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CHIRALITY TRANSFER DURING CYCLOBUTYL - CYCLOPROPYLMETHYL - HOMOALLYL CATION REARRANGEMENT AND SYNTHESIS OF (-)-ELDANOLIDE

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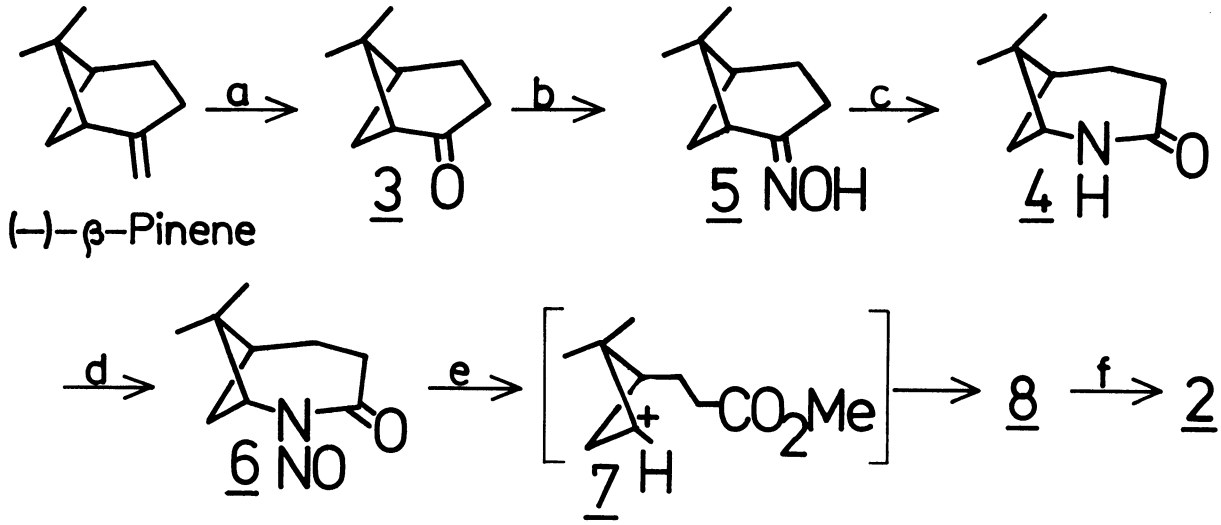
The (3*R*)-2,2-dimethyl-3-(2-methoxycarbonyl)ethylcyclobutyl cation rearranged to give (1*S*,2*S*)-1-(1-methoxy-1-methyl)ethyl-2-(2-methoxycarbonyl)ethylcyclopropane. The latter was transformed into (4*R*)-4-(3-methylbut-2-enyl)-4-butyrolactone with a high degree of chirality transfer. The γ-lactone was converted into (-)-eldanolide, an antipode of the wing gland pheromone of an African sugar-cane borer.

The recent development of the chemistry of small-ring compounds has presented a diversity of synthetic media, taking advantage of the synthetic facility and high reactivity of the cyclobutane and cyclopropane rings.[1] More importantly, a stereoselective interconversion between these two species provides one of the methods of yielding a specific configurational isomer.[2]

The cyclobutyl - cyclopropylmethyl - homoallyl cation rearrangement has been well studied and established.[3] Particularly, rearrangements of 2,2-dialkyl-3-alkenylcyclobutyl and 2,2-dialkyl-3-alkenylcyclopropylmethyl cations had been investigated in detail by several groups with special reference to the squalene biosynthesis.[4] Furthermore, the stereochemical study of the cyclopropylmethyl - homoallyl cation rearrangement of a rigid alicyclic system and its application to the synthesis of pseudoguaianolide (±)-confertin had been achieved by Marshall *et al.*[5]

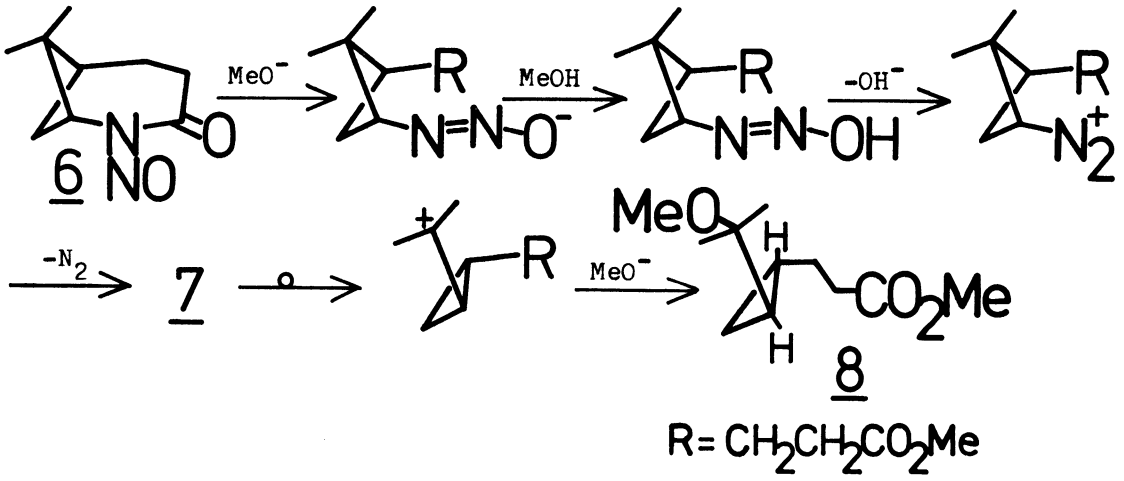
We have been interested in the behavior of the terpenoid cations,[6] especially in the intramolecular nucleophilic attack on them by a remotely suspended nucleophile during the course of the rearrangement. Here we report that the rearrangements of cyclobutyl and cyclopropylmethyl cations, whose precursors were derived from (-)-β-pinene, have been achieved with high stereoselectivity. Also reported is the synthesis of (-)-eldanolide ((-)-1),[7] an antipode of an insect pheromone, from the rearrangement product, (4*R*)-4-dimethylallyl-γ-lactone (2).

Scheme 1.

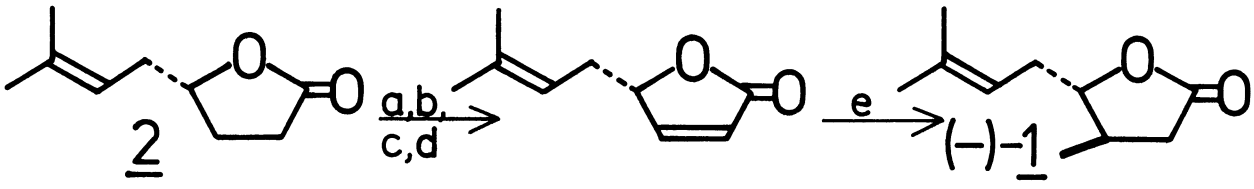


a: O_3/MeOH,-78°C; b: $NH_2OH \cdot HCl$/Pyr; c: p-TsCl/Pyr; d: $NaNO_2/Ac_2O$; e: NaOMe/MeOH,0°C; f: p-TsOH/PhH, reflux.

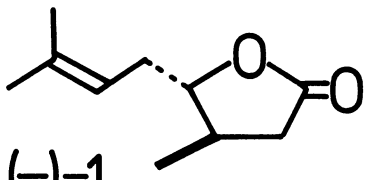
Scheme 2.



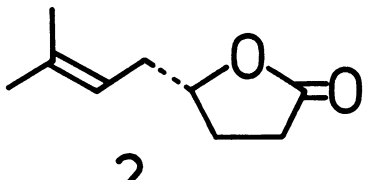
Scheme 3.



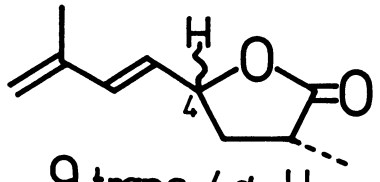
a: LDA/THF,-78°C; b: PhSSPh; c: mCPBA/CH_2Cl_2,-78°C; d: heat/CCl_4; e: $LiMe_2Cu/Et_2O$,-78°C.



(−)-1



2



9 trans 4α-H
cis 4β-H

Nopinone (3), derived from (-)-β-pinene,[8,9] was converted into the lactam (4) *via* the oxime (5).[10] The lactam was treated with excess sodium nitrite in acetic anhydride to give the N-nitrosolactam (6) (3 steps 64%). Compound 6, an immediate precursor of the cyclobutyl cation (7), was treated with catalytic amount of sodium methoxide in methanol at 0 °C. The reaction proceeded rapidly, and gave the methyl ester 8 in 90% yield. The spectral data (see below) and a possible base-initiated reaction mechanism, *i.e.* loss of nitrogen molecule from the intermediate diazonium ion followed by the cyclobutyl - cyclopropylmethyl cation rearrangement, suggest the structure of 8 as shown in Scheme 2. Through the rearrangement reaction, the stereochemistry of the bridgehead carbons of the nitrosolactam (6) (to be C-1 and C-2 carbons of 8) is undoubtedly immutable, therefore the relationship between the substituents of 8 is concluded to be *trans*.

The cyclopropane derivative (8) gave only the γ-lactone (2) when treated with *p*-TsOH in refluxing benzene (98%), by way of the cyclopropylmethyl - homoallyl cation rearrangement. Specific rotation of 2 ($[\alpha]_D^{22}$ -24.2°, c=1.32, MeOH) shows that 2 possesses 4*R* configuration (4*S*-2: $[\alpha]_D^{20}$ +20.0°, c=1.1, MeOH).[11] Therefore, the rearrangement would be terminated by the intramolecular S_N2 reaction with the ester moiety. The chirality transfer from (-)-β-pinene to (4*R*)-2 was thus achieved.

The γ-lactone (2) seems to be a good synthon to prepare optically active monoterpenoids such as marmelolactones (9) and its derivatives[12,13] and eldanolide (1). Recently, eldanolide, a sex pheromone of an African sugar-cane borer, *Eldana saccharina*, was isolated[7] and synthesized in both enantiomeric forms.[11,14] The syntheses showed the natural eldanolide to be (+)-(3*S*,4*R*)-1. We have carried out transformation of 2 into (-)-eldanolide ((-)-1) as in Scheme 3 (20% from 2). Specific rotation of the synthetic sample showed its satisfactory optical purity ($[\alpha]_D^{20}$ -49.1°, c=0.3, MeOH) (Lit.[11]: $[\alpha]_D^{20}$ +51.5°, c=1.15, MeOH). Other spectral data of it were identical with those of (+)-eldanolide synthesized by Mori *et al.*[14]

Characterization of products is as follows; 2: An oil, IR 1770 cm^{-1}, ^{1}H-NMR[15] δ 1.68 and 1.77 (each 3H, s), 4.42 (1H, quint, J = 6 Hz), 5.16 (1H, t, J = 7 Hz), MS m/z 154 (M^+); 6: A yellow oil, IR 1719 cm^{-1}, ^{1}H-NMR δ 0.57 and 1.35 (each 3H, s),

4.80 (1H, dd, J = 8, J = 4 Hz), MS m/z 154 $(M - N_2)^+$ and 152 $(M - NO)^+$; 8: An oil, IR 1735 cm^{-1}, ^{1}H-NMR δ 1.22, 1.25, 3.18, and 3.65 (each 3H, s), 0.15 - 0.5 (1H, m), 0.5 - 1.2 (3H, m), ^{13}C-NMR ($CDCl_3$) δ 7.17, 16.05, 23.96, 25.37, 26.13, 26.45, 35.12, 49.21, 51.48, 74.23, and 174.35; (-)-1: An oil, IR 1780 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 1.14 (3H, d, J = 6.4 Hz), 1.64 and 1.73 (each 3H, d, J = 1.5 Hz), 2.70 (1H, dd, J = 13.0, J = 4.7 Hz), 4.06 (1H, q, J = 6.6 Hz), 5.18 (1H, t-hep, J = 7.3, J = 1.4 Hz), ^{13}C-NMR ($CDCl_3$) δ 17.77, 17.99, 25.79, 32.18, 35.11, 37.06, 87.11, 117.99, 135.44, and 176.50, MS m/z 168 (M^+) and 99 (M - side chain)$^+$.

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