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REACTION OF 2,2-DISUBSTITUTED CYCLOPENTANONES WITH BROMINE AND ALKALI : FACILE PREPARATION OF 5,5-DISUBSTITUTED 2-HYDROXYCYCLOPENTENONES AND TRANSFORMATION TO THE 3,3-DISUBSTITUTED CYCLOPENTANONES

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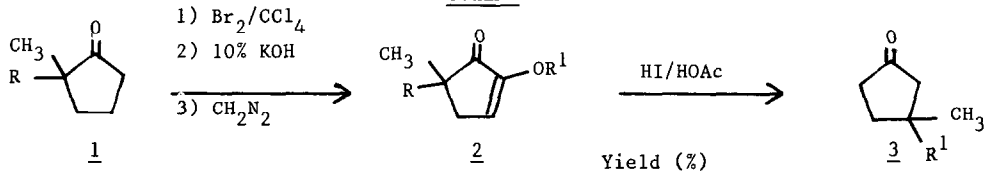
Summary: Reaction of 2,2-disubstituted cyclopentanones (1a-d) with bromine followed by aqueous alkali furnishes the 5,5-disubstituted 2-hydroxycyclopent-2-en-1-ones which were transformed to the 3,3-disubstituted cyclopentanones by reduction with hydriodic and acetic acids.

A recent report[1] regarding a structural revision prompts us to disclose our early results in a related area.

In a project operating in these laboratories towards the synthesis of some cyclobutane containing natural products exemplified by the boll weevil pheromone grandisol[2], it became of interest to explore ways of ring contraction of appropriately substituted cyclopentanone precursors to generate the cyclobutane moiety. Despite previous reports[3] relating to simple cyclopentanones remaining impervious to ring contraction under Favorskii reaction conditions we felt encouraged to initiate a series of fresh investigations addressed to solving this riddle following the earlier report[1] of a successful ring contraction of a cyclopentanone under Favorskii conditions. In this letter we report our initial results obtained from reaction of a few 2,2-disubstituted cyclopentanones with bromine and aqueous alkali.

2,2-Dimethylcyclopentanone (1a) was brominated with excess bromine and the crude dibromo compound treated at 80° with 10% aqueous potassium hydroxide. The product from the reaction was treated with diazomethane to afford 5,5-dimethyl-2-methoxycyclopent-2-en-1-one (2a) in 58% yield [UV 259nm; IR 1710, 1630 cm^{-1}; ^1H NMR δ 1.10 (s,6H), 2.33 (d,J 3Hz,2H), 3.71 (s,3H), 6.18 (t,J 3Hz,1H)]. Similar reaction with (1b-d) (Scheme) afforded the corresponding 2-hydroxycyclopentenones and were characterised as the methyl ethers (2b-d)[4].

SCHEME



1

a, R=CH_3
b, R=C_2H_5
c, R=C_6H_5
d, R=CH_2CH_2OMe

2

a, R=R^1=CH_3
b, R=C_2H_5, R^1=CH_3
c, R=C_6H_5, R^1=CH_3
d, R=CH_2CH_2OMe, R^1=CH_3

Yield (%)

(58)
(52)
(55)
(50)

3

a, R^1=CH_3
b, R^1=C_6H_5
c, R^1=CH_2CH_2I

Yields are based on starting cyclopentanones and are not fully optimised. No Favorskii type products were obtained from the reaction. The products were characterised from elemental analyses and spectral data, with (2b-d) showing characteristic ABX pattern in the ^{1}H NMR spectrum for the ring methylene protons on account of their nonequivalent nature.

Additional evidence in support of the assigned structures was obtained through treatment of the hydroxycyclopentenones with a combination of hydriodic and acetic acids, a condition developed by Reusch and Le Mahieu[5] for the reduction of 1,2-diketones to the monoketones, which in some cases affords a means for the transposition of the carbonyl function. The utility of this procedure does not appear to have been well explored. Reaction of the hydroxycyclopentenones [2a,c,d (R^1=H)] with hydriodic and acetic acid furnished the 3,3-disubstituted cyclopentanones (3a-c) in very good yield (>65%). (3a & b) were identified through comparison with authentic samples prepared independently and (3c) was assigned by analogy and from spectral features[6].

In conclusion even though a Favorskii type ring contraction of simple cyclopentanones is yet to be realised, the experiments described herein provide a convenient and inexpensive route to substituted 2-hydroxycyclopentenones[7], some of which are useful natural flavour constituents[8], and a three step transformation of 2,2-disubstituted cyclopentanones to 3,3-disubstituted cyclopentanones.

We are currently exploring the reaction of the bromocyclopentanones from (1a-d) with other nucleophilic bases and also the utility of substrates like (2) in natural product synthesis.

We thank Professor U.R. Ghatak for his kind interest.

REFERENCES AND NOTES

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2 U.K. Banerjee and R.V. Venkateswaran, *Tetrahedron Letters*, 24, 423 (1983).

3 A.A. Akhrem, T.K. Ustynyuk, and Yu. A. Titov, *Russian Chem. Revs.*, 39, 732 (1970).

4 Spectroscopic data:

(2b): UV 258nm; IR 1710, 1630 cm^{-1}; ^{1}H NMR, δ 0.76 (t,J 8Hz,3H), 1.06 (s,3H), 2.09 (q,A of ABX J_{AB}17.7, J_{AX}3.5 Hz,1H), 2.31 (q,B of ABX J_{BA}17.7, J_{BX}3.5 Hz,1H), 3.71 (s,3H), 6.23 (t,X of ABX J 3.5 Hz,1H).

(2c): UV 254nm; IR 1710, 1630, 1600 cm^{-1}; ^{1}H NMR δ 1.47 (s,3H), 2.57 (q, A of ABX J_{AB}17.7, J_{AX} 3 Hz,1H), 2.84 (q, B of ABX J_{BA}17.7, J_{BX} 3 Hz,1H), 3.71 (s,3H), 6.26 (t,X of ABX J 3 Hz,1H), 7.23 (brs,5H).

(2d): UV 256nm; IR 1710, 1630 cm^{-1}; ^{1}H NMR δ 1.06 (s,3H), 2.15 (q, A of ABX J_{AB}18, J_{AX}3Hz, 1H), 2.57 (q, B of ABX J_{BA}18, J_{BX}3 Hz,1H), 3.21-3.37 (m,5H), 3.70 (s,3H), 6.16 (t,X of ABX J 3Hz,1H).

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6 M.S; m/e 252 (M^+); IR 1745 cm^{-1}; ^{1}H NMR δ 1.10 (s,3H), 3.0-3.23 (m,2H).

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