233. Practical Asymmetric *Diels-Alder* Additions to Camphor-10-sulfonic-Acid-Derived Acrylates

Preliminary Communication[1])

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Summary

Starting from (+)-camphor-10-sulfonic acid (**1**) the chiral crystalline alcohols **3** and **11** were prepared in two steps. *Lewis*-acid-mediated [4 + 2]-additions of their acrylates to 1,3-dienes were studied. Notably, the crystalline acrylate **4** underwent $TiCl_2(OiPr)_2$-promoted *Diels-Alder* addition to cyclopentadiene giving after recrystallization efficiently the pure (2*R*)-adduct **5**.

The asymmetric *Diels-Alder* reaction, employing either chiral dienophiles [1] or dienes [2] has received considerable attention during the last years[2]). Thus, we have recently described almost perfectly diastereofacialselective *Lewis*-acid-promoted [4 + 2]-additions of cyclopentadiene (99.3% d.e.) [1j] and 1,3-butadiene (95.6% d.e.)[3]) to the *si*-face shielding acrylate **A** and to its *re*-face-blocking enantiomer *(Scheme 1)*. An analogous, neopentyloxy-biased allenic ester/cyclopentadiene cycloaddition (99% d.e.) served as a key step for the efficient enantioselective synthesis of (−)-β-santalene[3]) [4]. We then focussed our efforts on the design of chiral control elements which are *1*) even more readily accessible, *2*) highly crystalline and which impose crystallinity to dienophiles and adducts, and *3*) are easily and efficiently regenerated.

Prompted by the ready availability of (+)-(**1**) and (−)-camphor-10-sulfonic acid[4]) we studied the possibility of attaching an aryl- or another bulky group at C(10) of the camphor skeleton which was supposed to shield selectively one isobornyl-acrylate-π-

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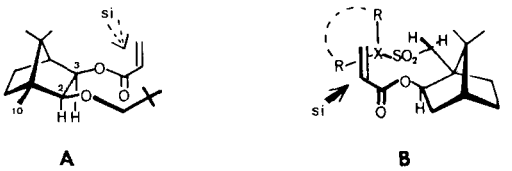
[1]) Reported partially *(Table,* entry a) by *W.O.* at the 14th Workshop Conference Hoechst 'Selectivity – a Goal for Synthetic Efficiency', Schloss Reisensburg, September 18, 1983; to be reported at the GDCh-Symposium 'Chiralität und Aktivität' *(W.O.)* September 29, 1983, Schliersee.

[2]) For non-catalyzed, highly π-facial-selective *Diels-Alder* reactions of H-bonded chiral acrylates see [1k]. Asymmetric [4 + 2]-addition of prochiral dienes and dienophiles using chiral acrylates have apparently not yet reached the same level of predictability and chiral efficiency [3].

[3]) Reported *(W.O.)* at the 8th International Symposium 'Synthesis in Organic Chemistry', Cambridge, UK, July 1983 (*D. Dupuis*, Diploma Work, Université de Genève 1983).

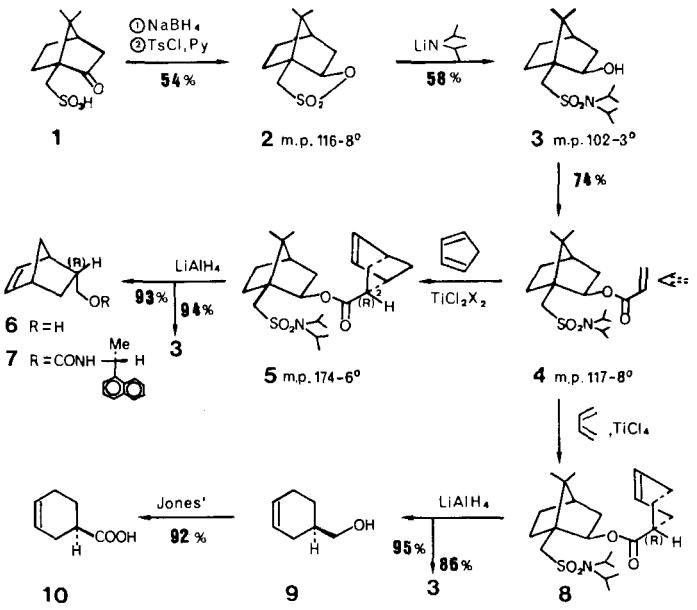
[4]) (−)-Camphor is easily available by *Jones'* oxidation of (−)-borneol *(Aldrich, EGA)*.

Scheme 1



face as depicted in the general formula **B**. Our results are summarized in *Schemes 2* and *3* and in the *Table*[5]). Thus, the crystalline alcohol **3** was prepared in two steps from **1** *via* nucleophilic opening of the crystalline sultone **2** [5] (LDA (6 mol-equiv.), Et_2O, 25°, 30 min, 58%). Esterification of **3** with β-chloropropionic acid (6 mol-equiv., trifluoroacetic anhydride (5 mol-equiv.) [6], slow addition of **3**, 25°, 3 h, m.p. 143–145°, 75%) and β-elimination (Et_3N (2 mol-equiv.), toluene, reflux, 2.5 h, 99%) afforded the crystalline acrylate **4**. The crucial *Diels-Alder* reaction was carried out as follows: 1.2 N cyclopentadiene (3 mol-equiv. in CH_2Cl_2) was added at −20° under N_2 to a stirred solution prepared from 1 N $TiCl_4$/Ti(OiPr)$_4$-mixture (1:1 in CH_2Cl_2), 1.5 mol-equiv.) and 0.1 N acrylate **4** (CH_2Cl_2). After 4 h at −20° the mixture was quenched with H_2O to give after workup the crude (2*R*)-adduct **5** (containing 3% of its *exo*-isomers) in 98% yield (entry a). Reduction of crude **5** with $LiAlH_4$ (Et_2O, 25°, 1 h) yielded the expected[6]) (2*R*)-alcohol **6** in 88% e.e. as determined by HPLC-analysis of **7** [1j] [8]. Moreover, by

Scheme 2



[5]) All new compounds were characterized by IR, ^{1}H-NMR and MS. The depicted diastereoface differentiation (d.e.) and the absolute configuration of the adducts agree perfectly with chiroptic measurements of **6** and **9**.

[6]) For X-ray evidence in favor of the depicted sulfonamide conformation see [7].

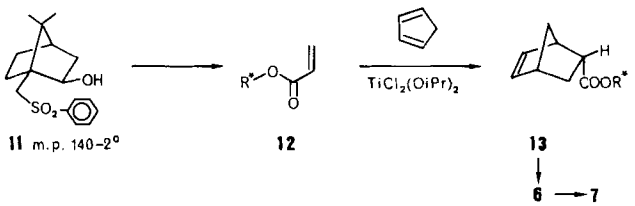
Table. *Asymmetric* Diels-Alder *Reactions* **4** → **5**, **4** → **8** *and* **12** → **13**

Entry	Dienophile	Diene	*Lewis* acid X	Reaction temp. [°C] (Time [h])	Adduct	Yield [%]	M.p.	*endo/exo*	d.e.%
a	**4**		OiPr	−20 (4)	**5**	98	155–62	97/3	88
		2 crystallizations			**5**	83	174–76	> 100/1	99
b	**4**		Cl	−20 (4)	**5**	89	–	98/2	77
		2 crystallizations			**5**	52	–	> 100/1	96
c	**4**		Cl	−8 (84)	**8**	98	125–32	–	78
		2 crystallizations			**8**	60	135–37	–	86
d	**12**		OiPr	−20 (14)	**13**	97	155–58	95/5	66

two simple crystallization (hexane) of crude **5** the very minor (2*S*)-*endo*- and its *exo*-isomers were easily removed giving virtually pure **5** in 83% yield. Cleavage of the latter with $LiAlH_4$ furnished 99% pure (2*R*)-**6** in 93% yield with 94% recovery of the recrystallized auxiliary **3**. The analogous, but slower $TiCl_4$-mediated addition of 1,3-butadiene to **4** proceeded with lower chiral efficiency than its addition to acrylate **A**[3])[7]). Nevertheless, simple recrystallization of the resulting crude **8** furnished enantiomerically almost pure adduct **8** as assessed by the reduction **8** → **9** and the oxidation **9** → **10**. The acid **10** was shown to be 86% enantiomerically pure according to HPLC-analysis [8] of its amide derived from (*R*)-α-naphthylethylamine[8]).

This result becomes even more significant since **9** and **10** are the correct enantiomers to serve as intermediates in the syntheses of (−)-sarkomycine [1e] and (−)-shikimic acid [10], respectively. The potential of this concept is further illustrated by nu-

Scheme 3



[7]) $TiCl_4$ is also a less suitable promotor for the process **4** → **5** (entry b).

[8]) Acid **10** was converted to its α-naphthylethyl-amide under non-epimerizing conditions [9][3]).

cleophilic opening of sultone **2** with phenyllithium (3.5 mol-equiv. Et_2O, 25°, 4 h) which afforded the crystalline sulfone **11** in 53% yield. Its acrylate **12** (m.p. 83–84.5°) added to cyclopentadiene with comparatively lower chiral efficiency (entry d); however the adduct **13** is again crystalline.

We are currently exploring the scope of camphor-10-sulfonamide- and -sulfone-derived diastereoface differentiation by introducing various shielding groups into **B** and are studying its application in asymmetric *Diels-Alder*-, ene-, 1,4-addition-, and ester enolate-substitution reactions.

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