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SIMPLE AND EFFICIENT ENTRIES TO THE BASIC CARBON SKELETONS OF SOME KINDS OF TERPENOIDS FROM A FUNCTIONALIZED TRICYCLO[6.3.1.0^{3,8}]DODEC-4-ENE

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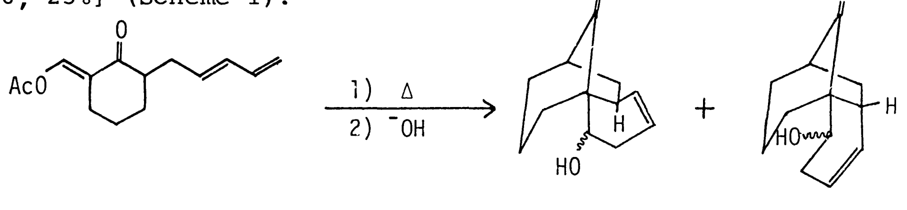
The basic carbocyclic frameworks of stemodane, cedrane, hydroazulene, and himachalene type terpenoids are newly synthesized from a common tricyclic ketone, which is readily obtained *via* an intramolecular Diels-Alder reaction of a trienone, by simple manipulations.

In our previous report[1] we have described a stereoselective intramolecular Diels-Alder reaction of several trienones (e.g. 5) into functionalized tricyclo[6.3.1.0^{3,8}]dodec-4-enes (e.g. 6), which would be a useful and common synthon for assembling basic carbocyclic frameworks of various kinds of natural products. We now wish to report the new methods for constructing some kinds of terpenoids carbon skeletons, e.g. stemodane (1),[2] cedrane (2),[3] hydroazulene (3),[3] and himachalene (4),[3] from the tricyclic ketone (6) as a common precursor.

The starting tricyclic ketone (6)[4] was synthesized stereoselectively from the acetate (5) *via* an intramolecular Diels-Alder reaction (40 mmol solution in mesitylene using a sealed tube, 220 °C, 50 h) followed by a basic hydrolysis [α-/β-OH = 12.0 : 2.6, 23%] (Scheme 1).



5 6 14.6 : 1 7

Scheme 1.

Sequential hydrogenation, ketalization, and Swern oxidation of the keto alcohol (6) provided the keto ketal (8)[5,6] [89% from the β-OH isomer and 86% from the α-isomer], which was then submitted to the conditions of Robinson type annulation[7] to give the enone (1),[8] with stemodane carbon skeleton, as a single product in 76%

yield. The β configuration at C-5H (steroid numbering) in 1 could be deduced from the use of a thermodynamic equilibration condition[9)] for the final aldol condensation step.

For assembling the cedrane skeleton (2), it is necessary to contract the cyclohexanone part in 8 to five membered ring. To this purpose, the keto ketal (8) was transformed to the diazoketone (9)[10)] [70%] by the diazo transfer procedure, then the methanol solution of 9 was photolized[11)] at 0 °C for 3 h to afford the desired ester (2)[12)] in 81% yield, stereoselectively. In order to convert the ester (2) to the hydroazulene (3) we resorted to a cleavage of the C-C bond between C-7 and C-11 in 2 *via* Baeyer-Villiger oxidation.[13)] Hydrolysis of the ketal of 2 followed by *m*-chloroperbenzoic acid treatment in the presence of lithium carbonate afforded the lactone (10)[14)] [83%] as a sole product, which was then converted to the diacetate (3)[15)] [65%] by sequential lithium aluminum hydride reduction and acetylation. The successful conversion of 3 into the corresponding acetonide (11)[16)] by a standard method implied that the configuration of carbomethoxy group at C-6 in 2 should be β orientation.

Finally, in the analogous way, the α-OH isomer[17)] of the ketone (6) was transformed into the himachalene skeleton (4)[18)] *via* a 5-step synthetic sequence [41% overall] as shown in Scheme 2.

Thus, we have demonstrated that the tricyclo[6.3.1.$0^{3,8}$]dodec-4-ene derivative (6) can be efficiently transformed into the four kinds of terpenoids carbon skeletons by simple manipulations and the tricyclic system can serve as a synthetically useful synthon.

Further application of this methodology to the synthesis of natural products is being pursued.

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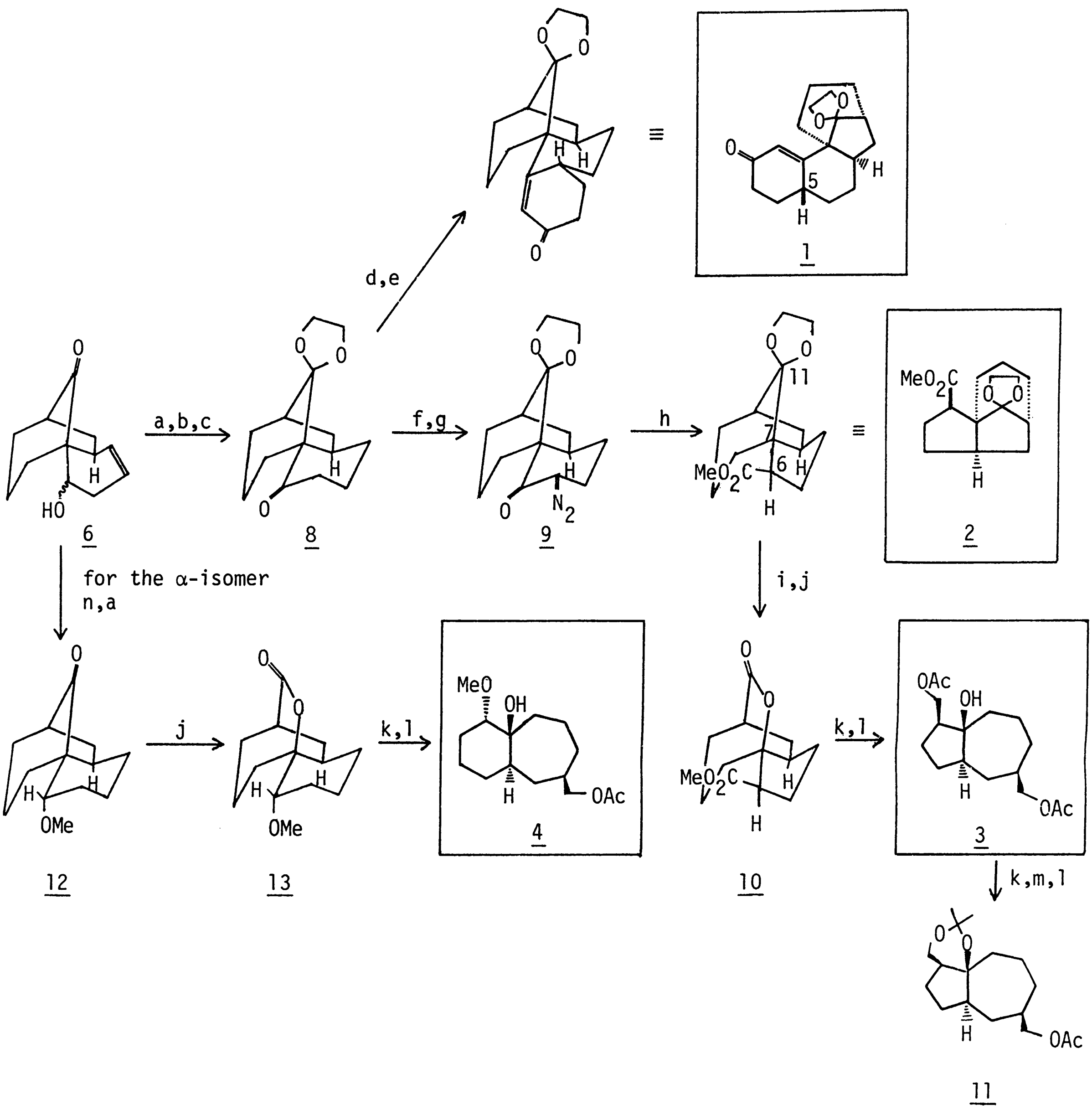
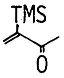
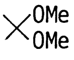


Key : a) H_2, 10% Pd-C. b) $HOCH_2CH_2OH$, CSA. c) $(COCl)_2$, DMSO, NEt_3. d) LDA, 

e) 5% NaOMe in MeOH. f) NaH, HCO_2Et. g) TsN_3, NEt_3. h) 400 W RIKO Hg lamp, Pyrex filter, MeOH. i) 10% HCl, acetone. j) MCPBA, Li_2CO_3. k) $LiAlH_4$. l) Ac_2O, Py., 4-DMAP. m) 

, CSA. n) NaH, MeI.

Scheme 2.

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2) E. Piers, B. F. Abeysekera, D. J. Herbert, and I. D. Suckling, J. Chem. Soc., Chem. Commun., 1982, 404.
3) For an excellent review of the total synthesis of sesquiterpenes, see C. H. Heathcock, S. L. Graham, M. C. Pirrung, F. Plavac, and C. T. White, "The Total Synthesis of Natural Products," Vol. 5, ed by J. ApSimon, John Wiley & Sons, New York (1983).
4) All compounds depicted are racemic but, for convenience, only one enantiomer is shown.
5) All new compounds gave statisfactory spectral and analytical (combustion and/or high-resolution mass spectral) data consistent with the structures shown.
6) Colorless oil; IR ($CHCl_3$), 1690 cm^{-1}; ^1H-NMR ($CDCl_3$, 100 MHz), δ 3.80 (4H, s); MS (m/z), 236 (M^+).
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8) Colorless oil; IR ($CHCl_3$), 1660 cm^{-1}; ^1H-NMR ($CDCl_3$, 100 MHz), δ 3.80 (4H, m), 6.16 (1H, d, J = 2.7 Hz); MS (m/z), 288 (M^+).
9) R. K. Boeckman, Jr., D. M. Blum,and S. D. Arthur, J. Am. Chem. Soc., 101, 5060 (1979).
10) Pale yellow oil; IR ($CHCl_3$), 2090, 1610 cm^{-1}; ^1H-NMR ($CDCl_3$, 60 MHz), δ 3.87 (4H, m); MS (m/z), 262 (M^+).
11) K. B. Wiberg, B. L. Furtek, and L. K. Olli, J. Am. Chem. Soc., 101, 7675 (1979); K. B. Wiberg, L. K. Olli, N. Golembeski, and R. D. Adams, ibid., 102, 7467 (1980); W. G. Dauben and D. M. Walker, Tetrahedron Lett., 23, 711 (1982).
12) Colorless oil; IR ($CHCl_3$), 1720 cm^{-1}; ^1H-NMR ($CDCl_3$, 100 MHz), δ 3.59 (3H, s), 3.74 (4H, m); ^{13}C-NMR ($CDCl_3$, 25 MHz), δ 19.491 (t), 28.180 (t), 29.061 (t), 33.112 (t), 34.227 (t), 36.106 (t), 42.858 (d), 45.500 (d), 51.078 (q), 51.430 (d), 58.416 (s), 63.466 (t), 64.170 (t), 117.421 (s), 174.253 (s); MS (m/z), 266 (M^+).
13) K. Narasaka, T. Sakakura, T. Uchimaru, and D. G. Vuong, J. Am. Chem. Soc., 106, 2954 (1984).
14) Colorless oil; IR ($CHCl_3$), 1735 cm^{-1}; ^1H-NMR ($CDCl_3$, 60 MHz), δ 3.72 (3H, s); MS (m/z), 238 (M^+).
15) Colorless oil; IR ($CHCl_3$), 3500, 1720 cm^{-1}; ^1H-NMR ($CDCl_3$, 100 MHz), δ 2.03 (6H, s), 3.85 (2H, d, J = 6.0 Hz), 4.04 (1H, dd, J = 12.0 and 6.0 Hz), 4.30 (1H, dd, J = 12.0 and 8.0 Hz); MS (m/z), 238 (M^+-AcOH).
16) Colorless oil; IR ($CHCl_3$), 1720 cm^{-1}; ^1H-NMR ($CDCl_3$, 100 MHz), δ 1.24 (3H, s), 1.36 (3H, s), 1.96 (3H, s), 3.42 (1H, dd, J = 12.0 and 3.0 Hz), 3.76 (2H, d, J = 8.0 Hz), 3.94 (1H, dd, J = 12.0 and 3.5 Hz); MS (m/z), 296 (M^+).
17) Although the β-isomer could also be converted to the corresponding himachalene skeleton, the lactonization step was very slow and the overall yield was slightly poor.
18) Colorless oil; IR ($CHCl_3$), 3560, 1720 cm^{-1}; ^1H-NMR ($CDCl_3$, 100 MHz), δ 1.96 (3H, s), 2.68 (1H, dd, J = 10.0 and 6.0 Hz), 3.26 (3H, s), 3.75 (2H, d, J = 5.5 Hz); MS (m/z), 270 (M^+).

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