$AlCl_3$-mediated Regioselective Migration of a Methoxy Group of *N*-Methoxy-*N*-phenylamides to the *ortho* Position of the Phenyl Ring

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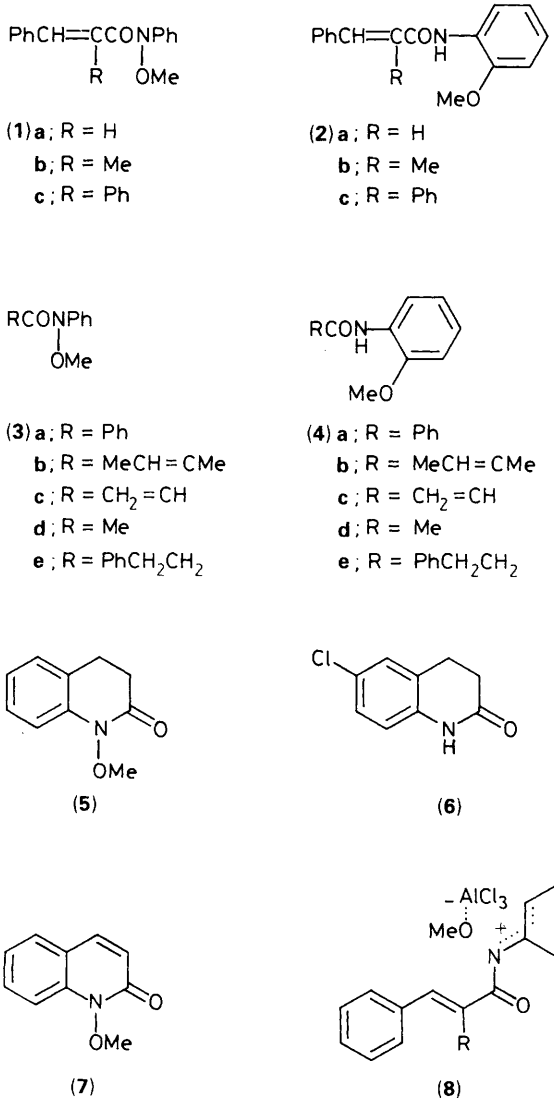
$AlCl_3$-mediated decomposition of *N*-methoxy-*N*-phenylamides in dichloroethane leads to regioselective intramolecular migration of the methoxy group from the nitrogen to the *ortho* position of the phenyl ring *via* a tight ion pair intermediate.

Although acid-catalysed hydrolysis of *N*-hydroxy-*N*-phenylacetamides in protic solvents has been studied[1a] in detail and found to give aminophenols through preferential hydrolysis of the amide group over N–O bond heterolysis, there have been no reports, to our knowledge, concerning the reaction of *N*-phenylhydroxamic acids with Lewis acids in aprotic solvents, although *N*-phenylhydroxamic acids have been reacted with benzene in the presence of trifluoromethanesulphonic acid to form aminobiphenyl derivatives.[2]

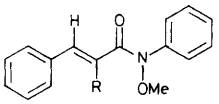
In this Communication we report that $AlCl_3$-mediated decomposition of *N*-methoxy-*N*-phenylamides in dichloroethane (DCE) provides a new source of *N*-acyl-*N*-arylnitrenium ions[3] and leads to the nucleophilic intramolecular migration of the methoxy group from the nitrogen to the *ortho* position of the phenyl ring. We have investigated the reaction of *N*-methoxy-*N*-phenylcinnamamide (**1a**) with various Lewis acids ($ZnCl_2$, $SnCl_4$, $FeCl_3$, $BF_3{\cdot}Et_2O$, and $AlCl_3$) in aprotic solvents (CH_2Cl_2, PhCl, $MeNO_2$, CS_2, and DCE) and found that the methoxy group migrated from the nitrogen, with $AlCl_3$† in DCE, to the *ortho* position of the phenyl ring in 79.4% yield; there was no migration to the *para* position. Two equiv. of $AlCl_3$ to (**1a**) were needed to obtain a high yield of *N*-(2-methoxyphenyl)cinnamamide (**2a**), and the use of 1.2 equiv. of $AlCl_3$ lowered the yield [(**2a**), 31.9%; (**1a**), 60.9%; 45 h). Prolonged reaction time or a higher reaction temperature brought about the demethylation of (**2a**). Several *N*-methoxy-*N*-phenylamides were reacted in this way, and the results are presented in Table 1.

Cinnamamides (**1b** and **c**) bearing α-substituent groups rearranged rapidly in high yields (runs 2,3), while *N*-methoxycarbostyrils [1-methoxy-2(1H)-quindinones] (**5**) and (**7**) did not, even with prolonged reaction times (runs 9 and 10). The most interesting aspect of this reaction is that rearrangement of (**1**) and (**3**) gave exclusively *N*-(*o*-methoxyphenyl)amides (**2**) and (**4**). The complete absence of the corresponding *para*-substituted products can be accounted for by assuming an intramolecular mechanism with a tight ion pair intermediate (**8**) which was formed by $AlCl_3$-mediated N–O bond heterolysis. A radical mechanism is not supported, as addition of a radical scavenger *N*,*N*-diphenylpicrylhydrazil did not affect this rearrangement. The configuration of the carbonyl oxygen and the methoxy oxygen in an *N*-methoxyamide group seems to influence the rate of this reaction. *N*-Phenylhydroxamic acids primarily have a configuration in which the two oxygens are on the same side;[4] however, (**1b** and **c**) are assumed to have a configuration where the two oxygens are on opposite sides owing to steric hindrance by the phenyl group.‡ Therefore, two moles of $AlCl_3$ co-ordinate with the oxygens to form a 2:1 complex, which enhances the rate of heterolytic N–O bond cleavage. On the other hand, (**5**) and (**7**) apparently have a configuration with two oxygens on the same side and one mole of $AlCl_3$ co-ordinates with these oxygens to form a 1:1 complex,[5] which retards the N–O bond cleavage. Even if the N–O bond is cleaved, the *ortho* position becomes remote from the methoxide anion generated but the latter is

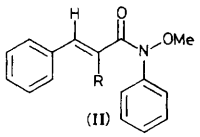


† Cinnamanilide (*N*-phenyl-3-phenylprop-2-enamide) (28.9%), *o*-chlorocinnamanilide (*o*-chloro-*N*-phenyl-3-phenylprop-2-enamide) (9.6%), and *N*-methoxy-*N*-phenyl-3-phenylprop-2-enamide (**1a**), (44.4%) were obtained with $FeCl_3$ and (**1a**) was recovered quantitatively with other acids.

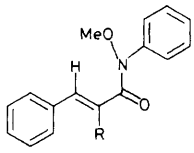
‡ The structures of cinnamamides are postulated as (**I**)—(**II**). (*E*)-Cinnamic acids were used as starting materials and the β-H signal (δ 7.80) of (**1a**) was shifted downfield owing to the deshielding effect of a carbonyl group compared with the corresponding H chemical shifts of (**1b**) (δ 6.84) and (**1c**) (δ 7.27), which supports the theory that the predominant structures of (**1a**, **b**, and **c**) are (**I**) (R = H) or (**II**) (R = H), (**III**) (R = Me), and (**III**) (R = Ph), respectively.



(I)



(II)



(III)

Table 1. Rearrangement of *N*-methoxy-*N*-phenylamides.[a]

Run	Starting material	Time/min	Product %
1	(**1a**)	120	(**2a**) (79.4)
2	(**1b**)	25	(**2b**) (84.0)
3	(**1c**)	27	(**2c**) (95.3)
4	(**3a**)	37	(**4a**) (59.6), (**3a**) (6.1)
5	(**3b**)	50	(**4b**) (69.2), (**3b**) (13.5)
6	(**3c**)	960	(**4c**) (32.0)[b]
7	(**3d**)	140	(**4d**) (22.8), (**3d**) (57.9)
8	(**3e**)	120	(**4e**) (41.7),[c] (**3e**) (27.4)
9	(**5**)	1440	(**5**) (30.0), (**6**) (49.3)[d]
10	(**7**)	4320	(**7**) (77.9)

[a] The reactions were carried out at room temperature with $AlCl_3$ (2 equiv.) in DCE. All new compounds reported in this Communication have been fully characterised by spectroscopic methods and elemental analyses. [b] Plus *ca.* 50% of a mixture of the *p*-chloroanilide and demethylated (**4c**). [c] Plus 18.6% of demethylated (**4e**). [d] A positive charge of a nitrenium ion generated by N–O bond heterolysis shifted to C-6 where a chloride anion was trapped.

held by $AlCl_3$, which still will be co-ordinated on the carbonyl oxygen side. The configuration of the methoxyamide group of other amides changes under different reaction conditions.

Compound (**1a**) was subjected to thermolysis (150 °C, 3 h), by which some *N*-acyloxy-*N*-arylamides were decomposed to give *N*-(*o*-acyloxyaryl)amides,[6] to recover the starting material in 94.9% yield. Usually, liquid *N*-methoxy-*N*-arylamides may be distilled below 150 °C under reduced pressure, and crystalline compounds can be stored for several years without decomposition. *N*-Acetoxy-*N*-phenylacetamide was subjected to this $AlCl_3$-mediated decomposition and *ortho*-substituted products were not obtained; however, *p*-chloroacetanilide and the starting material were isolated in 40.5% and 12.9% yields, respectively. However, *N*-ethoxy- and *N*-hydroxy-*N*-phenylamides were decomposed with $AlCl_3$ to give the corresponding *N*-(*o*-ethoxy- and hydroxy-phenyl)-amides in moderate yields.

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