Tetrahedron Letters,Vol.23,No.28,pp 2823-2824,1982 0040-4039/82/282823-02$03.00/0
Printed in Great Britain

AROMATIC ANNELATION. II. SYNTHESIS OF PHENOLS.

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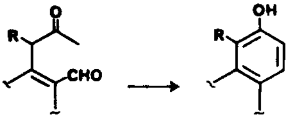
Summary: The preparation of substituted phenols from cycloalkanones by elaboration of an aromatic ring is described.

In the preceding note we described the preparation of ketoaldehydes 1 from cycloalkanones and their subsequent conversion in high yield to pyridines.[1] These versatile intermediates are precursors to substituted phenols 2 as well.[2] The intramolecular aldol reaction leading to the phenols proceeded readily (2-3h at 23°C) upon treatment of the ketoaldehydes with 2-3 equiv of methanolic potassium hydroxide. Other catalysts, including pyrrolidinium acetate, pyridinium tosylate and boron trifluoride etherate were ineffective. The examples listed in Table 1 demonstrate the utility of this process for the preparation of substituted phenols.[3] Experimental details follow.



1 2

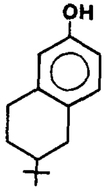
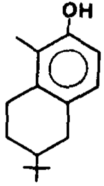
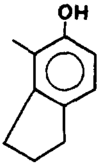
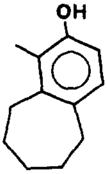
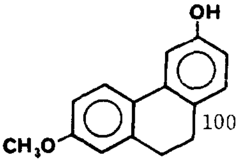
Preparation of 1-methyl-6,7,8,9-tetrahydro-5H-benzocyclohepten-2-ol (entry 4 of Table 1): Crude ketoaldehyde, derived from 120 mg of the corresponding olefin[1] was dissolved in 2 ml of anhydrous methanol and treated with 80 mg (ca. 2.1 equiv) of potassium hydroxide. After 2h the reaction mixture was diluted with ether and acidified with 1N aqueous hydrochloric acid. Extraction with ether, followed by washing with brine, drying (Na_2SO_4) and concentration furnished the crude product. Flash chromatography produced 87 mg (74% overall) of the phenol as an oil: ir_{max} 3420, 2925, 2850, 1595, 1450, 1280, 1060, 810 cm^{-1}; ^1H nmr ($CDCl_3$) δ 6.80 (d, J = 8 Hz, 1H, Ar-H), 6.49 (d, J = 8 Hz, 1H, Ar-H), 4.90 (br s, 1H, OH), 2.21 (s, 3H, CH_3); mass spectrum m/e 176 (p), 161 (p-CH_3), 148, 147, 135, 122, 121, 101.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for their generous support.

References and Notes

1. M. A. Tius, A. Thurkauf and J. W. Truesdell, preceding paper in this issue.
2. For earlier work on phenol annelations, see: (a) D. L. Boger and M. D. Mullican, *J. Org. Chem.*, **45**, 5002 (1980); (b) K. Takaki, M. Okada, M. Yamada and K. Negoro, *J. Chem. Soc., Chem. Commun.*, 1183 (1980); (c) T. H. Chan and P. Brownbridge, *Tetrahedron*, **37**, Supplement 1, 387 (1981), and references cited therein.
3. With the exception of entry 3 of Table 1, none of the phenols have been described in the literature.
4. R. E. Dean, A. Midgeley, E. N. White and D. McNeil, *J. Chem. Soc.*, 2773 (1961); m.p. 98.5-99.5°C.

Table 1

Phenol[a,b]		^{1}H 100-MHz nmr ($CDCl_3$, δ)	ir (ν_{max}, cm^{-1})	mass spectrum (m/e)
1. 	92% mp 89°C	6.92 (d, J = 8.7 Hz, 1H, ArH), 6.60 (m, 1H, ArH), 6.53 (br s, 1H, ArH), 4.60 (br s, 1H, OH), 0.91 (s, 9H, tBu)	3350, 2960, 1595, 1480, 1430, 1250, 1160, 760.	204 (p), 189 (p-CH_3), 161, 148, 147 (p-tBu), 133.
2. 	96% mp 95-96°C	6.82 (d, J = 8.55 Hz, 1H, ArH), 6.58 (d, J = 8.55 Hz, 1H, ArH), 4.50 (br s, 1H, OH), 2.11 (s, 3H, CH_3), 0.94 (s, 9H, tBu)	3350, 2980, 1600, 1460, 1360, 1280, 1060, 800.	218 (p), 203 (p-CH_3), 161 (p-tBu), 147, 146, 145, 135, 134.
3. 	80% mp 96-97°C Ref. 4	6.90 (d, J = 7.9 Hz, 1H, ArH), 6.57 (d, J = 7.9 Hz, 1H, ArH) 4.52 (s, 1H, OH), 2.14 (s, 3H, CH_3)	3580, 2950, 2850, 1600, 1475, 1330, 1250, 1150, 1050, 800.	148 (p), 147, 133 (p-CH_3), 90.
4. 	74%[c]	6.80 (d, J = 8 Hz, 1H, ArH), 6.49 (d, J = 8 Hz, 1H, ArH), 4.90 (br s, 1H, OH), 2.21 (s, 3H, CH_3)	3420, 2925, 2850, 1595, 1450, 1280, 1060, 810.	176 (p), 161 (p-CH_3), 148, 147, 135, 122, 121, 101.
5. 	100%	7.55 (d, J = 7.5 Hz, 1H, ArH), 7.13 (br s, 1H, ArH), 7.03 (d, J = 7.5 Hz, 1H, ArH), 6.75 (s, 1H, ArH), 6.70 (m, 2H, ArH), 3.80 (s, 3H, OCH_3).	3440, 3010, 1640, 1525, 1340, 1310, 1265, 1070, 840.	226 (p), 225, 211 (p-CH_3), 195 (p-OCH_3), 181, 165, 152.

(a) Yields refer to materials purified by flash chromatography.
(b) Melting points are not corrected.
(c) Overall yield for oxidation and cyclization.

(Received in USA 19 April 1982)