

Stereospecific Total Synthesis of (\pm)-Albene *via* a Prochiral Precursor

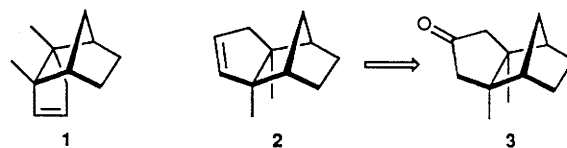
Adusumilli Srikrishna* and Sankuratri Nagaraju

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560012, India

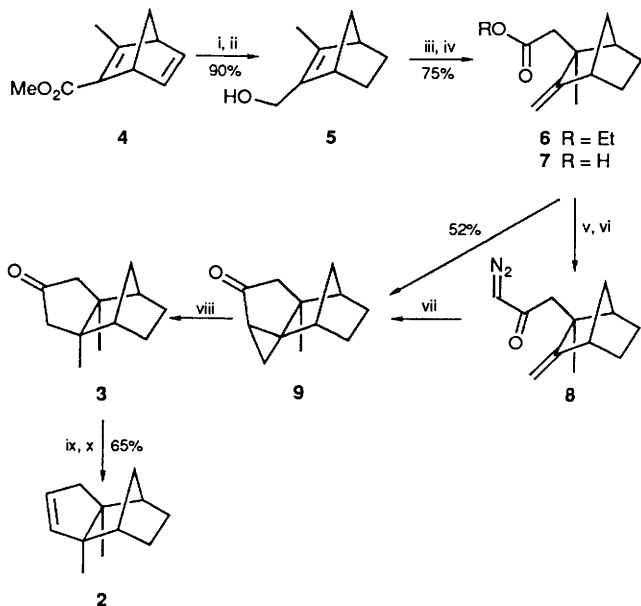
The total synthesis of racemic albene **2** *via* the prochiral precursor **3**, using a stereoselective Claisen rearrangement and an intramolecular diazoketone cyclopropanation as key reactions, is described.

The natural product albene was first isolated¹ in 1962 from *Petasites albus* and the structure, as the *exo* isomer **2**, was established² conclusively in 1978 after an initial assignment³ as the *endo* isomer **1** (now referred to as isoalbene). The unique 2,6-dimethyltricyclo[5.2.1.0^{2,6}]decane skeleton incorporating two contiguous quaternary carbons makes the compound an interesting synthetic target.⁴ As part of our interest⁵ in the application of the Claisen rearrangement in the stereospecific synthesis of natural products containing quaternary carbons, we now report a total synthesis of racemic albene **2** *via* the prochiral ketone **3**, using a combination of stereoselective Claisen rearrangement and copper catalysed intramolecular diazoketone cyclopropanation as key reactions.

The synthetic sequence starting from the cyclopentadiene-



methyl tetrolate Diels–Alder adduct **4** is depicted in Scheme 1. Diels–Alder reaction of cyclopentadiene with but-2-ynoic acid followed by esterification with ethereal diazomethane furnished, in 68% yield, the requisite starting material **4**.⁶ The allyl alcohol **5** required for the Claisen rearrangement was obtained, in 90% yield, by selective hydrogenation of the adduct **4** followed by

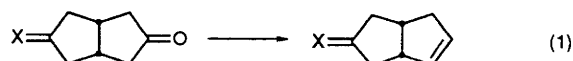


Scheme 1 i, $\text{H}_2/10\% \text{Pd-C}$, EtOAc , 2 h; ii, DIBAH, toluene, $-78^\circ\text{C} \rightarrow$ room temp., 1 h; iii, MeC(OEt)_3 , EtCO_2H , 180°C , 48 h; iv, $\text{MeOH-H}_2\text{O}$, NaOH , reflux, 6 h; v, $(\text{COCl})_2$, C_6H_6 , room temp., 2 h; vi, CH_2N_2 , Et_2O , room temp., 2 h; vii, anhydrous Cu_2SO_4 , W-lamp, C_6H_{12} , 5 h; viii, Li , liq. NH_3 , THF, 5 min, 80%; or $\text{H}_2/10\% \text{Pd-C}$, EtOH , 40 psi, 6 h, 100%; ix, TsNHNH_2 , EtOH , 80°C , 4 h; x, BuLi , $\text{Et}_2\text{O-TMEDA}$, $0^\circ\text{C} \rightarrow$ room temp., 6 h.

DIBAH reduction of the resultant dihydro compound. The ortho ester Claisen rearrangement⁷ of the allyl alcohol **5** using triethyl orthoacetate in the presence of a catalytic amount of propionic acid (sealed tube, 180°C , 48 h) stereoselectively furnished, in 86% yield, the ester **6** via the sterically preferred *exo* transition state. Hydrolysis of the ester **6** with aq NaOH furnished, in 87% yield, the acid **7**, m.p. 86°C .^{*} Treatment of the acid chloride, obtained from the acid **7** and oxalyl chloride, with an excess of ethereal diazomethane generated the key diazoketone **8**.^{*} Anhydrous copper sulphate-catalysed decompo-

sition⁸ of the diazoketone **8** in refluxing cyclohexane (tungsten lamp), and intramolecular insertion of the resultant keto carbene into the *exo*-methylene, gave stereospecifically the cyclopropyl ketone **9**.^{*} Regiospecific cleavage of the cyclopropane ring in **9**, using lithium in liquid ammonia, furnished cleanly the symmetric ketone **3**, in 80% yield.^{*} Alternatively, catalytic hydrogenation (10%Pd-C, EtOH) of the cyclopropyl ketone **9** quantitatively yielded the prochiral ketone **3**. The prochiral ketone **3** was transformed to albene **2** via its tosyl hydrazone. Thus, treatment of the ketone **3** with tosylhydrazine furnished the tosyl hydrazone, m.p. 162°C (decomp.). The tosyl hydrazone on reaction with an excess of BuLi in $\text{Et}_2\text{O-TMEDA}$, furnished, in 65% yield, albene **2**, m.p. 110°C (after sublimation) (lit.,³ $110\text{--}115^\circ\text{C}$); the ^1H NMR spectral results were identical with those reported in the literature.²

In conclusion, we have described here a stereospecific route to albene, via the prochiral ketone **3**. A recent report⁹ on the conversion of similar prochiral ketones into chiral alkenes [eqn. (1)], enhances the significance of the present sequence as a potential chiral route to albene **2**.



Acknowledgements

One of the authors (S. N.) thanks the Council of Scientific and Industrial Research, New Delhi, for the award of a research fellowship.

References

- L. Hochmannova, L. Novotny and V. S. Herout, *Collect. Czech. Chem. Commun.*, 1962, **27**, 2711.
- W. Kreiser and L. Janitschke, *Tetrahedron Lett.*, 1978, 601; *Chem. Ber.*, 1979, **112**, 408; W. Kreiser, L. Janitschke and L. Ernst, *Tetrahedron*, 1979, **34**, 131.
- K. Vokac, Z. Samek, V. Herout and F. Sorm, *Tetrahedron Lett.*, 1972, 1665.
- For earlier syntheses see: J. E. Baldwin and T. C. Barden, *J. Org. Chem.*, 1981, **46**, 2442; B. M. Trost and P. Renaut, *J. Am. Chem. Soc.*, 1982, **104**, 6668; G. G. G. Manzardo, M. Karpf and A. S. Dreiding, *Helv. Chim. Acta*, 1983, **66**, 627; D. P. Curran and M.-H. Chen, *J. Am. Chem. Soc.*, 1987, **109**, 6558; H. R. Sonawane, N. S. Bellur, J. R. Ahuja and D. G. Kulkarni, unpublished work.
- A. Srikrishna and K. Krishnan, *Tetrahedron Lett.*, 1989, **30**, 6577; A. Srikrishna and K. Krishnan, *Indian J. Chem., Sect. B*, 1990, **29**, 879; A. Srikrishna and G. Sundarababu, *Tetrahedron*, 1990, **46**, 6501.
- T. Gibson and Z. J. Barneis, *Tetrahedron Lett.*, 1972, 2207; F. M. Simmross and P. Weyerstahl, *Liebigs Ann. Chem.*, 1981, 1089.
- W. S. Johnson, L. Werthermann, W. R. Bartlett, T. J. Brocksom, T. Li, D. J. Faulkner and M. R. Petersen, *J. Am. Chem. Soc.*, 1970, **82**, 741. For a two step ortho ester Claisen rearrangement see: H. Monti, C. Corroil and M. Bertrand, *Tetrahedron Lett.*, 1982, **23**, 947.
- A. Tahara, M. Shimagaki, S. Ohara and T. Nakata, *Tetrahedron Lett.*, 1973, 1701.
- H. Kashiwara, H. Suemune, T. Kawahara and K. Sakai, *J. Chem. Soc., Perkin Trans. 1*, 1990, 1663.

Paper 0/05236A
Received 21st November 1990
Accepted 5th December 1990

^{*} Selected spectral data (*J* values in Hz). For **7**: (Found: C, 73.4; H, 9.08. $\text{C}_{11}\text{H}_{16}\text{O}_2$ requires C, 73.3; H, 8.95); ν_{max} (Nujol)/ cm^{-1} 3000br, 1707, 1240, 935 and 888; δ_{H} (90 MHz, CDCl_3): δ 4.83 (1 H, s), 4.57 (1 H, s), 2.79 (1 H, br s), 2.48 (1 H, br s), 2.48 and 2.27 (2 H, AB q, *J* 16), 1.3–1.8 (6 H, m) and 1.2 (3 H, s); δ_{C} (22.5 MHz, CDCl_3) 179.0 (s), 164.5 (s), 101.3 (t), 46.9 (d), 45.5 (t), 45.0 (d), 44.2 (s), 37.3 (t), 29.3 (t), 23.7 (t) and 23.1 (q). For **8**: ν_{max} (film)/ cm^{-1} 3075, 2105, 1635 and 880; δ_{H} (60 MHz, CCl_4) 5.08 (1 H, s), 4.65 (1 H, s), 4.41 (1 H, s), 2.66 (1 H, br s), 2.5 (1 H, br s), 2.2 (2 H, ABq, *J* 14), 1.3–1.9 (6 H, m) and 1.13 (3 H, s). For **9**: ν_{max} (film)/ cm^{-1} 1730, 1205 and 957; δ_{H} (90 MHz, CDCl_3) δ 2.48 and 2.02 (2 H, ABq, *J* 18), 2.16 (1 H, br s), 1.2–2.0 (10 H, m) and 0.98 (3 H, s); δ_{C} (22.5 MHz, CDCl_3) 215.1 (s), 56.0 (t), 50.8 (s), 48.2 (d), 42.0 (d), 40.5 (s), 37.7 (t), 35.2 (d), 25.0 (2 C, t), 23.1 (q) and 17.2 (t) (Found: M^+ , 176.1195. $\text{C}_{12}\text{H}_{16}\text{O}$ requires *M*, 176.1201). For **3**: ν_{max} (film)/ cm^{-1} 1735, 1465, 1405, 1385, 1090 and 625; δ_{H} (90 MHz, CDCl_3) 2.32 (4 H, s), 1.9 (2 H, br s), 1.2–1.8 (6 H, m) and 1.12 (6 H, s); δ_{C} (22.5 MHz, CDCl_3) 219.5 (s), 55.4 (2 C, t), 50.5 (2 C, d), 46.2 (2 C, s), 34.8 (t), 23.7 (2 C, t) and 21.1 (2 C, q) (Found: M^+ , 178.1364. $\text{C}_{12}\text{H}_{18}\text{O}$ requires *M*, 178.1358).