Synthesis of the Tricyclo[5,2,2,$0^{1,5}$]undecane Skeleton Related to Isoeremolactone

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Summary Synthesis of 8,8-dimethyltricyclo[5,2,2,$0^{1,5}$]undecan-4,9-dione (**3**) has afforded the basic skeleton of the diterpene, isoeremolactone.

Isolation of eremolactone (**1**) and several related compounds from *Eremophila fraseri*[1] and *E. freelingii*[2] introduced a new family of diterpenes which was shown by *X*-ray studies on isoeremolactone (**2**)[3] to possess the previously undescribed tricyclo[5,2,2,$0^{1,5}$]undecane skeleton. We report the synthesis of this skeleton in the ketone (**3**), a system suitable for exploring further conversion into (**2**).

Reaction of the cyclohexanone (**4**)[4] with methyl acrylate and trimethylamine at room temperature for 5 days[5] gave compound (**5a**) which was deformylated (EtOH–KOH) to give (**5b**) [60% from (**4**)]. Bromination (Br_2–CCl_4) gave the crude (**5c**) which was dehydrobrominated (LiCl–Li_2CO_3–DMF) (DMF = dimethylformamide) to give (**6a**) [66% from (**5b**)]. Unless care was taken to dissolve the LiCl before addition of the Li_2CO_3, the keto-lactone (**10**) was formed in addition to (**6a**).

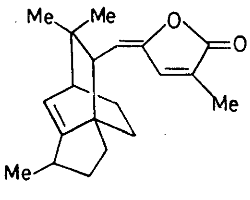
Bromination of (**6a**) (*N*-bromosuccinimide–CCl_4)[6] gave predominantly the bromide (**6b**) in excellent yield [τ(CCl_4) 3·25br (1H, d, J 2·5 Hz, C=CH) and 4·99 (1H, m, CHBr)]. In decoupling experiments on (**6b**), irradiation at τ 3·25 caused the multiplet at τ 4·99 to collapse into a triplet (J 7 Hz), and irradiation at τ 4·99 caused the signal at τ 3·25 to appear as a broad singlet. Dehydrobromination (LiCl–Li_2CO_3–DMF) of (**6b**) gave the cyclohexa-1,3-dienone (**7**) [91% from (**6a**); λ_{max} 240 and 310 nm].

Reaction of (**7**) with ethyl acrylate followed by chromatography over silica gel gave a mixture of epimers (**8**) (68%). This mixture was hydrogenated (Pd–C, MeOH) to give the keto-diester (**9**) as a mixture of epimers at C-6.[7] Dieckmann condensation of this mixture (NaH–MeOH–benzene) gave, after acidic work-up, the epimeric mixture (**3**) which was purified by preparative g.l.c. (48%) [ν_{max} 1743 and 1718 cm^{-1}].

The mixture of stereoisomers at C-5 in (**3**) is inconsequential as the asymmetry at this point ultimately disappears in the planned synthesis of (**2**).

Compound (**3**) and a closely related ketone synthesized by Birch[8] represent the first syntheses of the basic skeleton of isoeremolactone.

All new compounds, with the exception of the labile (**5a**), (**5c**), and (**6b**) gave satisfactory combustion analyses.



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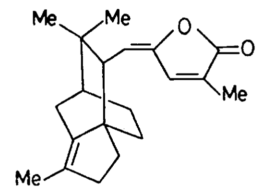

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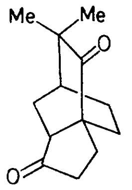

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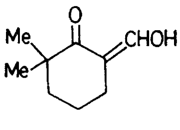

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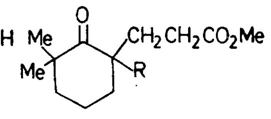
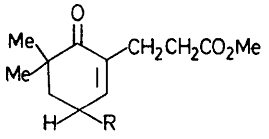


(5)

a; R = CHO

b; R = H

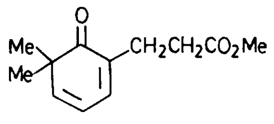
c; R = Br



(6)

a; R = H

b; R = Br



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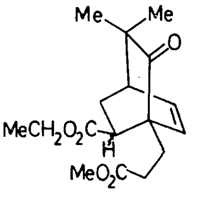

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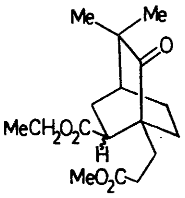

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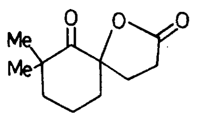

(10)

All compounds gave parent peaks in their mass spectra in accord with theory. Structural assignments are, in every case, supported by i.r. and n.m.r. data.

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[7] Cyclohexa-1,3-dienones are generally assumed to obey the *endo* rule in Diels–Alder additions. In this case epimerization may have occurred during chromatography. See S. Danishefsky and D. Dumas, *Chem. Comm.*, 1968, 1287; K. Somekawa, T. Matsuo, and S. Kumamoto, *Bull. Chem. Soc. Japan*, 1969, **42**, 3499.

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