutadienes **1** with methyl acrylate and 3-acryl-1,3-oxazolidin-2-one[a]

Run	Diene	Conditions Lewis acid(equiv)	Solvent	T / °C	Time	Product	Yield[b] (%)	*exo:endo*[c]
1	**1a**	none	PhH	RT	9 d	**5a**	97	81:19
2		none	PhH	80	6 h	**5a**	98	77:23
3		$SnCl_4$ (1.0)	CH_2Cl_2	RT	0.5 h	**5a**	96	60:40
4		BF_3OEt_2 (1.0)	CH_2Cl_2	RT	10 min	**5a**	96	67:33
5		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**5a**	99	83:17
6		$TiCl_4$ (0.1)	CH_2Cl_2	RT	48 h	**5a**	91	82:18
7		none	CH_2Cl_2	RT	48 h	**6a**	99	90:10
8		$TiCl_4$ (1.0)	CH_2Cl_2	RT	0.5 h	**6a**	99	88:12
9	**1b**	none	PhH	RT	10 d	**5b**	98	72:28
10		none	PhH	80	5 h	**5b**	99	72:28
11		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**5b**	99	78:22
12	**1c**	none	PhH	RT	7 d	**5c**	96	76:24
13		none	PhH	80	6 h	**5c**	99	75:25
14		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**5c**	97	83:17

[a] Reaction was carried out in a molar ratio of **1**: dienophile = 1.0 : 1.2-2.0 for uncatalyzed reaction, and of **1**: dienophile : Lewis acid = 1.2 : 1.0 : 1.0 (0.1) for Lewis acid-promoted reaction. [b] Isolated yield.
[c] Determined by ^1H NMR spectroscopy.

Table 2
Asymmetric hetero Diels–Alder reaction of thiabutadienes **1** with dimethyl maleate (Runs 1–6) and dimethyl fumarate (Runs 7–12)[a]

Run	Diene	Conditions Lewis acid(equiv)	Solvent	T / °C	Time	Product	Yield[b] (%)	*exo:endo*[c]
1	**1a**	none	PhMe	110	45 h	**7a**	98	>99:1
2		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**7a**	99	>99:1
3	**1b**	none	PhMe	110	49 h	**7b**	96	>99:1
4		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**7b**	99	>99:1
5	**1c**	none	PhMe	110	11 h	**7c**	98	>99:1
6		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**7c**	99	>99:1
7	**1a**	none	PhMe	110	4 h	**8a**	97	50:50
8		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**8a**	99	75:25
9	**1b**	none	PhMe	110	5 h	**8b**	95	50:50
10		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**8b**	99	78:22
11	**1c**	none	PhMe	110	4 h	**8c**	99	51:49
12		$TiCl_4$ (1.0)	CH_2Cl_2	RT	10 min	**8c**	99	75:25

[a] Reaction was carried out in a molar ratio of **1**: dienophile = 1.0 : 1.2-2.0 for uncatalyzed reaction, and of **1**: dienophile : Lewis acid = 1.2 : 1.0 : 1.0 for Lewis acid-promoted reaction. [b] Isolated yield.
[c] Determined by ^1H NMR spectroscopy. No *endo* isomers were detected for Runs 1-6.

H-3 and H-4 in the *exo/endo* isomers were observed without marked differences (J 3.7–4.8 Hz) from each other.[7] Finally, the stereochemistry of the cycloadducts was determined by comparison of their ^{1}H NMR spectra with that of *exo*-**5b**, the structure of which was unequivocally confirmed by X-ray crystallographic analysis.[8]

Thus, the present work provides a facile and useful synthetic method for novel and optically active bornene ring-fused dihydrothiopyrans.[9]

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References

1. *Asymmetric Synthesis*; Morrison, J. D., Ed.; 1983; Vol. 2, and 1985; Vol. 5; Money, T. *Natural Prod. Reports* **1985**, 253; Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969; Blaser, H.-U. *Chem. Rev.* **1992**, *92*, 935; Arai, Y.; Koizumi, T. *Sulfur Reports* **1993**, *15*, 41.
2. For recent literatures, see: Verdaguer, X.; Vázquez, J.; Fuster, G.; Bernardes-Génisson, V.; Greene, A. E.; Moyano, A.; Percàs, M. A.; Riera, A. *J. Org. Chem.* **1998**, *63*, 7037; Morris, D. G.; Ryder, K. S. *Synthesis* **1997**, 620; Sewald, N.; Wendisch, V. *Tetrahedron: Asymmetry* **1996**, *7*, 1269; de Vries, A. H. M.; Imbos, R.; Feringa, B. L. *Tetrahedron: Asymmetry* **1997**, *8*, 1467; Tanaka, K.; Matsui, J.; Suzuki, H. *J. Chem. Soc., Perkin Trans. 1* **1993**, 153.
3. Motoki, S.; Saito, T.; Karakasa, T.; Kato, H.; Matsushita, T.; Hayashibe, S. *J. Chem. Soc., Perkin Trans. 1* **1991**, 2281; Saito, T.; Fujii, H.; Hayashibe, S.; Matsushita, T.; Kato, H.; Kobayashi, K. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1897; Saito, T.; Karakasa, T.; Fujii, H.; Furuno, E.; Suda, H.; Kobayashi, K. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1359; Saito, T.; Kawamura, M.; Nishimura, J. *Tetrahedron Lett.* **1997**, *38*, 3231; Saito, T.; Suda, H.; Kawamura, M.; Nishimura, J.; Yamaya, A. *Tetrahedron Lett.* **1997**, *38*, 6035; Saito, T.; Takekawa, K.; Nishimura, J.; Kawamura, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2957; Saito, T.; Takekawa, K.; Takahashi, T. *J. Chem. Soc., Chem. Commun.* **1999**, 1001.
4. Sen, D. C. *J. Indian Chem. Soc.* **1936**, *13*, 523.
5. Andrieu, C. G.; Metzner, P.; Debruyne, D. *J. Mol. Struct.* **1977**, *39*, 263.
6. Lamazouere, A.-M.; El-Batouti, N.; Sotiropoulos, J. *Z. Kristallogr.* **1995**, *210*, 597.
7. Compound *exo*-**5b**: mp 75°C; $[\alpha]_D^{20}$ +169 ($CHCl_3$, *c* 2); δ_H ($CDCl_3$) 0.73 (3H, s), 0.85 (3H, s), 0.97 (3H, s), 0.68–2.22 (4H, m), 2.06 (1H, d, J=3.3), 2.91 (1H, dt, J=4.8, 4.8), 3.10 (2H, d, J=4.8), 3.65 (3H, s), 4.03 (1H, d, J=4.8), 7.10–7.30 (5H, m). HRMS found: M^+ 342.1646. Calcd: M 342.1653; Compound *endo*-**5b**: mp 64–65°C; $[\alpha]_D^{20}$ +244 ($CHCl_3$, *c* 0.24); δ_H ($CDCl_3$) 0.76 (3H, s), 0.89 (3H, s), 1.01 (3H, s), 0.88–1.70 (4H, m), 2.10 (1H, d, J=3.3), 2.84 (1H, ddd, J=1.1, 2.6, 13.2), 3.08 (1H, ddd, J=2.6, 4.8, 12.5), 3.17 (1H, dd, J=12.5, 13.2), 3.51 (3H, s), 4.01 (1H, d, J=4.8), 7.02–7.04 (2H, m), 7.19–7.26 (3H, m).
8. Crystal data of *exo*-**5b**. $C_{21}H_{26}O_2S$, M=342.48. Orthorhombic, a=8.533(1), b=14.604(2), c=15.329(2) Å, U=1910.3(4) Å^3, space group $P2_12_12_1$, Z=4, D_{calc}=1.191 Mgm^{-3}. Crystal dimensions 0.11×0.32×0.57 mm, μ(Mo-Kα)=0.170 mm^{-1}, F(000)=736. Enraf–Nonius CAD-4 diffractometer, $\omega/2\theta$ scan mode, ω scan speed ca. 4 deg min^{-1} (h, 0 to 11; k, 0 to 18; l, 0 to 19; 4°<2θ<55°), graphite-monochromated Mo-Kα radiation (λ=0.71073 Å), 2509 reflections measured, 1785 unique reflections with $|F_0| \geq 3\sigma(|F_0|)$. Final R and Rw values are 0.045 and 0.048, respectively.
9. The cycloadducts can be used as useful chiral compounds by further manipulation, e.g., as a chiral sulfide catalyst in asymmetric epoxidation and aziridination (for reviews, see: Aggawal, V. K. *Synlett* **1998**, 329; Li, A.-H.; Dai, L.-X.; Aggawal, V. K. *Chem. Rev.* **1997**, *97*, 2341). Results regarding this study will be published elsewhere. (Saito, T.; Akiba, D.; Kanazawa, S. presented at the 76th Annual Meeting of the Chemical Society of Japan, Yokohama, 1999, Vol. II, p. 810).