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ASYMMETRIC DIELS-ALDER REACTIONS OF ACRYLATES DERIVED FROM 3-ALKYL-BORNEOLS AND -ISOBORNEOLS

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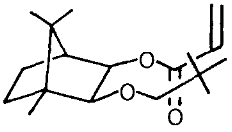
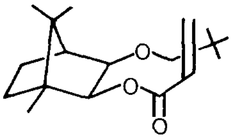
Abstract: Starting from (+)-camphor the chiral alcohols 7 and 8 have been prepared; their acrylates 9 and 13 underwent $TiCl_2(OiPr)_2$-mediated Diels-Alder additions to cyclopentadiene with stereoface-differentiations of 66% d.e. and 94% d.e., respectively.

Two years ago we have reported high levels of stereodifferentiation in $TiCl_2(OiPr)_2$-promoted Diels-Alder additions of cyclopentadiene to acrylates 1 (99.3% d.e.) and 2 (97% d.e.)[1].

Scheme 1



1

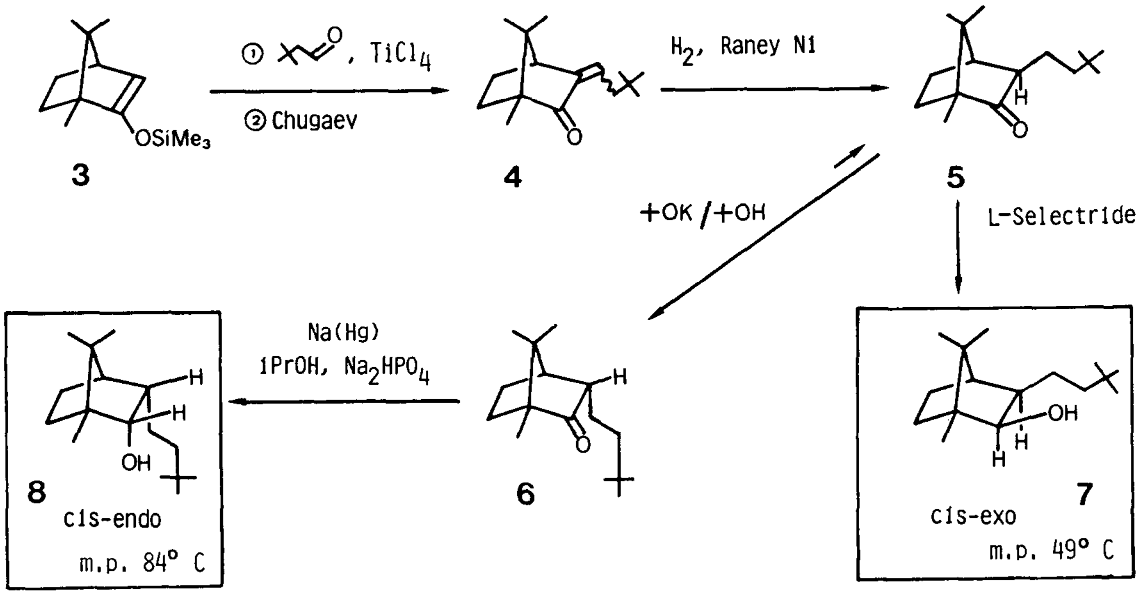


2

Although the auxiliary alcohol of acrylate 1 is readily accessible from (+)-camphor (and its antipode from (-)-camphor) by a sequence of six steps in 60% overall yield (after recrystallization) the development of other chiral auxiliaries remained a fascinating challenge[2].

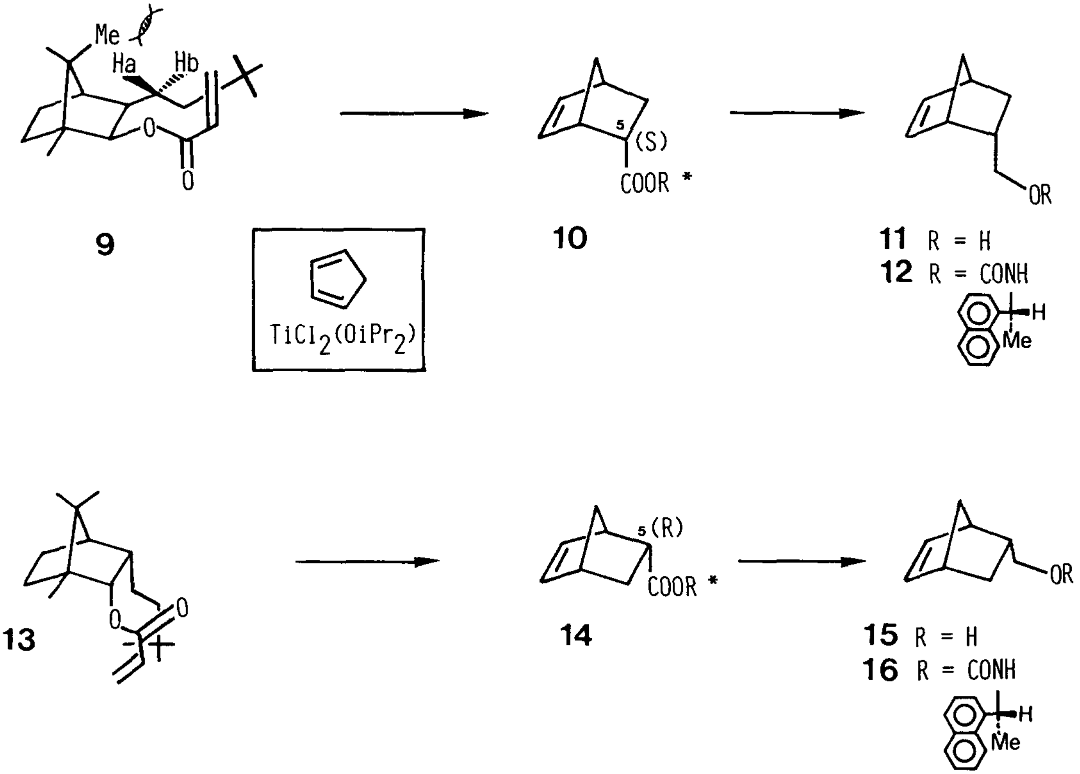
Thus, we next focussed our attention on the possibility of linking the sterically demanding *t*-butyl group to the borneol-/isoborneol skeleton by a carbon chain (Scheme 2).

Scheme 2



TiCl$_4$-mediated aldolization[3] of silylenol ether 3[4] with 3,3-dimethylbutanal[5] and elimination[6] afforded enone 4 (6:1 - stereoisomer mixture, 75%)[7] which on hydrogenation (4.7 mmol, 110 mg Raney Ni, MeOH, 60°, 4.3 atm, 14 h) yielded a 83:17-mixture of the *exo*- and *endo*-ketones 5[7] and 6[7] (80%). Reduction of the purified major isomer 5 with L-Selectride (1.1 eq, -78°, THF, 1 h) gave cleanly the crystalline *cis-exo*-alcohol 7[7] (92%). Base-induced equilibration (KO*t*Bu (4.5 eq), *t*BuOH, ↑↓, 48 h) of the mixture 5/6 gave predominantly the more stable *endo*-ketone 6[7] (88% yield; 5/6 = 83:17 → 8:92). The latter was reduced with Na(Hg) in buffered isopropanol[8] to give the crystalline *cis-endo* alcohol 8[7] (63%). Esterification of 7 and 8 with acryloyl chloride/AgCN[9] furnished acrylates 9[7] (77%) and 13[7] (85%), respectively. To determine the sign and extent of the topological bias provided by each auxiliary the TiCl$_2$(OiPr)$_2$-promoted additions to cyclopentadiene served as a test reaction[10] (Scheme 3). Regenerative cleavage of the auxiliary from the adducts with LiAlH$_4$ furnished alcohols 11 and 15 which were analyzed by means of their chiroptic properties and by HPLC-measurements of their carbamates 12 and 16, respectively[1].

Scheme 3



Dienophile	Reaction Temperature	Product	Yield%	Endo%	d.e.%
9	-30°C	10	75	89	66
13	-20°C	14	89	92	94.3

Interestingly, it turned out that the signs of induction agree with our expectation but that the *exo*-control element 7 exerts a significantly lower chirality directing influence than its *endo*-counterpart 8. Thus, the stereoface selectivity of the reaction 9 → 10 was rather modest (66% d.e.) relative to that of the transformation 13 → 14 (94.3% d.e.) and to the analogous addition of the neopentyl ether 2 (97% d.e.). This may be attributed to H_a/CH_3-repulsion in 9 impairing the alignment of the blocking chain along the acrylate π-face. Another reason for the advantageous conformational role of the ether oxygen in 1 (and 2) could be a chelation of the carbonyl- and the ether oxygens by titanium.

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[2] For the most recent achievements in this area see: *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.

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[4] *G. Simchen* and *W. Kober*, Synthesis 1976, 259.

[5] Obtained by oxidation of 3,3-dimethylbutanol with PDC: *E.J. Corey* and *G. Schmidt*, Tetrahedron Lett. 1979, 399.

[6] i) NaH (1 eq), THF/HMPA 7:1, imidazole (0.3 eq), → ↑↓; ii) CS_2 (8.5 eq), ↑↓ 3 h; iii) $(CH_3O)_2SO_2$ (2.2 eq) ↑↓, 0.5 h.

[7] All new compounds were characterized by IR, ^{1}H-NMR and MS. The following optical rotations $[\alpha]_D^{25}$ (EtOH) were recorded: 7: +23.4° (c 0.95); 8: +17.1 (c 2.75).

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[9] *S. Takimoto*, *J. Inanaga*, *T. Katsuki* and *M. Yamaguchi*, Bull. Chem. Soc. Jpn. 49, 2335 (1976).

[10] i) Add 1N mixture of $TiCl_4/Ti(OiPr)_4$ (1:1, 1.5 eq) in CH_2Cl_2 to 0.1N acrylate in CH_2Cl_2; ii) cyclopentadiene (3 eq), 4 h.

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