Can *N*-Alkyl- and *N*-Arylimidazoles be Prepared Directly from Alcohols and Phenols with *N*,*N*'-Carbonyldiimidazole?

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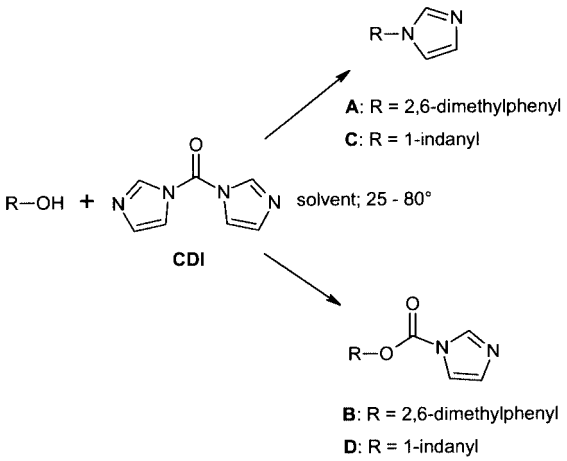
Abstract: The report that *N*-alkyl- and *N*-arylimidazoles can be prepared directly by reactions of *N*,*N*'-carbonyldiimidazole (CDI) with alcohols or phenols was shown to be erroneous. Under the described conditions only (*N*-alkoxy-carbonyl)- and (*N*-aryloxy-carbonyl)-imidazoles (carbamates) were obtained.

Key words: alcohols, phenols, imidazoles, carbonyl diazole reagents, heterocycles

Introduction

Recently Njar has reported a high-yielding synthesis of imidazoles and triazoles from alcohols and phenols.[1] According to the procedures described *N*-alkyl- and *N*-arylimidazoles were prepared directly from alcohols or phenols with *N*,*N*'-carbonyldiimidazole (CDI) under very mild conditions. Our interest in *N*-arylimidazoles as precursors for catalyst ligands prompted us to study these striking and unexpected reactions.



Scheme

Reaction of CDI with 2,6-Dimethylphenol

We repeated exactly the reported procedure of synthesis of 2,6-dimethylphenyl-1-imidazole (**A**) (Lit.[1]: Table, **38**, Entry 31) by reacting 2,6-dimethylphenol with 1.3 equivalents of CDI in dichloromethane at reflux for 5 hours. We isolated as single product the corresponding carbamate, (2,6-dimethylphenoxy)-carbonyl-1-imidazole (**B**), in 91% yield, as a colourless oil that solidified on standing, mp 63–64 °C (in a patent[2] 2,6-dimethylphenyl-1-imidazole, structure **A**, prepared by an umambiguous method, is mentioned with mp 82–82.5 °C; Lit.[1] mentions **38** to be a viscous oil).

The ^{1}H NMR-spectrum (300 MHz, $CDCl_3$) of our compound **B** was identical with the data published for **A**;[1] however the elemental analysis clearly supported the structure **B**: $C_{12}H_{12}N_2O_2$ (MW: 216.24) requires C, 66.65; H, 5.59; N, 12.95; O, 14.80; found: C, 66.74; H, 5.73; N, 12.91; O, 14.83.

The structure **B** was further supported by a strong IR-absorption (KBr) at 1769 cm^{-1} (C=O stretch vibration).

Additional chemical evidence for structure **B** was found when the product was hydrolysed in ethanolic aqueous NaOH solution on standing or brief heating to reflux: Only 2,6-dimethylphenol, identified by ^{1}H NMR, was formed besides some imidazole.

Reaction of CDI with 1-Indanol

We next repeated the reported synthesis of 1-(1*H*-imidazol-1-yl)indane (**C**) (Lit.[1]: Table, **25**; Entry 17) by reacting 1-indanol with 1.3 equivalents of CDI in acetonitrile at reflux for 1 hour. We isolated (1-indanyloxy)carbonyl-1-imidazole (**D**) in 42% yield, mp 89–90 °C. Indene was formed as the only identifiable side product. This instability of **D** was also mentioned in the literaure.[1]

Again the ^{1}H NMR-spectrum (300 MHz, $CDCl_3$) was identical with the published data for **C**;[1] however the elemental analysis clearly supported the structure **D**: $C_{13}H_{12}N_2O_2$ (MW 228.25) requires C, 68.41; H, 5.30; N, 12.27; O, 14.02; found: C, 68.42, H, 5.43; N, 12.23; O, 13.81.

The structure **D** was further supported by a strong IR-absorption (KBr) at 1743 cm^{-1} (C=O stretch vibration) typical for a *N*-alkoxycarbonyl-imidazole.[3]

Additional chemical evidence for structure **D** was found when the product was hydrolysed in ethanolic aqueous NaOH solution on standing, only 1-indanol and indene, identified by ^{1}H NMR, were formed besides some imidazole.

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^{1}H NMR Considerations

The above mentioned facts given, we assume that more examples in the literature,[1] both with alcohols and phenols, gave similarly only carbamates instead of the postulated *N*-alkyl- or *N*-arylimidazoles, respectively. Careful inspection of the ^{1}H NMR data[1] further supports this assumption; most spectra mention one peak (imidazole; H-2, s) at lower field than 8 ppm (mostly 8.1–8.3 ppm). *N*-Phenylimidazole, however, gives the H-2- peak at 7.83 ppm;[4a] *N*-alkyl- and *N*-allyl-imidazoles give the H-2-peak even at as highfield as 7.4–7.5 ppm.[4b–d] On the other hand ethyl 1-imidazole-carboxylate gives the H-2-peak at 8.14 ppm,[4e] typical for a imidazolyl-carbamate.

This argument holds throughout all imidazole examples, with one exception, compound **2** (Entries 1,2)[1] is described with a H-2-peak of 7.50 ppm, typical for a *N*-alkyl-imidazole. This single exception and the triazole cases remain to be elucidated.

In one case in the literature[1] the corresponding carbamate was prepared by independent synthesis (compound **40**; H-2-peak at 8.13 ppm). It was 'decarboxylated' by just refluxing in acetonitrile (carbamate **40**, 'alkyl imidazole' **14**; Entries 9–11).[1] However both compounds **40** and **14** have essentially the same melting points (Lit.[1]: 168–170 °C for **40** vs. 168–169 °C for **14**). More importantly their ^{1}H NMR spectra are essentially identical with respect to all of their chemical shifts in $CDCl_3$. This suggests that **40** does not react in refluxing acetonitrile at all and **40** and **14** appear to be identical.

Conclusion

There is strong evidence that most *N*-alkyl- and *N*-arylimidazoles described in the literature[1] were in fact carbamates. This was unambiguously proven in two cases by elemental analyses, by hydrolysis to the respective alcohols and phenols, and by spectroscopic evidence (IR-spectra). The argument was extended to most other cases by further spectroscopic evidence (^{1}H NMR-spectra).

Since *N*-alkyl- and *N*-arylimidazoles are important intermediates in organic chemistry it seems adequate to inform the scientific community that they generally cannot be prepared as reported in the literature.[1]

References

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