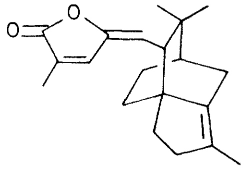
A Simple Synthesis of a Functionalized Tricyclo[5.2.2.$0^{1,5}$]undecene as a Synthon for Isoeremolactone

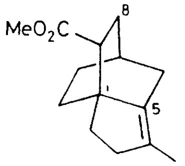
By WALTER WEBER, DIETRICH SPITZNER, and WOLFGANG KRAUS*
(*Department of Chemistry, University of Hohenheim, D-*7000 *Stuttgart* 70, *W. Germany*)

Summary Methyl 4-methyltricyclo[5.2.2.$0^{1,5}$]undec-4-ene-9-carboxylate (**2**) was synthesised by using the easily available 6-methyl-7-t-butoxybicyclo[4.3.0]non-1-en-3-one (**3**) as a starting material.

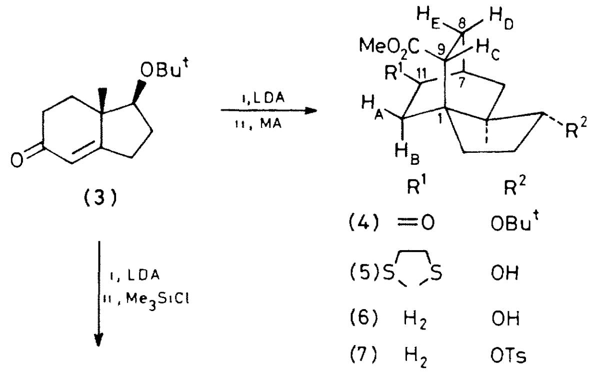
Isoeremolactone (**1**), a diterpene from the crude oil of *Eremophila fraseri* and *E. freelingii*,[1] possesses the unique tricylo[5.2.2.0^{1,5}]undecene carbon framework as shown by *X*-ray analysis.[2] To our knowledge no synthesis of (**1**) has been described in the literature so far. Krantz[3] and Mirrington[4] reported preparations of tricyclo[5.2.2.0^{1,5}]-undecenone and tricyclo[5.2.2.0^{1,5}]undecane-4,9-dione precursors of (**1**) by quite different sequences. We report on the synthesis of this skeleton in the ester (**2**), starting with the racemic ketone (**3**) which has been used as the common synthon for rings *C* and *D* in various steroid syntheses.[5]†

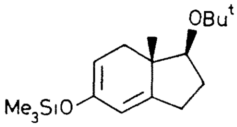
Treatment of the ketone (**3**) under rigorous anaerobic and anhydrous conditions with 1·1 equiv. of lithium di-isopropylamide (LDA) in tetrahydrofuran at −23 °C generated the kinetically controlled anion. Double Michael reaction[6] with methyl acrylate (MA) gave (**4**) as the sole product in almost quantitative yield, ^{1}H-n.m.r. ($CDCl_3$): δ 0·87 (s, 3H, 5-Me), 1·16 (s, 9H, $OCMe_3$), 1·99 (dddd, ${}^2J$ 14·0 Hz, ${}^3J$ 9·0 and 2·0 Hz, ${}^4J$ 2·0 Hz, 1H, H_E), 2·06 (ddd, ${}^2J$ 14·0 Hz, ${}^3J$ 10·0 and 4·0 Hz, 1H, H_D), 2·37 (m, 1H, 7-H), 2·57 [AB-system: 2·98 (d, ${}^2J$ 18·7 Hz, 1H, H_A), 2·16 (dd, ${}^2J$ 18·7 Hz, ${}^4J$ 2·0 Hz, 1H, H_B)], 2·92 (ddd, ${}^3J$ 10·0 and 9·0 Hz, ${}^4J$ 2·0 Hz, 1H, H_C), and 3·72 (s, 3H, OMe); ^{13}C-n.m.r. ($CDCl_3$): δ 216·1 (s, C-11), 175·3 (s, CO_2Me), 78·1 (d, C-4), 72·4 (s, $OCMe_3$), 51·4 (q, CO_2Me), 47·8 and 45·1 (s, C-1 and C-5), 43·1 and 40·7 (d, C-7 and C-9), 42·3, 38·2, 32·3, 28·7, and 27·8 (t, C-2, C-3, C-6, C-8 and C-10), 28·5 (q, $OCMe_3$), and 17·4 (q, 5-Me) p.p.m.; i.r. ν (film) 1730 cm^{-1} (C=O).


(1)

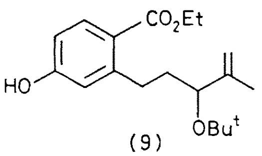


(2)





(8)



(9)

Thioacetalization (dithian, BF_3–Et_2O) of (**4**) to give (**5**), followed by reduction with Raney-Nickel in anhydrous EtOH gave the alcohol (**6**) [>80% yield from (**3**)] which was treated with toluene-*p*-sulphonyl chloride in pyridine (0 °C, 24 h) to give (**7**) (83% yield after crystallization), ^{1}H n.m.r. δ($CDCl_3$) 1·03 (s, 3H, 5-Me), 2·45 (s, 3H, Ar-*Me*), 3·65 (s, 3H, OMe), and 7·56 (AA′BB′ system, 4H, Ar-H). Solvolysis of the tosylate (**7**) in aqueous acetone (100 °C, 1·5 days) yielded (**2**) (80% yield after chromatography over silica gel), ^{1}H n.m.r. δ($CDCl_3$) 1·59 (s, 3H, 4-Me) and 3·68 (s, 3H, OMe). Extensive nuclear Overhauser effect and decoupling experiments, as well as ^{13}C-n.m.r. measurements and comparison with other tricyclo[5.2.2.0^{1,5}]undecanes, are in full accord with the proposed structure (**2**).

A mixture of (**4**) and its C-9 epimer could also be obtained in a ratio of 3 : 1 from the trimethylsilyl ether (**8**) and methyl acrylate *via* a Diels–Alder reaction[7] (110 °C, 2 days, 40% yield). Several attempts to introduce two methyl groups at C-8 directly by using methyl dimethylacrylate as Michael-acceptor or dienophile failed. Ethyl propiolate as dienophile gave the aromatic product (**9**).[8]

This work was supported by Deutsche Forschungsgemeinschaft and Fonds der Chemischen Industrie.

(*Received*, *7th August* 1980; *Com.* 875.)

---

† All new compounds except the labile silyl ether (**8**) gave satisfactory combustion analyses and/or high resolution m.s.-data, and their structures were determined by i.r., ^{1}H n.m.r., and ^{13}C n.m.r. spectroscopy.

[1] P. R. Jefferies, J. R. Knox, and E. J. Middleton, *Aust. J. Chem.*, 1962, **15**, 532; A. J. Birch, J. Grimshaw, and J. P. Turnbull, *J. Chem. Soc.*, 1963, 2412; A. J. Birch, G. S. R. Subba Rao, and J. P. Turnbull, *Tetrahedron Lett.*, 1966, 4749.

[2] Y.-L. Oh and E. N. Maslen, *Tetrahedron Lett.*, 1966, 3291.

[3] A. Krantz and C. Y. Lin, *J. Am. Chem. Soc.*, 1973, **95**, 6552.

[4] G. I. Feutrill and R. N. Mirrington, *J. Chem. Soc., Chem. Commun.*, 1976, 589.

[5] Z. G. Hajos, R. A. Micheli, D. R. Parrish, and E. P. Oliveto, *J. Org. Chem.*, 1967, **32**, 3008; U. Eder, H. Gibian, G. Neef, K. Prezewowsky, G. Sauer, and R. Wiechert, *Chem. Ber.*, 1978, **111**, 939.

[6] R. A. Lee, C. McAndrews, K. M. Patel, and W. Reusch, *Tetrahedron Lett.*, 1973, 965; D. Spitzner, *ibid.*, 1978, 3349.

[7] C. Girard and J. M. Conia, *Tetrahedron Lett.*, 1974, 3327; K. B. White and W. Reusch, *Tetrahedron*, 1978, **34**, 2439.

[8] P. Yates and F. M. Walliser, *Can. J. Chem.*, 1976, **54**, 3508, report a similar retro-Diels–Alder reaction.