Tetrahedron Letters No. 25, pp 2165 - 2166, 1978. 0040-4039/78/0615-2165$02.00/0

A NOVEL STEREOSELECTIVE SYNTHESIS OF 1,2,3-TRISUBSTITUTED CYCLOPENTANES

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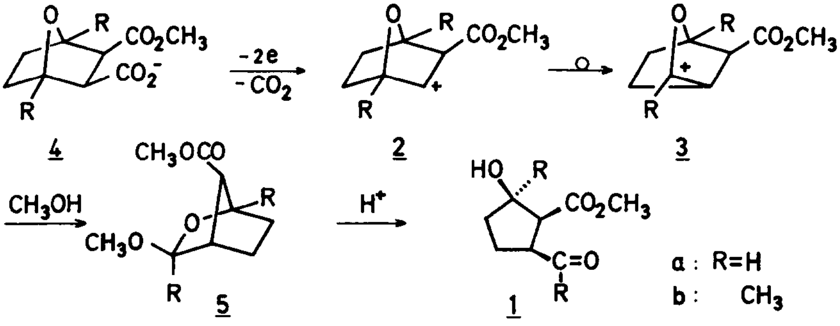
(Received in Japan 22 March 1978; received in UK for publication 21 April 1978)

The construction of five-membered rings presents a general attractive problem[1] in organic synthesis in view of the increasing appearance of cyclopentanoids in large numbers of natural products.

We wish to report a unique stereoselective method for synthesizing 1,2,3-trisubstituted cyclopentanes (1), based on the Wagner-Meerwein rearrangement of 7-oxabicyclo[2.2.1]heptyl-2-cation (2) into 2-oxabicyclo[2.2.1]heptyl-3-cation (3)[2] by virtue of the participation of the oxygen atom as shown below. The 7-oxabicyclo[2.2.1]heptyl-2-cation (2), otherwise being difficult to obtain, was generated by electrolysis (so-called abnormal Kolbe reaction or Hofer-Moest reaction) of the anion of 3-methoxycarbonyl-7-oxabicyclo[2.2.1]heptane-2-carboxylic acids (4), which were readily obtained[3] by the Diels-Alder reaction of maleic anhydride and furans, followed by hydrogenation and methanolysis.



The experimental details are illustrated as follows.[4] A CH_3OH (100 ml) solution of 4b (4.44 g; 19.5 mmol) containing 93.3 mg of Na (4.1 mmol) was electrolyzed at 0°C using 36.6 cm^2 of carbon anode which was placed 0.3 cm apart from carbon cathode and current intensity was maintained at 300 mA.

After 1.6 times of the theoretical amount of current (calculated on the basis of two-electron transfer) was passed (340 min.), followed by usual work-up, compound 5b was distilled; bp 130-132°C/28mmHg (3.45 g, 82.9 %). ^{1}H-NMR ($CDCl_3$): δ 1.33 (s, 3H), 1.60 (broad s, 7H), 2.37 (s, 1H), 2.80 (s, 1H), 3.10 (s, 3H) and 3.65 ppm (s, 3H); IR (neat): 1735 cm^{-1}. Similarly 5a was prepared from 4a in 87 % yield. In this case, two stereoisomers were obtained, which were 3-exo and 3-endo-methoxy (1 : 1) derivatives, being separated by column chromatography (silica gel, PhH : AcOEt = 9 : 1). To a solution of 5b (1.53 g; 7.14 mmol) in THF (15 ml) was added 0.5 ml of 1.5N $HClO_4$ solution at 0°C under stirring for 30 min. Extractive work-up and subsequent distillation afforded the pure compound 1b (120-125°C/20 mmHg, 1.42 g, 99.0 % yield). ^{1}H-NMR ($CDCl_3$) δ 1.43 (s, 3H), 1.5-3.6 (m, 6H), 2.16 (s, 3H), 3.17 (s, 1H) and 3.68 ppm (s, 3H); IR (neat): 3370, 1735 and 1710 cm^{-1}; MS: m/e 182 (M^+-H_2O). Similarly 1a was obtained from 5a in 87 % yield. Stereochemistry of the products is unequivocal as judged from the reaction sequence.

The cyclopentanes thus obtained are versatile intermediates for the synthesis of monoterpenoids and prostanoids. An important feature in the novel cyclopentane synthesis is as follows. (a) Each substituent is in different oxidation state and in fixed arrangement. (b) In addition, 2-oxabicyclo[2.2.1]heptane structure (5) plays the protective role of two groups. Application in the synthesis of natural products is under investigation.

References and Notes

1. *Inter alia*, M. E. Jung and J. P. Hudspeth, J. Am. Chem. Soc., 99 5508 (1977), and references cited therein.
2. J. C. Martin and P. D. Bartlett, J. Am. Chem. Soc., 79 2533 (1957).
3. a) The addition reaction between maleic anhydride and furans in ether solution yields the exo-isomer exclusively [H. Stockmann, J. Org. Chem., 26 2025 (1961)]. The exo-cis derivatives 4, which were prepared according to the published method, were used as starting materials.

   b) J. Jolivet, Ann. chim. (Paris), 5 1165 (1960); CA, 55 13403i (1961).
4. Acceptable ^{1}H- and ^{13}C-NMR, IR and mass spectra and elemental analyses were obtained for all new compounds.