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ASYMMETRIC DIELS-ALDER REACTIONS : FACILE PREPARATION AND STRUCTURE OF SULFONAMIDO-ISOBORNYL ACRYLATES

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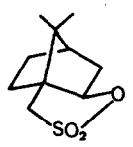
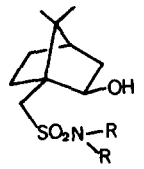
Abstract: The crystalline chiral auxiliaries 2, 3 and 4 were prepared from camphor-10-sulfonyl chlorides in 2 steps. Their readily accessible acrylates underwent efficient asymmetric Diels-Alder additions to cyclopentadiene, the topicity of which agrees with X-ray evidence.

The control of the absolute topicity in Diels-Alder reactions and other carbon,carbon-bond forming processes by means of removable chiral auxiliaries has attracted considerable attention recently[1]. Thus, we have reported the nucleophilic opening of sultone 1 (1 → 2) and the use of the crystalline

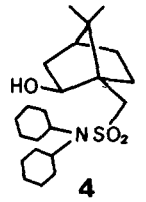
Scheme 1



1



2 R = iPr
3 R = cyclohexyl



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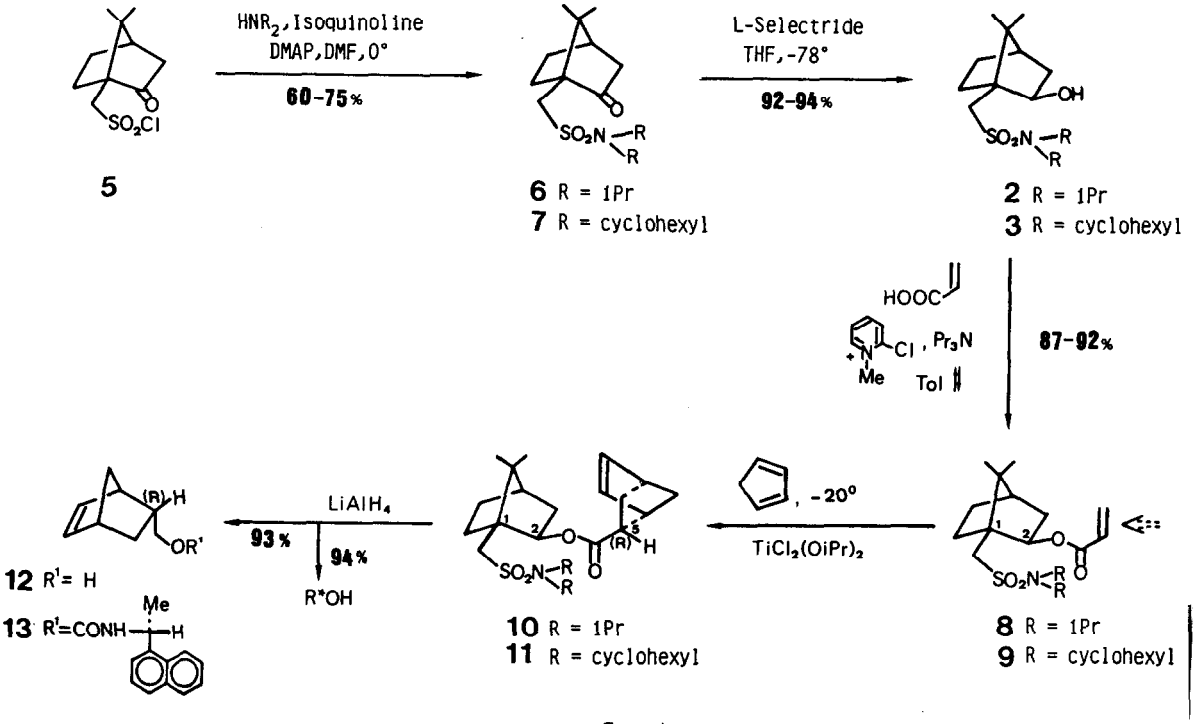
sulfonamide-isoborneol 2 as a practical acrylate-stereoface-directing moiety in the Diels-Alder addition to cyclopentadiene[2]. We present here a more efficient preparation and esterification of the auxiliary alcohol 2 as well as of the new, mutually antipodal control elements 3[3] and 4[3] (Scheme 2).

Scheme 2



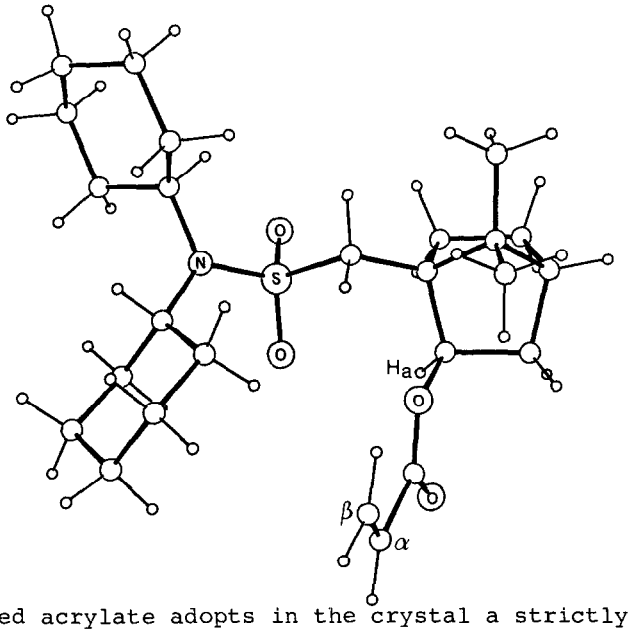
Entry	Dienophile	Product	Cryst. m.p. °C	Yield%	Endo%	d.e.%
a	8	10	crude	98	97	88
	8	10	174-176	83	100	99
b	9	12	crude	97	96	93

Amidation[4] of (+)-camphor-10-sulfonyl chloride (5) with diisopropylamine furnished 6[3] (75%, m.p. 52-54.5°) which on reduction with L-Selectride[4] gave, after crystallization, alcohol 2 (89%, m.p. 102-103°). Acylation[4,5] of 2 afforded acrylate 8[3] (94% recrystallized, m.p. 117-118°). Despite the good dienophile stereoface discrimination in the Diels-Alder reaction 8 → 10[2] (and the facile purification of adduct 10 by crystallization (Table, entry a)) we searched for an even more powerful π-face shielding sulfonamide moiety. Analogous amidation of 5 with dicyclohexylamine[4] yielded 7[3] (60%, m.p. 134-135°) which was reduced[4] to give 3[3] (92% recrystallized, m.p. 163-164°).

Efficient esterification[4,5] furnished acrylate 9[3] (87% after crystallization, m.p. 198-199°) which on $TiCl_2(OiPr)_2$-mediated addition to cyclopentadiene provided the crystalline *endo*-adduct 11[3] in excellent yield and with improved

topological selection[6] (entry b). (The auxiliary 3 was simply regenerated by reduction of the adduct 11 with $LiAlH_4$ and separation from alcohol 12 by crystallization.) This result was readily rationalized based on an X-ray diffraction analysis of acrylate 9[7].

Scheme 3



The uncomplexed acrylate adopts in the crystal a strictly antiplanar disposition of the C_α,C_β- and the C=O bond which in turn is out of the C-H_a-plane by an angle of about 30°. The p lone pair on the planar nitrogen bisects the O-S-O-angle[9]; thus the surface of one cyclohexane ring is projected firmly on top of the olefinic C_α-*re*-face.

To achieve identical C_α-*si*-face shielding the antipodal control element 4[3] was prepared in a strictly analogous way from (-)-camphor-10-sulfonic acid[10]. The rather universal sulfonamide-derived π-face-shielding in esters of 3 and 4 applies also to other reactions such as asymmetric 1,4-additions and enolate alkylations which shall be published in due course.

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REFERENCES AND NOTES

[1] Review: "Asymmetric Synthesis", Ed. *J.D. Morrison*, Academic Press, Vol. 2, 1983; Vol. 3, 1984; see also *D.A. Evans, K.T. Chapman* and *J. Bisaha*, J. Am. Chem. Soc. 106, 4261 (1984); *W. Oppolzer, C. Chapuis* and *G. Bernardinelli*, Helv. Chim. Acta 67, 1397 (1984) and references mentioned therein.

[2] *W. Oppolzer, C. Chapuis* and *M.J. Kelly*, Helv. Chim. Acta 66, 2358 (1983).

[3] All new compounds were characterized by IR, ^{1}H NMR- and MS. $[\alpha]_D^{21°}$-values (EtOH, c= g/100 ml): 2: -34.4° (4.74); 3 -25.7° (0.76).

[4] The following experimental data are representative: 1) Amidation: 5 (7.52 g, 30 mmol in DMF (30 ml)) was added over 2 h to a stirred mixture of DMAP (0.73 g), isoquinoline (7.74 g) and the corresponding amine (60 mmol) in DMF (30 ml) at 0°. Stirring at 0° for 1h, shaking with CH_2Cl_2/10% aq. citric acid, drying of the organic phase ($MgSO_4$), evaporation and chromatography or crystallization (hexane) gave 6 or 7. ii) Reduction: Dropwise addition of 1N L-Selectride in THF (15.3 ml) to 6 or 7 (13.9 mmol) in THF (20 ml) at -78°, stirring of the mixture at -78° for 30 min, then at +21° for 45 min, quenching by successive slow addition of H_2O (3.3 ml), EtOH (12 ml), 3N aq. NaOH (16 ml) and 30% aq. H_2O_2 (12 ml, over 30 min) at 0°, followed by saturation of the aq. phase with K_2CO_3, extraction with Et_2O/THF (1:1), drying of the organic phase, evaporation and crystallization (hexane) gave 2 or 3. iii) Acylation: A mixture of alcohol 2 or 3 (0.56 mmol), $N(nPr)_3$ (5.6 mmol) and acrylic acid (1.41 mmol) in toluene (3.8 ml) was added to α-chloro-N-methylpyridinium iodide (720 mg, 3.8 mmol). Heating of the mixture at reflux for 1 h, dilution with toluene (15 ml), successive washing with 10% aq. HCl, sat. aq. $NaHCO_3$, sat. aq. NaCl, drying, evaporation and crystallization gave acrylate 8 or 9, respectively. For the cycloaddition and cleavage reactions see ref. [2].

[5] *T. Mukaiyama, M. Usui, E. Shimada* and *K. Saigo*, Chem. Lett. 1045 (1975).

[6] The asymmetric induction was determined by HPLC-analysis of 13, s. ref.[2].

[7] Crystallographic data have been deposited at the *Cambridge Crystallographic Data Center*. Observed and calculated structure factors may be obtained from one of the authors (*G.B.*) upon request. The crystals (hexane) are orthorhombic, a=9.248(2), b=13.407(3), c=20.786(6)A, space group P $2_12_12_1$, z=4, d_c=1.164 g.cm^{-3}. Data were collected on a *Philips PW 1100* diffractometer (MoKα). The structure was solved by a direct method (Multan-80) and refined by a full matrix least-squares analysis. The absolute configuration was confirmed by least-squares refinement of the enantiomorph-polarity parameter x[8] (x=0.05(26)). The final R-factor, based on 1732 observed reflections ($|F_o| > 3\sigma(F_o)$ and $|F_o| > 8.0$) was 0.057.

[8] *H.D. Flack*, Acta Crystallogr. Sect. A 39, 876 (1983).

[9] For a similar spatial arrangement of a N,N-disubstituted sulfonamide see: *S. Pokrywiecki, C.M. Weeks* and *W.L. Duax*, Cryst. Struct. Comm. 2, 67 (1973).

[10] (-)-Camphor: *R.V. Stevens, F. Gaeta, D. Lawrence*, J. Am. Chem. Soc. 105, 7713 (1983); (-)-camphor-10-sulfonyl chloride: *P.D. Bartlett* and *L.H. Knox*, Org. Synth. Vol. V, 194, 196 (1973).

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