Intramolecular Diels–Alder Reaction of a Sulphonyl-activated 1,3,9-Triene

Andreas Weichert and H. Martin R. Hoffmann*
Department of Organic Chemistry, University of Hannover, Schneiderberg 1 B, D-3000 Hannover, Federal Republic of Germany

The eudesmane precursor (**6**) containing a *trans* ring fusion has been prepared stereoselectively by an inverse electron-demand, intramolecular (4 + 2) π cycloaddition with phenylsulphonyl as controlling group.

The intramolecular Diels–Alder reaction (IMDA) has attracted continued interest as a method for the regio- and stereo-selective construction of molecules with several chiral centres.[1] Hitherto, π-components which are activated by sulphonyl substituents have hardly been studied, although recently Craig *et al.*[2a] and Battiste and his co-workers[2b] have described IMDA reactions of vinylic sulphones.

In an approach towards *trans* fused octahydronaphthalenes of the eudesmane type[3a] we have investigated an IMDA reaction of a dienyl sulphone, *i.e.* a Diels–Alder cyclization with inverse electron-demand. Preparation of a suitably functionalized 1,3,9-triene began with isopulegol (**1**), which was cleaved oxidatively to the aldehyde (**2**).[3b] Coupling of (**2**) with phenyl vinyl sulphone in the presence of DABCO (1,4-diazabicyclo[2.2.2]octane)[4,5] afforded the allylic alcohol (**4a**) which was mesylated and subjected to elimination–cyclization [(**4a**)→(**5**)→(**6**)]. Flash chromatography (ether–petroleum, 2:1) yielded an oily mixture of four diastereoisomers (4 acetoxycarbonyl signals in the ^{13}C NMR spectrum) in reproducible fashion. 400 MHz ^1H NMR showed two pairs of isomers which were epimeric at C-7 and C-10, respectively (Table).

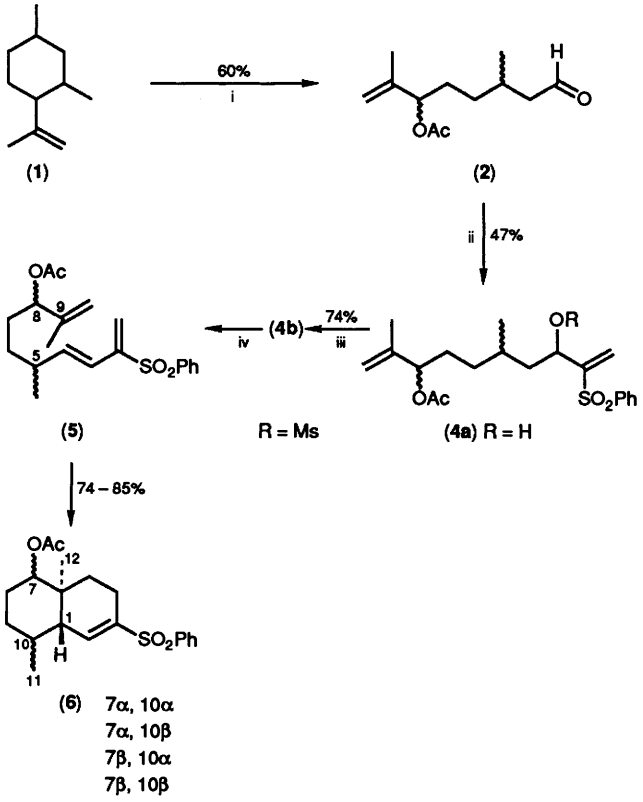
A priori, 8 diastereoisomers (2^4 stereoisomers) are possible for a decalin with 4 chiral centres. Since only 4 diastereoisomers were formed, the ring junction had to be either *cis* or *trans*. Fractional crystallization (Et_2O) yielded the major isomer, m.p. 189 °C, which was submitted to X-ray crystal structure analysis (Figure 1), showing *trans* ring fusion. Therefore, the 3 remaining diastereoisomers were also *trans* fused decalins.

Clearly, the preferred transition state is *endo* with respect to the olefinic methyl group, which becomes angular or axial in the product (Figure 2). Previously, Wilson,[6] and Taber[7] have studied related IMDA reactions of 1,3,9-trienes with an olefinic methyl group at C-9 [as is also present in our triene (**5**)] and a second methyl group at C-3. In this case, high *trans* stereoselectivity has been ascribed to steric bulk at C-3.[6–8] The triene (**5**) lacks the 3-methyl group and has a bulky phenylsulphonyl group at the more remote C-2. In our case, the angular methyl group appears to control the steric outcome, possibly in combination with an electronically altered

Table. Characteristic 400 MHz ^{1}H NMR data[a,b] of (6).

Diastereoisomer[c]	Ratio[d]	2-H[d]	7-H	14-H	11-H	12-H
(6) (7α,10α)	1	6.88 (m)	4.54 (dd, 11/5)[e]	2.01 (s)	0.97 (d, 7.5)[g]	0.83 (s)
(7α,10β)	2	7.04 (m)	4.54 (dd, 11/5)[e]	2.02 (s)	1.04 (d, 6.5)[g]	0.75 (s)
(7β,10α)	2	7.26 (m)	4.69 (dd, 2.5)[f]	2.07 (s)	1.07 (d, 7.0)[g]	0.70 (s)
(7β,10β)	4	7.14 (m)	4.73 (dd, 2.5)[f]	2.04 (s)	1.08 (d, 6.0)[g]	0.76 (s)

[a] Bruker instrument. [d] Determined in $CDCl_3$ with Me_4Si as internal standard; coupling constants ^3J in Hz. [c] Diastereoisomeric at C-7 and C-10; *cf.* formula (6). [d] The intensity of the well resolved 2-H signal gave the diastereoisomeric ratio. [e] The large coupling constant (11 Hz) demands an axial proton at C-7, which is coupled to the *trans* diaxial proton at C-8 [*cf.* (6) (7α,10α); (6) (7α,10β)]. [f] The equatorial proton is coupled equally with the 8-methylene protons (dd, apparent triplet) [*cf.* (6) (7β,10α); (6) (7β,10β)]. [g] The smaller ^3J coupling constant is observed for the methyl group which is equatorial at C-10, the larger one for the axial epimer (*cf.* T. M. Moynehan, K. Schofield, R. A. Y. Jones, and A. R. Katritzky, *J. Chem. Soc.*, 1962, 2637; J. A. Marshall and J. J. Partridge, *Tetrahedron*, 1969, **25**, 2159).



Scheme. *Reagents and conditions:* i, $Pb(OAc)_4$, benzene, reflux 2 h; ii, CH_2=$CHSO_2Ph$ (3), DABCO, room temp., 8 weeks; iii, MsCl, $EtNPr^i_2$, catalyst DMAP, −20 °C, 20 h; iv, pyridine, toluene, 170 °C, 24 h, sealed tube.

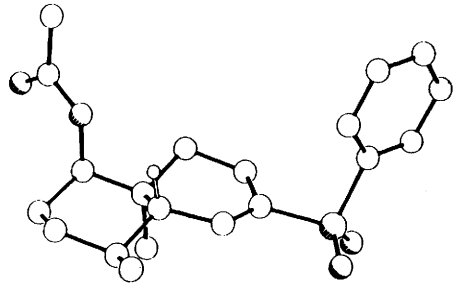


Figure 1. X-Ray crystal structure of (6) (major isomer 7β,10β).

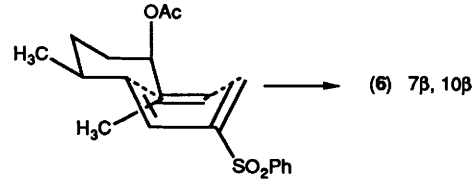


Figure 2.

transition state due to the electron-attracting phenylsulphonyl group.[9]

Experimental

For the preparation and spectral properties of 8-acetoxy-2-phenylsulphonyl-5,9-dimethyl-3-hydroxydeca-1,9-diene (**4a**) *cf.* ref. 4*a*.

8-Acetoxy-5,9-dimethyl-3-methylsulphonyloxy-2-phenylsulphonyldeca-1,9-diene (**4b**).—Methanesulphonyl chloride (0.55 g, 4.73 mmol) in dry CH_2Cl_2 (6 ml) was added to a solution of the allylic alcohol (**4a**) (1.5 g, 3.94 mmol), ethyldiisopropylamine (1.53 g, 11.8 mmol), and a catalytic amount of *p*-dimethylaminopyridine (DMAP) in CH_2Cl_2 (6 ml) at −20 °C and the mixture was stirred for 20 h under nitrogen. The solution was then poured into ice-cooled 1M HCl and the organic layer was separated, washed with saturated aqueous $NaHCO_3$ and water, dried ($MgSO_4$), filtered, and evaporated under reduced pressure. The crude brown oil was purified by flash chromatography (ether–light petroleum, 5:1) on silica gel to give the mesylate (**4b**) as a colourless oil (1.34 g, 74%) (diastereoisomeric mixture) (Found: M^+ − COMe, 415.1248. $C_{21}H_{30}O_7S_2$ requires *M*, 415.1249); ν_{max}($CHCl_3$) 1 730 (C=O), 1 370 and 1 175 (OSO_2CH_3), and 1 320 and 1 145 cm^{-1} (SO_2Ph); δ_H(200 MHz, $CDCl_3$) 7.96–7.54 (5 H, m, Ar), 6.63/6.61 (1 H, d, ^2J 1.5 Hz, 1-H), 6.26 (1 H, br s, 1-H), 5.26 [1 H, m, C(*H*)OAc], 5.13/5.08 [1 H, t, ^3J 7 Hz, C(*H*)OMs], 4.91 (2 H, m, =CH_2), 2.76/2.74 (3 H, OSO_2Me), 2.08/2.05 (3 H, s, $COCH_3$), 1.73/1.69 (3 H, s, CCH_3), 1.67–1.01 (7 H, m), and 0.87/0.82 (3 H, d, ^3J 6 Hz, $CHCH_3$); δ_C(50 MHz, $CDCl_3$) 170.22/170.16 (s, C=O), 150.49/149.97 (s, C-2), 143.12/143.01 (s, *C*=CH_2), 139.42 (s, Ar), 134.31, 129.63, 128.61 (d, Ar), 127.41/126.68 (t, C-1), 112.93/112.70 (t, C=CH_2), 77.26/77.21, 75.58/75.42 (d, CHOMs, CHOAc), 44.16/43.96 (t, C-4), 38.56/38.47 (q, OSO_2Me), 32.61/31.02 (t, C-7), 29.75/29.58 (d, $CHCH_3$, 29.12/28.91 (t, C-6), 21.12/19.60 (q, C-12), 19.41/19.03 (q, $CHCH_3$); *m/z* (220 °C) 458 (1%, M^+), 415 (14), 320 (32), 302 (17), 161 (100), 125 (56), 109 (82), 94 (30), 78 (45), and 43 (54).

For spectral data of 8-acetoxy-5,9-dimethyl-2-phenylsulphonyldeca-1,3,9-triene (**5**) *cf.* ref. 4*a*.

7β-*Acetoxy*-6,10β-*dimethyl*-3-*phenylsulphonylbicyclo*[4.4.0]-*dec*-2-*ene* (**6**) (*Major Isomer*).—Dry pyridine (25 ml) was added to the mesylate (**4b**) (2.0 g, 4.37 mmol) in dry toluene (290 ml, 0.015M) and the solution was heated at 170 °C for 24 h in a sealed tube. After dilution with ether, the reaction mixture was washed with 1M HCl solution and water. The organic layer was dried ($MgSO_4$), filtered, and concentrated. The residue when subjected to flash chromatography (silica gel, ether–light petroleum, 2:1) afforded an oil (1.34 g, 85%) (diastereoisomeric mixture, 4:2:2:1, cf. Table), from which the major isomer 7β,10β (0.59 g, 37%) crystallized selectively (m.p. 189 °C) upon addition of ether (Found: C, 66.3; H, 7.25. $C_{20}H_{26}O_4S$ requires C, 66.27; H, 7.23%) (Found: M^+ 362.1552. $C_{20}H_{26}O_4S$ requires 362.1552); $\nu_{max}(CHCl_3)$ 3 020, 2 960, 2 940, 1 725, 1 445, 1 370, 1 315, 1 305, 1 250, 1 150, 1 090, and 910 cm^{-1}; δ_H(300 MHz, $CDCl_3$) 8.05–7.50 (5 H, m, Ar), 7.14 (1 H, m, =CH), 4.73 (1 H, dd, ^3J 2.5 Hz, CHOAc), 2.36–1.26 (13 H, m), 2.04 (3 H, s, $COCH_3$), 1.08 (3 H, d, ^3J 6 Hz, $CHCH_3$), and 0.76 (3 H, s, CCH_3); δ_C(75 MHz, $CDCl_3$) 170.38 (s, C=O), 139.51 (s, *C*=CH), 138.96 (d, C=*C*H), 138.74 (s, Ar), 133.18, 129.14, 128.02 (d, Ar), 75.90 (d, *C*HOAc), 45.17 (d, =CH*C*H), 36.12 (s, *C*CH_3), 31.22, 30.56 (t, C-4, C-8), 29.19 (d, *C*HCH_3), 25.87, 20.84 (t, C-5, C-9), 21.15 (q, CO*C*H_3), 19.47 (q, C*C*H_3), and 16.32 (q, CH*C*H_3); *m/z* (100 °C) 362 (8%, M^+), 320 (5), 303 (90), 161 (100), 145 (22), 125 (34), 104 (30), 91 (22), 78 (28), and 43 (44).

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8 Ref. 1*a*, p. 221; ref. 1*d*, p. 48.

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