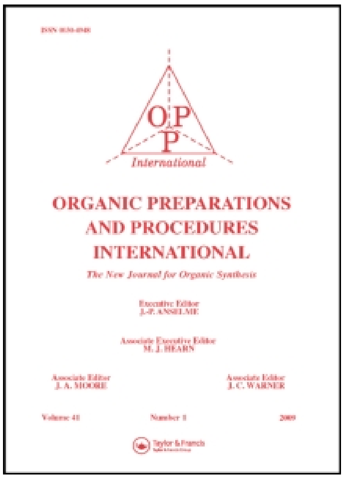


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

TETRAHYDRO-4-PYRONE

Ramesh M. Kanojia[a]; Richard E. Adams[a]
[a] Division of Organic Chemistry, Ortho Research Foundation, Raritan, New Jersey

To cite this Article Kanojia, Ramesh M. and Adams, Richard E.(1972) 'TETRAHYDRO-4-PYRONE', Organic Preparations and Procedures International, 4: 2, 59 — 61

To link to this Article: DOI: 10.1080/00304947209458262

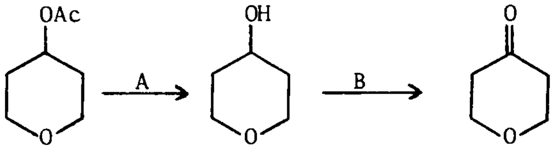
URL: http://dx.doi.org/10.1080/00304947209458262

ORGANIC PREPARATIONS AND PROCEDURES INT. 4(2), 59-61(1972)

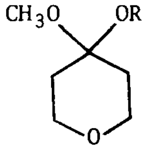
TETRAHYDRO-4-PYRONE

Ramesh M. Kanojia and Richard E. Adams
Division of Organic Chemistry, Ortho Research Foundation
Raritan, New Jersey 08869

Recently the use of the methoxytetrahydropyranyl moiety 4 as a symmetrical alternative to the tetrahydropyranyl group for protection of alcoholic hydroxyl functions in nucleotide chemistry[1] and in other branches of natural product chemistry[2] has proved to offer many advantages. Preparation of tetrahydro-4-pyrone 3, the key ketonic intermediate required for the ketal derivatives, by the following sequence has been reported.[3,4]



1 2 3



4

In these procedures, use of methanolic hydrogen chloride in step A for the hydrolytic conversion of 4-acetoxytetrahydropyran 1 to 4-hydroxytetrahydropyran 2 was originally reported[3] to afford a 99% yield, was found by Fukui *et al.*,[4] to proceed in 65% yield, and in our hands afforded only a 30% yield. The use of methanolic potassium hydroxide (5% solution) gave only 22% yield of 2. In the oxidation step B for preparation of tetrahydro-4-pyrone 3 from 2, use of Beckmann Mixture (sodium dichromate, water and sulfuric acid) was reported by Olsen *et al.*,[3] to afford a 56% yield, by Fukui *et al.*,[4] to afford a 20% yield and gave in our hands a yield of 16%. One of the principal reasons for these erratic results appears to be the losses encountered by virtue of the water solubility of both 2 and 3.

We wish to report modified experimental conditions, which have avoided or minimized the use of water in steps A and B, proved very reproducible, and gave high yields. The use of sodium bicarbonate in methanol for the hydrolytic step A improved the yield of 2 from 1 to 93% and the use of Jones reagent[5] in the oxidation step B improved the yield of 3 from 2 to 80%.

EXPERIMENTAL

4-Hydroxytetrahydropyran (2). A mixture of 24.0 g (0.138 mole) of 4-acetoxytetrahydropyran[3] 1 and 11.47 g (0.137 mole) of sodium bicarbonate in 100 ml of methanol was stirred and heated at reflux for 16 hrs. Methanol was removed under reduced pressure and the residue was extracted with ether by collecting the solids in a funnel and washing well with ether. The filtrate and washes were combined, ether was removed on the rotary evaporator, and the residual yellow oil was distilled under reduced pressure to afford a colorless oil, 13.09 g (93%), bp 99 - 101° (25 mm), n_D^{25} 1.4598, [lit.[3] bp 88.5° (13 mm), n_D^{20} 1.461].

Tetrahydro-4-pyrone (3). To a cold (10°) and vigorously stirred solution of 10.2 g (0.1 mole) of 4-hydroxytetrahydropyran 2 in 400 ml of purified acetone was added, from a burette, 25 ml of Jones reagent[5] over a ten minute period, maintining the temperature between 10° - 15°. The mixture was allowed to warm to room temperature and then the residue of chromium salts was removed by filtration and washed well with acetone. The combined filtrate and washes were stripped of acetone on a rotary evaporator. The residual oil was taken up in 250 ml of chloroform, washed with a saturated solution of sodium chloride (3 x 40 ml), dried over anhydrous sodium sulfate and the chloroform was removed in vacuum. Distillation of the residue under reduced pressure afforded a colorless oil, 8.0 g (80%), bp 76° - 78° (31 mm), n_D^{24} 1.450, [lit.[3] bp 57° - 59° (11 mm), n_D^{20} 1.451].

Acknowledgment: We wish to thank Dr. J. Settepani for his encouragement and interest.

REFERENCES

1. C.B. Reese, R. Saffhill and J.E. Sulton, Tetrahedron, **26**, 1023 (1970).
2. A.D. Cross and J.A. Edwards, U.S. Patent 3,520,881 (1970).
3. S. Olsen and R. Bredock, Chem. Ber. **91**, 1589 (1958).
4. K. Fukui, T. Takino and H. Kitano, Bull. Japan Petrol. Inst. **3**, 27 (1961).
5. A solution of 26.73 g of chromium trioxide and 23 ml of concentrated sulfuric acid diluted to 100 ml with water.

(Received February 28, 1972)