# Electrophilic Amidoalkylation of Benzene and Dimethyl Malonate with Cyclic *N*-Formyl-2-methoxyamines

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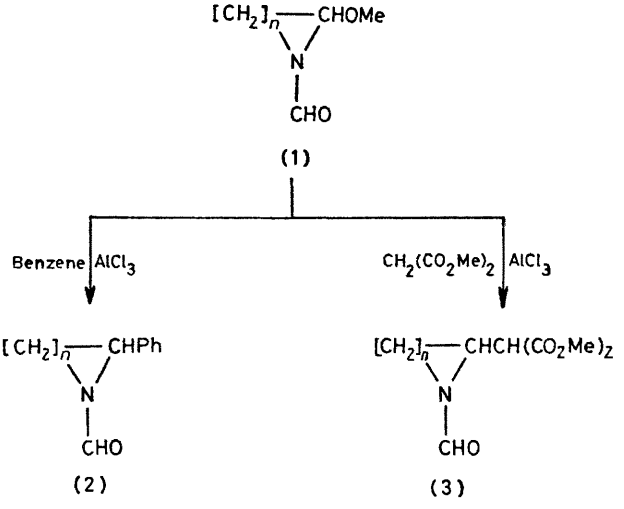
*Summary* Cyclic *N*-formyl-2-methoxyamines (derived from pyrrolidine, piperidine, and hexahydroazepine) amidoalkylate benzene and dimethyl malonate using $AlCl_3$ as a catalyst in 44—55 and 70—73% yields respectively.

ELECTROPHILIC amidoalkylation of aromatic compounds and enolizable carbonyl derivatives is well documented.[1,2] Most of these reactions have been performed with reagents of the type $R^1CON(R^2)CH_2X$ ($R^2$ = H or Me), where X is a leaving group. This limitation may result from difficulties encountered in the synthesis of other more complex reagents. We have recently shown that electrophilic reagents, where X is attached to a secondary or tertiary carbon atom, can be prepared in a simple anodic procedure by oxidizing an *N*-formylamine in methanol,[3] the synthesis being applicable on any desired scale. Here we report on the use of some of these reagents (**1**, $n$ = 2—4) in amidoalkylation.

The methoxy compounds (**1**) react with benzene (used as solvent) in the presence of $AlCl_3$, using a molar ratio of $AlCl_3$ to (**1**) of 1·4:1 at reflux temperature. The products are cyclic *N*-formyl-2-phenylamines (**2**), formed in the yields shown in the Scheme.† Previous synthesis of (**2**) has only




SCHEME. (**2**): $n$ = 3, 52%, b.p. 127 °C at 0·9 mmHg; $n$ = 4, 44%, b.p. 133—134 °C at 0·9 mmHg; $n$ = 5, 55%, b.p. 134 °C at 1·2 mmHg. (**3**): $n$ = 3, 70%, b.p. 145—152 °C at 1 mmHg; $n$ = 4, 73%, m.p. 66—71 °C; $n$ = 5, 73%, m.p. 79—81 °C.

† Experimental procedures. Benzene: (**1**) (0·1 mol) dissolved in benzene (0·2 mol) was added dropwise to a stirred solution of $AlCl_3$ (0·14 mol) in benzene (0·8 mol) at reflux temperature. The mixture was then refluxed for 1 h. Water (100 ml) was added and the organic phase was separated, washed with water, dried ($MgSO_4$), and filtered. The products (**2**) ($n$ = 3, 4, and 5) were isolated by distillation *in vacuo*. Dimethyl malonate: (**1**) (0·1 mol) and dimethyl malonate (0·12 mol) dissolved in dichloromethane (20 ml) were added dropwise to a stirred solution of $AlCl_3$ (0·14 mol) in dichloromethane (80 ml). The resulting solution was stirred overnight at room temperature. Water (100 ml) was added and the organic phase was separated, washed with water, dried ($MgSO_4$), and filtered. The solvent was evaporated off and the products (**3**) were isolated by distillation *in vacuo* ($n$ = 3), or were crystallized by addition of diethyl ether ($n$ = 4 and 5).

been reported for $n = 3$ (from benzoylcyclopropane),[4] but the unformylated compounds are known.[5]

In the second reaction, (**1**) is treated with $AlCl_3$ (molar ratio as before) in the presence of dimethyl malonate in dichloromethane (*ca.* 1 M in each reactant). The reaction is exothermic and causes the solvent to boil. The products are substituted malonates (**3**), in the yields shown in the Scheme.† None of the products or their unformylated analogues have been reported previously.[6]

The choice of catalyst is important. A protonic acid catalyst, such as trifluoroacetic acid[7] or sulphuric acid,[1,2] results in elimination of methanol from (**1**) followed by polymerization of the enamide formed.[8]

We believe that there should be a wide scope for the use of reagents of type (**1**), since they are easily prepared and both the acyl group and the alkyl groups at the nitrogen atom can be varied. The reactions shown in the Scheme exemplify simple routes to derivatives of 2-substituted cyclic amines.

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