

## Short Communications

Pakistan J. Sci. Ind. Res., Vol. 23, Nos. 1-2, Feb.-April, 1978

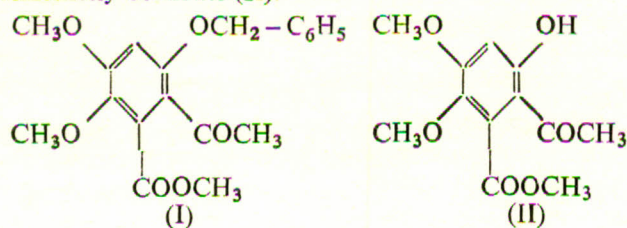
## SYNTHESIS OF METHYL-2-ACETYL-3-HYDROXY-5, 6-DIMETHOXYBENZOATE

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(Received May 27, 1978 ; revised June 21, 1978)

Treatment of 2, 5-dihydroxy-4-methoxy acetophenone (I) with allyl bromide yielded the allyl ether (II) which was benzylated to allyl benzyl ether<sup>1</sup> The Claisen rearrangement of this ether readily gave 2-allyl-6-benzyloxy-3-hydroxy-4-methoxy acetophenone. The methyl ether of this, when refluxed with 25% alcoholic potassium hydroxide, provided 6-benzyloxy-3, 4-dimethoxy-2-propenyl acetophenone. Oxidation<sup>2</sup> of this benzyl ether with potassium permanganate led in a moderate yield to an *o*-acetyl benzoic acid.<sup>1</sup> Methylation of this acid with diazomethane gave the methyl ester (I). This ester was hydrogenolyzed with Pd catalyst to give the desired methyl 2-acetyl-3-hydroxy 5, 6-dimethoxy benzoate (II).



*Methyl-2-acetyl-3-benzyloxy-5, 6 - dimethoxybenzoate*<sup>3</sup> (I). Methylation of 2-acetyl-3-benzyloxy-5, 6-dimethoxy benzoic acid<sup>1</sup> (0.5 g) in methanol (10 ml.) with an excess of ethereal diazomethane gave the methyl ester (0.45 g), which separated from methanol in colourless needles. Recrystallization from the same solvent afforded methyl-2-acetyl-3-benzyloxy-5, 6-dimethoxybenzoate (I) in colourless needles, m.p. 140° (found C, 66.3 ; H 5.9, C<sub>19</sub>H<sub>20</sub>O<sub>6</sub> requires C, 66.2 ; H 5.8%.  $\nu_{max}$  1745 and 1605 cm<sup>-1</sup>. Nmr signals at  $\tau$  7.49 (3H, S), 6.22 (3H, S), 6.12 (3H, S), 6.15 (3H, S), 4.88 (2H, S), 3.42 (1H, S. Ar), 2.62 (5H, S. Ar). m/e (means spectrum) = 282.

*Methyl 2-acetyl-3-hydroxy-5, 6-dimethoxybenzoate*<sup>3</sup> (II). Methyl 2-acetyl-3-benzyloxy-5, 6-dimethoxybenzoate (500 mg.) and palladium charcoal (20%, 75 mg) in acetic acid (25 ml.) were shaken with hydrogen. Absorption ceased after 15 min. (35 ml. uptake). The suspension was filtered, and the acid solution was taken up in ether (100 ml.), washed with aqueous sodium bicarbonate, water, dried (MgSO<sub>4</sub>), and concentrated under reduced pressure to leave a thick yellow oil which on

crystallization from petroleum gave methyl 2-acetyl-3-hydroxy-5, 6-dimethoxybenzoate (430 mg.) m.p. 79°. (Found C, 57.0 ; H. 5.6 ; C<sub>12</sub>H<sub>14</sub>O<sub>6</sub> requires C, 56.6, H. 5.5%).  $\nu_{max}$  1722 and 1615 cm<sup>-1</sup>. Nmr signals at  $\tau$  7.55 (3H, S), 6.21 (3H, S) 6.8 (3H, S), 6.05 (3H, S) 3.48 (1H, S), 2.8 (1H, S) m/e (mas spectrum) = 254.

## References

1. F. M. Dean, D. R. Randall and G. Winfield, J. Chem. Soc., 1071 (1959).
2. F. M. Dean and D. R. Randall, J. Chem. Soc., 798 (1961).
3. S. Ayub Ali, Ph.D. Thesis, University of London, 1971.

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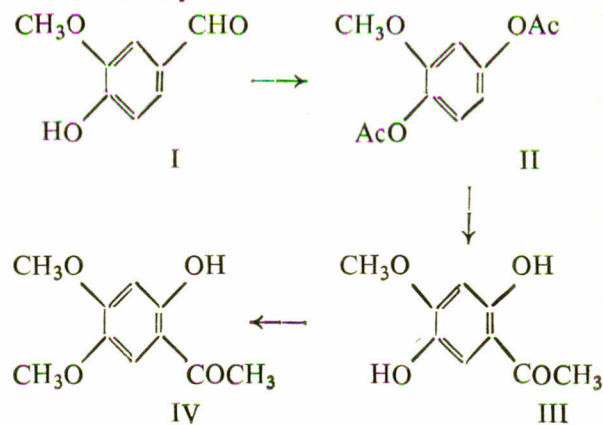
## A NEW ROUTE TO THE SYNTHESIS OF 2-HYDROXY-4,5-DIMETHOXY ACETOPHENONE

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(Received May 17, 1978; revised June 21, 1978)

In an attempt to prepare 2-hydroxy-4, 5-dimethoxy acetophenone from 1,2-dimethoxybenzene where the yields were variable, it was decided to try and simplify the reaction sequence. Consequently it was found that the required ketone could be prepared in an excellent yield by the methylation of 2,5-dihydroxy 4-methoxy acetophenone.<sup>2</sup> For this purpose vanillin (I) was oxidized with hydrogen peroxide in alkaline medium and converted into a diacetate (II). Fries migration of the diacetate with boron trifluoride and hydrolysis of the resultant product afforded 2,5-dihydroxy-4-methoxy acetophenone (II). Treatment of this ketone with methyl iodide yielded the desired 2-hydroxy-4,5-dimethoxy acetophenone (IV) in an excellent yield.





*Methoxyquinol diacetate.* Vanillin (I) (40 g) was suspended in aqueous sodium hydroxide (120 ml 1N) and oxidized with hydrogen peroxide (100 vol. 40 ml) in water (90 ml) at 0°. The whole of the solid dissolved, forming a dark brown solution. After 2 hr. aqueous sodium hydroxide (80 ml. 10N) and crushed ice (400 g) were added with vigorous agitation, followed by acetic anhydride (70 ml). The brown crystalline solid which separated was collected, dried at room temperature and recrystallized to afford methoxy quinol diacetate (II) in white needles, (45 g). m. p. 94° (literature value, 95°)<sup>2</sup>.

$\nu_{\max}$ . 1770  $\text{cm}^{-1}$ . Nmr signals at  $\tau$  7.75 (6H, S) 6.22 (3H, S); 2.9-3.4 (3H, Ar).

*2,5-Dihydroxy-4-methoxyacetophenone (III).* A solution of methoxyquinol diacetate (25 g) in acetic acid (90 ml). was saturated with boron trifluoride and the resulting reddish solution was poured into 5N hydrochloric acid (225 ml.) and boiled for 15 min. On cooling, the solution deposited a brown powder which was crystallized from alcohol to yield 2,5-dihydroxy-4-methoxyacetophenone (III) in yellow needles, (12.5 g), m.p. 166° (literature value, 166°)<sup>2</sup>.  $\nu_{\max}$ . 3380 ( $\nu_{\text{H}}$ ) and 1675  $\text{cm}^{-1}$  (C=O)

N.m.r. signals at  $\tau$  7.5 (3H, S), 6.1 (3H, S), 4.72 (1H, 3) 3.65 (1H, Ar), 2.8 (1H, Ar).

*2-Hydroxy-4, 5-dimethoxyacetophenone.* 2, 5-Dihydroxy-4-methoxyacetophenone (4 g) was methylated with methyl iodide (6 ml.) and anhydrous potassium carbonate (6 g) in dry acetone (150 ml) at reflux temperature for 6 hr. The mixture was filtered hot and the filter-cake washed well with acetone. Removal of the solvent under reduced pressure and crystallization of the product from methanol afforded 2-hydroxy-4, 5-dimethoxyacetophenone (IV) (3.5 g) m.p. and mixed m.p. 112°.<sup>3</sup> The product gave a deep blue ferric reaction.

$\nu_{\max}$ . 1640  $\text{cm}^{-1}$  (carbonyl). Nmr signals at  $\tau$  7.5 (3H, S), 6.19 (3H, S), 6.12 (3H, S), 3.62 (1H, Ar), 3.95 (1H, Ar).

### References

1. S. Ayub Ali, Ph.D. Thesis, University of London, (1971).
2. F. M. Dean, D. R. Randell and G. Winfield, J. Chem. Soc., 1071, (1959).
3. G. H. Jones, J. B. D. Mackenzie, A. Robertson and W. B. Whalley, J. Chem. Soc., 562, (1949).