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Unprecedented Grob-type Fragmentation of 5-dioxolan-bicyclo[4.2.0]octan-2-ones into 3-(methoxycarbonylmethyl)cyclohexanones

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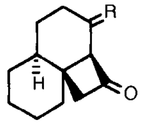
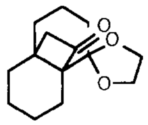
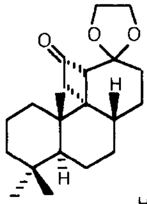
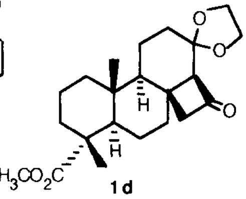
***Abstract*:** The unprecedented Grob-type fragmentations of 5-dioxolan-bicyclo[4.2.0]octan-2-ones **1** into 3-(methoxycarbonylmethyl)cyclohexanones **2** are described. This fragmentation, in combination with the allene photoannelation used to produce compounds **1**, might constitute an indirect way for achieving conjugate addition of methyl acetate; new syntheses of kaurane, stemarane and thirsiflorane diterpenes might be also envisaged from **2c** and **2d**. © 1997 Elsevier Science Ltd.

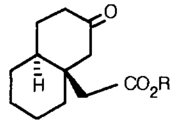
In the course of our continuing effort towards the synthesis of tetracyclic diterpenes we found that 5-dioxolan-bicyclo[4.2.0]octan-2-one **1a**[1-3] is quantitatively converted into 3-(methoxycarbonylmethyl)cyclohexanone **2a**[4] by the action of a 4:1 mixture of MeOH/1N HCl at r.t. for 2h. The reaction proceeds cleanly and the corresponding bicyclo[4.2.0]octan-2,8-dione **3** and 9-(carboxymethyl)-2-decalone **4** were not detected in the course of the reaction. The same unprecedented outcome was recorded by us when this reaction was applied to **1b**[5], **1c**[6] and **1d**[7] from which **2b**[8], **2c**[9] and **2d**[10] were obtained respectively.

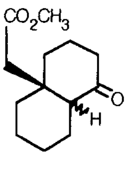

1a R= OCH_2CH_2O
3 R= O

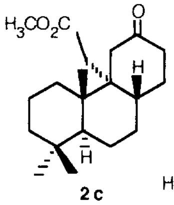

1b

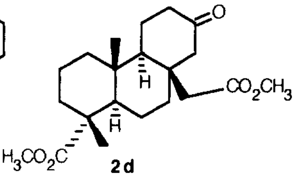

1c


1d


2a R= CH_3
4 R= H

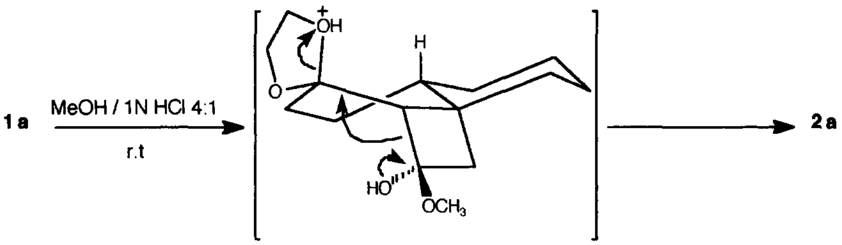

2b


2c


2d

The conversion of compounds **1** into **2**, which gives rise to two C-atoms at a different level of oxidation, is unique in the sense that the cyclobutane and dioxolane rings are opened "simultaneously".[11a] These Grob-type[11b-c] fragmentations appear to occur because of the peculiar *antiperiplanar* arrangement, in the emiacetalic intermediate, of the CH-C(OH)OCH_3 cyclobutane bond and one of the dioxolane C-O bond, as described for the conversion of **1a** into **2a** in the scheme.

This fragmentation is, in our opinion, quite interesting, not only because is novel and constitutes therefore a further variant of these processes, but also because compounds of type **1** are efficiently available by stereoselective allene photoaddition to the proper α,β-unsaturated ketone and simple functionality manipulations; the whole sequence might be therefore very useful, in alternative to the various conjugate addition methodologies, for the introduction of an angular methyl acetate side chain. Finally **2c** and **2d** are precursors of 3-(formylmethyl)cyclohexan-1-one intermediates from which new syntheses of kaurane, stemarane and thirsiflorane diterpenes, by intramolecular reductive coupling[12] and rearrangement[13] of the cyclization products, might be envisaged.



Scheme. A plausible reaction pathway for the conversion of **1a** into **2a**

Acknowledgments

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References and Notes

1. The elemental composition of all compounds, described in this communication, has been determined by elemental analysis or high resolution mass spectrometry; IR in cm^{-1}, NMR in δ.
2. IR (CCl_4): 1776; ^{1}H-NMR ($CDCl_3$): 2.35 (dd, J = 5.5, 18.5 Hz, 1H), 2.60-2.70 (m, 1H), 2.97 (dd, J = 3.0, 18.5 Hz, 1H), 3.70-3.90 (m, 4H); ^{13}C-NMR ($CDCl_3$): 22.8, 24.3, 25.9, 29.5, 32.0, 35.4, 37.3, 38.5, 49.3, 64.0, 64.4, 70.0, 108.0, 206.1; colourless oil.
3. Obtained from the corresponding olefin as described for the preparation of **1d** in ref.7.
4. TLC (SiO_2): (petroleum ether (40-70°)/Et_2O) 6:4. $R_{f2a} < R_{f1a}$; IR (CCl_4): 1734, 1717; ^{1}H-NMR ($CDCl_3$): 3.61 (s, 3H); ^{13}C-NMR ($CDCl_3$): 20.5, 25.8, 27.3, 28.3, 32.7, 37.0, 39.6, 41.0, 44.5, 51.1, 52.7, 172.1, 210.8; low melting oil (38-39°C).
5. A. Bartoletti, M. Berettoni, F. Catteruccia, G. De Chiara, R. Marini Bettolo, C. Mastrangeli, R. Scarpelli, C. Tozzi, D. Lamba, *Gazz. Chim. Ital.*, **1996**, 126, 223.
6. Derived from (+)-podocarpic acid; IR (CCl_4): 1774; ^{1}H-NMR ($CDCl_3$): 0.80 (s, 3H), 0.82 (s, 3H), 1.01 (s, 3H), 3.80-4.00 (m, 4H); ^{13}C-NMR ($CDCl_3$): 15.5, 18.0, 21.0, 21.7, 24.5, 30.0, 30.4, 30.5, 31.3, 32.9, 33.0, 39.0, 42.0, 45.6, 46.1, 47.5, 63.2, 64.2, 64.4, 108.8, 208.4; m.p. (petroleum ether (40-70°)/Et_2O): 99.5-100.6°C.
7. Derived from (-)-abietic acid; M. Berettoni, G. De Chiara, T. Iacoangeli, P. Lo Surdo, R. Marini Bettolo, L. Montagnini di Mirabello, L. Nicolini, R. Scarpelli, *Helv. Chim. Acta*, **1996**, 79, 2035.
8. TLC (SiO_2): (petroleum ether (40-70°)/Et_2O) 6:4; $R_{f2b} < R_{f1b}$; IR (CCl_4): 1734, 1711, as epimeric mixture at C(9).
9. TLC (SiO_2): (petroleum ether (40-70°)/Et_2O) 1:1, $R_{f2c} > R_{f1c}$; IR (CCl_4): 1711, 1733; ^{1}H-NMR ($CDCl_3$): 0.85 (s, 6H) 1.05 (s, 3H), 3.55 (s, 3H); ^{13}C-NMR ($CDCl_3$): 15.8, 18.3, 21.4, 21.7, 28.3, 28.6, 29.5, 30.1, 32.9, 33.0, 34.0, 34.3, 37.9, 40.3, 41.5, 41.9, 44.2, 45.3, 47.3, 173.7, 211.8; colourless oil.
10. TLC (SiO_2): (petroleum ether (40-70°)/Et_2O) 4:6, $R_{f2d} > R_{f1d}$; IR (CCl_4): 1735; ^{1}H-NMR ($CDCl_3$): 0.82 (s, 3H), 1.08 (s, 3H), 3.54 (s, 3H), 3.57 (s, 3H); ^{13}C-NMR ($CDCl_3$): 16.0, 16.2, 17.3, 20.4, 20.9, 35.6, 36.5, 36.9, 38.5, 38.9, 40.7, 40.8, 47.4, 51.1, 51.7, 54.4, 57.5, 172.0, 179.1, 210.1; m.p. (petroleum ether (40-70°)/Et_2O): 136.8-137.1°C.
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