Nitrous Oxide

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Synthesis of Azoimidazolium Dyes with Nitrous Oxide**

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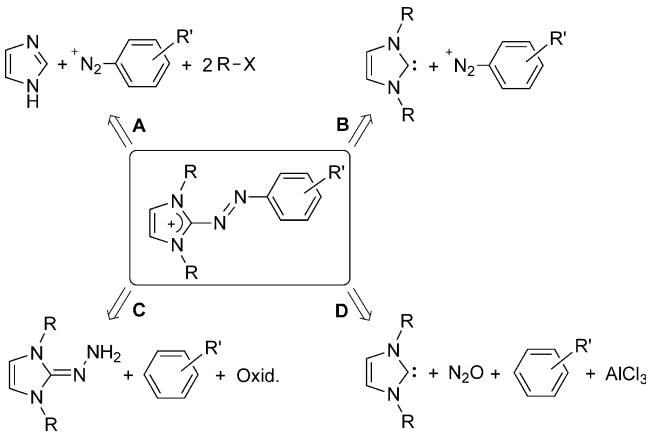
Abstract: *A new method for the synthesis of industrially important azoimidazolium dyes is presented. The procedure is based on a reagent which is rarely used in the context of synthetic organic chemistry: nitrous oxide ("laughing gas"). N_2O is first coupled to N-heterocyclic carbenes. Subsequent reaction with aromatic compounds through an $AlCl_3$-induced C–H activation process provides azoimidazolium dyes in good yields.*

Once used and abused as an anesthetic and recreational drug, nitrous oxide (N_2O, "laughing gas") is nowadays making the headlines as a greenhouse gas and ozone-depleting substance.[1,2] Human activities contribute significantly to the increased concentration of N_2O in the atmosphere. The extensive use of fertilizers, for example, fosters the enzymatic production of N_2O during nitrification and denitrification.[3] Nitrous oxide is also formed as a side product in important industrial processes, for example, during the synthesis of adipic and nitric acid.[4] Obviously, there is strong incentive to do something "useful" with N_2O. Two main directions have been explored so far. On one hand, people have exploited the high oxidation potential of N_2O. Due to the inert character of N_2O, most efforts have focused on oxidation reactions at elevated temperature and/or pressure in the presence of heterogeneous catalysts.[5] However, solution-based oxidation reactions have also shown some success.[6] A second, and much less explored direction is the utilization of N_2O as a building block for more complex organic molecules.[7–10] Organometallic compounds of the alkali[7] and earth alkaline metals[8] are known to react with N_2O under mild conditions. The products contain nitrogen atoms from N_2O, but the reactions are often not very attractive from a synthetic point of view (e.g., poor yields are obtained or alternative procedures give better results). Of particular relevance for the present study is a report published in 1953 by Meier and Rappold.[8c] The authors describe that azobenzene is formed in low yield by reaction of phenylcalcium iodide with N_2O. The reaction was recently reinvestigated by Hays and Hanusa.[8b] Under optimized reaction conditions, they were able to increase the yield of azobenzene to 61%, but they mentioned problems with reproducibility and the substrate scope was very narrow. Below, we report a simple, efficient, and versatile method for the synthesis of azo dyes from N_2O.

Azoimidazolium salts are of interest because they are strongly colored dyes. They are produced industrially (e.g., Basic Red 51) and used for a variety of applications such as dying of natural and synthetic fibers.[11] Furthermore, these compounds have been examined as photochromic ionic liquids.[12] Different methods for the synthesis of azoimidazolium dyes have been described in the literature. One route starts with an azo coupling of imidazole and diazonium salts, followed by N-alkylation (Scheme 1 A).[13] The patent literature reports a procedure which allows to prepare azoimidazolium dyes with aryl substituents at the heterocycle from N-heterocyclic carbenes and diazonium salts (Scheme 1 B).[14] A method without diazonium salts was developed by Hünig et al.: under oxidative conditions, hydrazones can be coupled to arenes (Scheme 1 C).[15,16] However, this procedure is limited to highly activated aromatic compounds such as anilines. In the following, we describe a novel procedure which is based on N-heterocyclic carbenes, N_2O, arenes, and $AlCl_3$ (Scheme 1 D).



Scheme 1. Retrosynthetic analysis of azoimidazolium dyes. Published procedures include the coupling of imidazole with diazonium salts, followed by alkylation (A),[13] the direct coupling of N-heterocyclic carbenes with diazonium salts (B),[14] and the oxidative coupling of hydrazones with activated arenes.[15,16] The new procedure is based on N-heterocyclic carbenes, N_2O, arenes, and $AlCl_3$ (C).

In 2012, we have reported that N-heterocyclic carbenes (NHCs) are able to form stable covalent adducts with N_2O.[17] While exploring the reactivity of these adducts with different organic and inorganic reagents, we observed rupture of the N–N bond or cleavage of the N–C bond of the N_2O group.[18] This type of chemistry is intriguing from a fundamental point of view, but the reaction products are less interesting from

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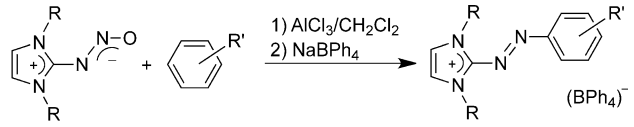
a synthetic chemistry point of view. In continuation of these investigations, we have studied the reaction of the adduct IMes–N_2O (IMes = 1,3-dimesitylimidazol-2-ylidene) with $AlCl_3$. Unexpectedly, we observed cleavage of the terminal N–O bond as detailed below.

Addition of $AlCl_3$ (2 equiv) to a benzene/CH_2Cl_2 (1:1) solution of IMes–N_2O led to an immediate color change to dark red. Workup after 1 h allowed the isolation of the azoimidazolium dye **1** in the form of a tetraphenylborate salt in 94% yield (Table 1). A similar procedure could be used to couple IMes–N_2O with aromatic compounds containing electron-donating and electron-withdrawing substituents. The corresponding dyes **2**–**5** were isolated in the form of orange/red powders with yields between 72% and 93% (Table 1). Whereas the reaction with fluorobenzene provided exclusively the *para* isomer, a mixture of *ortho* and *para* isomers (o/p = 1:2.5) was observed for the reaction with chlorobenzene. Typically, the aromatic coupling partner was added as co-solvent (200–700 equiv), but for the reaction with the electron-rich 1,3,5-trimethoxybenzene, it was possible to reduce the amount of arene to 5 equivalents with respect to IMes–N_2O.

Table 1: Synthesis of azoimidazolium dyes by Lewis acid-induced reaction of arenes with NHC–N_2O adducts.



R = Mes, *i*Pr, Me

1–**17**

Dye	R	Aryl	Yield [%][a]
1	Mes	Ph	94
2	Mes	Mes	93
3	Mes	2,4,6-$(MeO)_3C_6H_2$	75
4	Mes	ClC_6H_4	74[b]
5	Mes	*p*-FC_6H_4	72
6	*i*Pr	Ph	70
7	*i*Pr	Mes	93
8	*i*Pr	2,4,6-$(MeO)_3C_6H_2$	77
9	*i*Pr	*p*-ClC_6H_4	62
10	*i*Pr	*p*-FC_6H_4	70
11	Me	Ph	59
12	Me	Mes	61 (84)[c]
13	Me	2,5-$(MeO)_2C_6H_3$	52
14	Me	2,4,6-$(MeO)_3C_6H_2$	55
15	Me	$(Me_2N)C_6H_4$	71[d]
16	Me	ClC_6H_4	52[e]
17	Me	*p*-FC_6H_4	54

[a] Yield of the isolated product. [b] o/p = 1:2.5; [c] The value in bracket gives the yield for perchlorate salt; [d] Isolated as perchlorate salt, o/p = 1:1.3, [e] o/p = 1:7.8. Mes = mesityl.

The synthesis of IMe–N_2O from N_2O and the free carbene IMes[17] or the corresponding imidazolium salt[18] is straightforward. Nevertheless, we were interested whether preisolation of IMes–N_2O is necessary for the synthesis of the azoimidazolium dyes. This turned out not to be the case: the dyes **1**, **2**, and **4** could be obtained by a one-pot procedure starting directly from 1,3-dimesitylimidazolium chloride (for details see the Supporting Information). The isolated yields were comparable to what was found for the two-step procedure (**1**: 87%; **2**: 92%; **4**: 73%).

Next, we have examined reactions of N_2O adducts of carbenes featuring aliphatic substituents at the N atoms (*i*Pr, Me). As in the case of IMes–N_2O, we were able to obtain the corresponding azoimidazolium dyes (**6**–**16**, Table 1). It was found to be advantageous to start the reaction at a lower temperature (−40 °C). The reactions with chlorobenzene were more selective, with the *para* isomer **9** being the sole product in reactions with I*i*Pr–N_2O. Overall, the *i*Pr derivatives were isolated with yields between 62–93%. Somewhat lower yields were obtained for the IMe-based compounds **11**–**16** (52–61%). However, further optimization seems possible. For example, when $NaClO_4$ instead of $NaBPh_4$ was used as the precipitating agent for the synthesis of dye **12**, we were able to increase the yield of the desired product from 61 to 84%.[19]

It is noteworthy that *N*,*N*-dimethylaniline is a suitable coupling partner as evidenced by the synthesis of dye **15** as a mixture of two isomers (o/p = 1:1.3) in a combined yield of 71%. Azoimidazolium dyes with aminobenzene substituents are of special interest for industrial applications.[11] They are typically prepared by reaction of fluoro- or chlorobenzene derivatives such as **4** or **5** with amines (through nucleophilic substitution).[13a,b,e] Our direct methodology thus allows to circumvent an additional reaction step.

Polycyclic arenes appeared to be interesting reaction partners because the resulting dyes would feature an extended π-system. Therefore, we have examined the reaction of IMe–N_2O with naphthalene and pyrene. In both cases, we were able to obtain the corresponding azoimidazolium dyes in acceptable yields (Figure 1, **18** and **19**). For naphthalene, the reaction was highly regioselective, with C–H activation occurring exclusively at the 1-position. As expected, the dyes **18** and **19** show absorption bands at

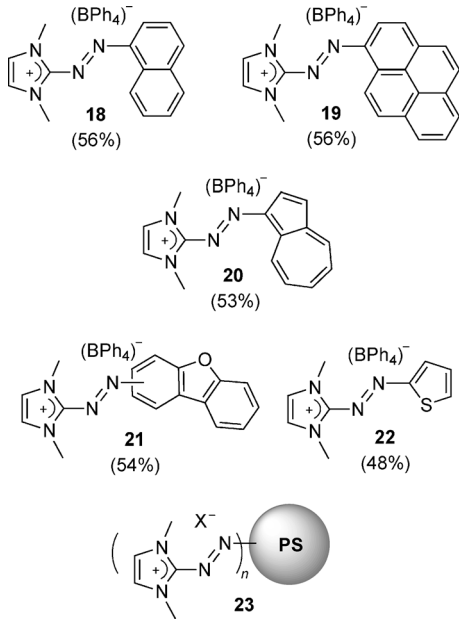


Figure 1. Structures of the dyes **18**–**23** (PS = polystyrene).

higher wavelengths compared to the simple benzene compound **11** (λ_{max}(**11**) = 368 nm, λ_{max}(**18**) = 462 nm, λ_{max}(**19**) = 573 nm).

The 10-π-electron system azulene is an isomer of naphthalene. In contrast to naphthalene, it exhibits a strong blue color and a large dipole moment. The incorporation of azulene into polyconjugated systems has been investigated extensively, because the resulting chromophores can display unique properties.[20] We managed to couple IMe–N_2O with azulene to give dye **20** in 53% yield. As expected, the azo coupling occurred selectively at the electron-rich five-membered ring of azulene. It should be noted that compound **20** would be difficult to prepare by standard synthetic procedures (Scheme 1 A,B) because 1-azulenyldiazonium salts[21] as well as the precursor 1-aminazulene,[22] are unstable compounds.

Reactions with heterocyclic compounds are likewise possible as evidenced by the successful synthesis of **21** and **22** (Figure 1). The reaction with dibenzofuran occurred in a nonselective fashion to give a mixture of all four possible isomers (ratio ~1:2:2:12; yield 54%). On the other hand, C–H activation of thiophene occurred selectively at the 2-position (yield: 48%). Attempts to couple NHC–N_2O adducts with pyridine or pyrrole were not successful. Possibly, $AlCl_3$ is deactivated by these strongly Lewis basic compounds.

The fact that simple arenes such as benzene and mesitylene are suitable coupling partners prompted us to investigate if our method could be used for the postfunctionalization of polystyrene with azoimidazolium groups. This was indeed possible: upon reaction of IMe–N_2O with an excess of polystyrene in dichloromethane, we were able to isolate the functionalized polymer **23**. Polymer **23** absorbs light at λ_{max} = 385 nm, and elemental analysis suggests a dye content of 4%.

The azo dyes **1**–**22** were comprehensively characterized by elemental analysis, high-resolution mass spectrometry, UV/Vis, and NMR spectroscopy. In addition, we have performed single-crystal X-ray analyses of **2** and **4**. For the crystallographic analyses, we have focused on dyes with aryl substituents at the heterocycle because these compounds are mainly described in the patent literature[14] and analytical data are scarce.

The cations of both compounds display the expected *trans* geometry (Figure 2). Interestingly, compound **4** crystallizes as a mixture of isomers. With an *ortho* to *para* ratio of 27:73, the solid- state composition reflects approximately the isomer distribution of the product. The two cations of **2**, *para*-**4**, and *ortho*-**4** show N–N bond lengths of 1.2649(19) Å (**2**), 1.266(7) Å, and 1.24(2) Å, respectively. These values are close to those of azoimidazolium salts with alkyl substituents at the heterocycle.[12c]

The mechanism of the reactions described above likely involves an initial complex between $AlCl_3$ and the NHC–N_2O adducts. In reactions with other metallic Lewis acids such as $CrCl_3$, Cu(OTf), $CuCl_2$, Fe(OTf)$_2$, Zn(C_6F_5)$_2$, and $SnCl_3Ph$, we had observed that NHC–N_2O adducts can act as N-donors, as O-donors, or as chelating N,O-donors.[18] For the hard Lewis acid $AlCl_3$, coordination through the oxygen atom seems likely (Scheme 2, **A**). Such a coordination should result in an elongation of the N–O bond, similar to what was observed for adducts between IMes–N_2O and $CrCl_3$ or the organic Lewis acid tritylium.[18] Oxygen abstraction, possibly facilitated by further $AlCl_3$, would then result in the formation of a diazonium salt, which could undergo azo coupling with the aromatic reaction partner (Scheme 2). A dicationic diazonium compound of type **B** is expected to be highly reactive, which would explain the fact that we observe coupling reactions with benzene and even deactivated arenes such as chloro- and fluorobenzene. First attempts to isolate or detect the putative intermediate **B** were not successful. When the reaction of IMes–N_2O with $AlCl_3$ was performed without an additional arene coupling partner, a complex mixture of products was obtained. A more detailed study of the reaction mechanism, as well as of the elusive diazonium dication **B**, is currently underway in our laboratory.

To conclude, we have reported the synthesis of azoimidazolium dyes by an $AlCl_3$-mediated coupling of aromatic compounds with NHC–N_2O adducts. The latter can be obtained by reaction of NHCs (preformed or generated in situ) with N_2O. A key advantage of our new procedure is its flexibility. The heterocyclic coupling partner can be decorated with aliphatic as well as aromatic substituents on the nitrogen atoms. Furthermore, it is possible to use a wide range of aromatic coupling partners including deactivated C_6H_5F, heterocycles, and polymers such as polystyrene. As such, our method complements existing procedures, each of which

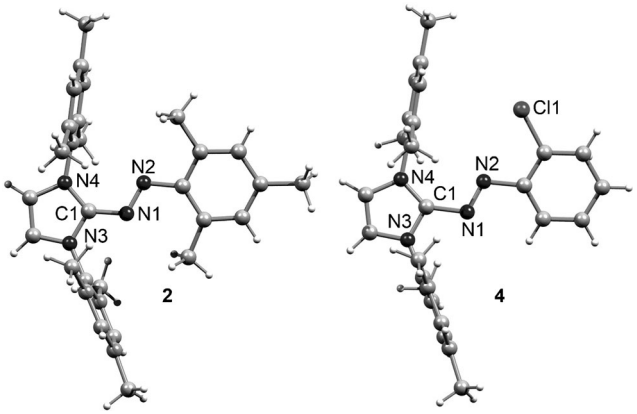
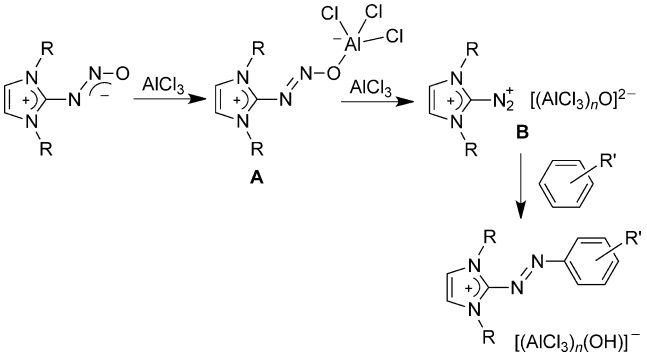


Figure 2. Ball-and-stick representations of the molecular structures of **2** and **4** in the solid state. Only the *ortho* isomer of **4** is shown. BPh_4^- anions are omitted for clarity.



Scheme 2. Proposed mechanism for the $AlCl_3$-mediated coupling of NHC–N_2O adducts with arenes.

has its own limitations. For example, the postfunctionalization of polymers with simple phenyl side chains would be difficult to achieve with the known synthetic protocols. In this communication, we have focused on imidazolium dyes, but it is conceivable that a similar procedure can be employed for other heterocyclic azo dyes.[23] From a more general point of view, our results are further evidence that N_2O can be used as an efficient N_2 donor in synthetic organic chemistry.

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[23] Preliminary results show that cationic azo dyes with benzothiazolium groups can be prepared in a related fashion (see compound **24**, Supporting Information).

