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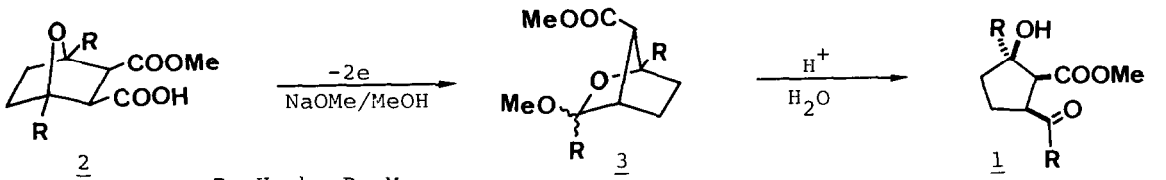
STEREOSPECIFIC SYNTHESIS OF t,t-1,2,3-TRISUBSTITUTED CYCLOPENTANES AND OF ANGULARLY DISUBSTITUTED t-HYDRINDANOLS

Takeshi Imagawa, Syuichi Sugita, Tetsuo Akiyama,[1] and Mituyosi Kawanisi*
Department of Industrial Chemistry, Kyoto University, Kyoto 606, Japan

Summary: Anodic oxidative decarboxylation of endo-3-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane-endo-2-carboxylate anion gave exclusively an oxygen-assisted Wagner-Meerwein-rearranged product, methyl 3-methoxy-2-oxabicyclo[2.2.1]heptane-anti-7-carboxylate, constituting a method for the stereospecific synthesis of c-3-acyl-t-2-methoxycarbonyl-r-1-cyclopentanols. Synthesis of 7a-methoxycarbonyl-t-hydrindane-3a,1-carbolactones was also attained.

The general importance of cyclopentane derivatives in natrual products has led to the development of various methodology for the synthesis of such systems, especially introducing of the multi-substituents in stereospecific manner.[2] We wish to report a method of stereospecific synthesis of the titled compounds.

Previously, we reported[3] a stereospecific synthesis of c-3-acyl-c-2-methoxycarbonyl-r-1-cyclopentanols (1) by the oxygen-assisted Wagner-Meerwein rearrangement of the cation induced by anodic oxidative decarboxylation and its application to the synthesis of a variety of iridoid monoterpenes.[4] Diels-Alder



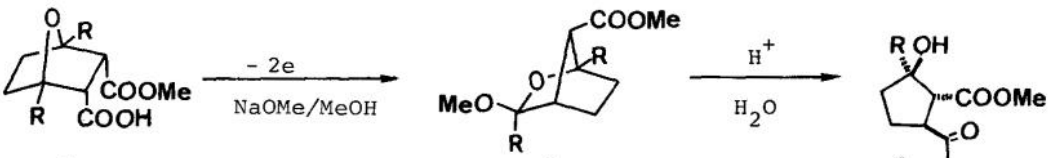
2 3 1

a: R = H; b: R = Me

reaction of furans, as a step to obtain the starting material, gives exclusively exo-adducts.[5] Accordingly, there is an unavoidable limitation that the methanolysis of the hydrogenated adducts, 1,4-dialkyl-7-oxabicyclo[2.2.1]heptane-exo,cis-dicarboxylic anhydrides, gives exo,cis-half esters of the dicarboxylic acid (2), which confines the syn-configuration of the methoxycarbonyl group in the rearranged products 3 and consequently all-cis configuration of the substituents of the final cyclopentane derivatives (1). In the present investigation, we intend to broaden the scope of this 1,2,3-trisubstituted cyclopentane synthesis and to appreciate the endo-carboxy group as the leaving group in the Wagner-Meerwein rearrangement.

The requisite endo,cis-half esters (4) (a: mp 115-117°C; b: mp 138-141°C) were derived from the endo-acid anhydrides by methanolysis, available through the Diels-Alder adducts of dimethyl acetylenedicarboxylate and the furans.[6)]

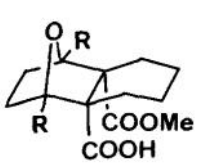
Electrolysis of 4a in MeOH in the presence of 1/10 equivalents of NaOMe in an undivided cell using graphite electrodes gave only a Wagner-Meerwein rearranged product 5a[7)] having anti-methoxycarbonyl and exo-3-methoxy group in 75% yield [^{1}H NMR ($CDCl_3$): δ 1.1-2.0(m, 4H), 2.70(m, 1H), 3.21(m, 1H), 3.35(s, 3H), 3.70(s, 3H), 4.50(bs, 1H), 4.53(s, 1H)]. None of the unrearranged products was detected and in addition the product having endo-3-methoxy group was not obtained. The arrangement of the methoxy group in 5a was readily assigned on the basis of the fact that the proton at the 3-position in the ^{1}H NMR spectrum appeared at δ 4.50[8)] not as a doublet but as a singlet. Treatment of 5a with perchloric acid in aq. THF gave the expected c-3-formyl-t-2-methoxycarbonyl-r-1-cyclopentanol (6a)[9)] in 83% yield.



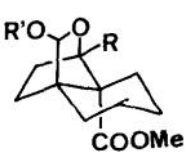
4 a: R = H; b: R = Me 5 6

Similarly to 4a, the electrolysis of 4b gave exclusively 5b in 97% yield [^{1}H NMR ($CDCl_3$): δ 1.37(s, 3H), 1.48(s, 3H), 1.70(m, 4H), 2.20(s, 1H), 2.60(m, 1H), 3.26(s, 3H), 3.70(s, 3H)]. The exo arrangement of the methoxy group could be deduced from the ^{1}H and ^{13}C NMR chemical shifts.[8)] Acid-catalyzed hydrolysis of 5b afforded c-3-acetyl-1-methyl-t-2-methoxycarbonyl-r-1-cyclopentanol (6b)[9)] in 86% yield.

Encouraged by the occurrence of Wagner-Meerwein rearrangement even in the case of the electrolysis of endo-2-carboxylic acid, we tried to synthesize angularly disubstituted trans-hydrindanol derivatives from the formal double Diels-Alder adducts of acetylenedicarboxylic acid with furan and butadiene.



7 a: R=H; b:R=Me



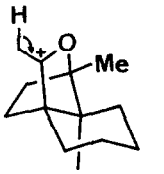
8 a: R=H; R'=Me b: R=H; R'=H

9 a: R=H; b: R=Me

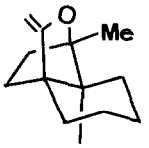
Electrolysis of 7a (mp 98-100°C)[10)] in a similar condition gave in 76% yield a single stereoisomer of hydrindane derivative 8a [^{1}H NMR ($CDCl_3$): δ 1.2 - 2.2(m, 12H), 3.47(s, 3H), 3.67(s, 3H), 4.27(s, 1H), 5.15(s, 1H), characterized to have

an endo-methoxy group based on the chemical shift of the methoxy group in the ^1H NMR spectrum[8] and on the stereochemical consideration. Acid-catalyzed hydrolysis of 8a gave only an intramolecular hemiacetal 8b in 54% yield [^1H NMR ($CDCl_3$): δ 1.2 - 2.3(m, 12H), 3.68(s, 3H), 4.23(s, 1H), 5.68(s, 1H)], and not the expected hydroxy-aldehyde. Jones' oxidation of 8b gave a lactone 9a in 79% yield [IR (neat): 1790 and 1740 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.2 - 2.2(m, 12H), 3.74(s, 3H), 4.71 (s, 1H)].

On the other hand, the dimethyl derivative 7b (mp 153.5-155.5°C)[11] gave on electrolysis a complex mixture, acid-catalyzed hydrolysis of which afforded a single lactone 9b in 68% over-all yield [IR (neat): 1790 and 1740 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.1-2.4(m, 12H), 1.57(s, 3H), 3.78(s, 3H)]. The structure of 9b is deduced from the comparison with 9a in IR, NMR, and mass spectra.[12] The mechanism of the formation of this unexpected product 9b can be rationalized as follows.



10 COOMe



11 COOMe

The carbocation formed by the anodic oxidative decarboxylation of 7b rearranges into the cation 10. For the sake of steric hindrance, however, the usual nucleophilic attack of the solvent MeOH to 10 is hampered and the cation is quenched by the release of a proton into an enol ether (11). Finally, anodic oxidative cleavage of 11 gives the orthoester form[12] of the lactone 9b. Anodic oxidative cleavage of the enol ether has some precedents.[13]

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References and Notes

1) Present address; Department of Fine Arts, Kyoto City University of Arts, Kyoto 610-11, Japan.
2) Inter alia, R. F. Newton and S. M. Roberts, Tetrahedron, 36, 2163 (1980).
3) T. Akiyama, T. Fujii, H. Ishiwari, T. Imagawa, and M. Kawanisi, Tetrahedron Lett., 2165 (1978).
4) (a) T. Imagawa, N. Murai, T. Akiyama, and M. Kawanisi, Tetrahedron Lett., 1691 (1979), (b) T. Imagawa, T. Sonobe, H. Ishiwari, T. Akiyama, and M. Kawanisi, J. Org. Chem., 45, 2005 (1980).
5) M. W. Lee and W. C. Herndon, J. Org. Chem., 43, 518 (1978) and references

cited therein.

6) The method of synthesis is based essentially on the reported one. To avoid stereomutation at the saponification stage, the Diels-Alder adduct of dimethyl acetylenedicarboxylate and furan or 2,5-dimethylfuran was successively half hydrogenated, saponified, fully hydrogenated, and distilled. (a) O. Diels and K. Alder, Ann., 490, 243 (1931), (b) T. A. Eggelte, H. de Koning, H. O. Huisman, J. Chem. Soc. Perkin I, 980 (1978).

7) All new compounds gave satisfactory elemental analyses and spectral data.

8) Generally in the ^{1}H NMR spectra of the present system the singlet due to the endo-OMe group appears at δ 3.40 - 3.50 whereas the singlet due to the exo-OMe group appears at δ 3.10 - 3.35. In the ^{13}C NMR spectra, if C-3 is not further substituted such as 3a and 5a, the exo-3-OMe carbons appear at δ 53.5 - 55 ppm and the endo-OMe carbons at δ 56 - 57 ppm and the endo-3-OMe group shows the so-called γ effect to C-5; if C-3 is further substituted by a methyl group, the endo-OMe carbons always absorb at lower fields relative to exo-OMe, but the chemical shifts are rather dispersed.

9) NMR spectral data ($CDCl_3$ solution) for 1 and 6 are as follows. 6a: ^{1}H NMR: δ 9.72(d, 1H), 4.32(m, 1H), 3.72(s, 3H); ^{13}C NMR: δ 22.9(t), 33.4(t), 52.0(d), 52.3(q), 52.4(d), 75.9(d), 173.7(s), 201.0(d). 1a: ^{1}H NMR: δ 9.74(d, 1H), 4.59(m, 1H), 3.80(s, 3H); ^{13}C NMR: δ 23.6(t), 32.7(d), 50.6(d), 52.1 (d), 52.5 (q), 72.9(d), 172.7(s), 202.6(d). 6b: ^{1}H NMR: δ 1.26(s, 3H), 2.27(s, 3H), 3.75(s, 3H); ^{13}C NMR: δ 24.5(q), 25.5(t), 29.0(q), 40.0(t), 52.0(d), 52.5(q), 56.7(d), 80.5(s), 173.4(s), 209.0(s). 1b: ^{1}H NMR: δ 1.43(s, 3H), 2.16(s, 3H), 3.68(s, 3H); ^{13}C NMR: δ 26.4(t), 26.8(q), 29.3(q), 40.2(t), 51.9(q), 53.4(d), 55.0(d), 80.4(s), 173.5(s), 209.1(s).

10) The compound 7a was easily obtained from the known compound; (a) K. Alder and K. H. Backendorf, Ann., 535, 101 (1938), (b) G. Stork, E. E. van Tamelen, L.J. Friedman, A. W. Burgstahler, J. Am. Chem. Soc., 75, 384 (1953).

11) The procedure of ref. 10 essentailly gives 7b, but the reaction of dimethyl 7-oxabicyclo[2.2.1]hept-2-ene-2,3-dicarboxylate with butadiene is exceedingly sluggish. For this reason, the anhydride was used as the starting material for the Diels-Alder reaction. Cf. G. Maier and W. A. Jung, Tetrahedron Lett., 21, 3875 (1980).

12) Y. Nakashima, T. Imagawa, and M. Kawanisi, Syn. Comm., 9, 889 (1979).

13) (a) S. Torii, H. Tanaka, T. Fukuoka, and H. Hirai, Bull. Chem. Soc. Jpn., 46, 2534 (1973), (b) T. Shono, Y. Matsumura, H. Hamaguchi, T. Imanishi, K. Yoshida, ibid., 51, 2179 (1978).

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