Rearrangements of Bicyclo[3,2,0]heptan-6-ones. Synthesis of Potential Prostanoid Precursors

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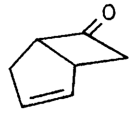
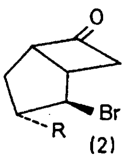
Summary 3-*endo*-Alkoxy-2-*exo*-bromobicyclo[3,2,0]heptan-6-ones rearrange under basic conditions and in the presence of cyanide ion to give 5-*endo*-alkoxy-7-*anti*-cyanobicyclo[2,2,1]heptan-2-ones.

Bicyclo[3,2,0]hept-2-en-6-one (**1**)[1] reacted with *N*-bromoacetamide in methanol, in benzyl alcohol, and in aqueous acetone to give the bromoethers (**2a**,**b**) and the bromohydrin (**2c**), respectively, in 85—95% yield. The alcohol (**2c**) was quantitatively converted into the tetrahydropyranyl (THP) ether (**2d**) in the usual manner.[2] The additions to the cyclopentene ring appeared to be stereospecific on the bases of chromatographic and n.m.r. spectroscopic analyses of the crude products.[3]

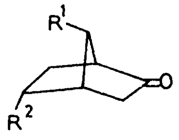


(1)



(2)

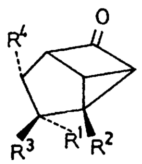
a; R = OMe
b; R = OCH$_2$Ph
c; R = OH
d; R = OTHP
e; R = Br



(3)

a; R^1 = CN, R^2 = OMe
b; R^1 = CN, R^2 = OCH$_2$Ph
c; R^1 = CN, R^2 = OTHP
d; R^1 = OEt, R^2 = Br

Treatment of the bromo-ethers (**2a**,**b**,**d**) with a catalytic amount of NaOMe in MeOH saturated with KCN yielded the corresponding 5-*endo*-alkoxy-7-*anti*-cyanobicyclo[2,2,1]heptan-2-ones (**3a**—**c**) in 85—90% yield. Physical data were consistent with the proposed structures and the n.m.r. spectra suggested that isomers totalled <3% of the crude products. Signals in the n.m.r. spectrum of the methoxy-compound (**3a**) were assigned as follows: δ (CCl_4) 4·14 (1H, ddd, *J* 9·0, 4·0, 3·5 Hz, 5-H), 3·18 (3H, s, OMe) 3·00br (1H, dd, *J* 4·5, 4·0 Hz, 4-H), 2·92 (1H, dt, *J* 2·5, 1·5 Hz, 7-H), 2·69br (1H, d, *J* 5·0 Hz, 1-H), 2·45 (1H, ddd, *J* 13·0, 9·0, 5·0 Hz, 6-*exo*-H), 2·42 (1H, d, *J* 17·5 Hz, 3-*endo*-H), 1·95 (1H, dd, *J* 17·5, 4·5 Hz, 3-*exo*-H), and 1·39 (1H, ddd, *J* 13·0, 3·5, 2·5 Hz, 6-*endo*-H). The assignments were confirmed by solvent-shift and double-irradiation techniques. Particularly noteworthy is the W coupling between 6-*endo*-H and 7-H (*J* 2·5 Hz); this defines the configuration of the cyano-group.[4]



(4)

a; R^1 = Br, R^2 = R^3 = R^4 = H
b; R^1 = R^3 = Me, R^3 = R^4 = Ph

The reaction conditions employed in the synthesis of the cyano-ketones (**3a**—**c**) were adapted from those reported to convert 2-*exo*,3-*endo*-dibromobicyclo[3,2,0]heptan-6-one (**2e**) into 5-*endo*-bromo-7-*anti*-ethoxybicyclo[2,2,1]heptan-2-one (**3d**) through the tricyclic intermediate (**4a**).[5] More recently Paquette has reported that the tricyclo[3,2,0,0^{2,7}]-heptan-6-one (**4b**) is attacked by hydride ion in like fashion, furnishing a bicyclo[2,2,1]heptane derivative.[6]

The stereochemistry and functionality of the bicyclo[2,2,1]heptanones (**3a**—**c**) suggest a potential use as prostaglandin precursors. In this connection the oxidative ring expansion[7] and the photochemical rearrangement[8] of these compounds are currently under investigation.

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