Reactions between 1-Methyl-2-phenyl-3-nitrosoindole, Activated with Benzoyl Chloride, with Indole and Indolizine Derivatives as Nucleophiles: a Case of 1,3-Migration

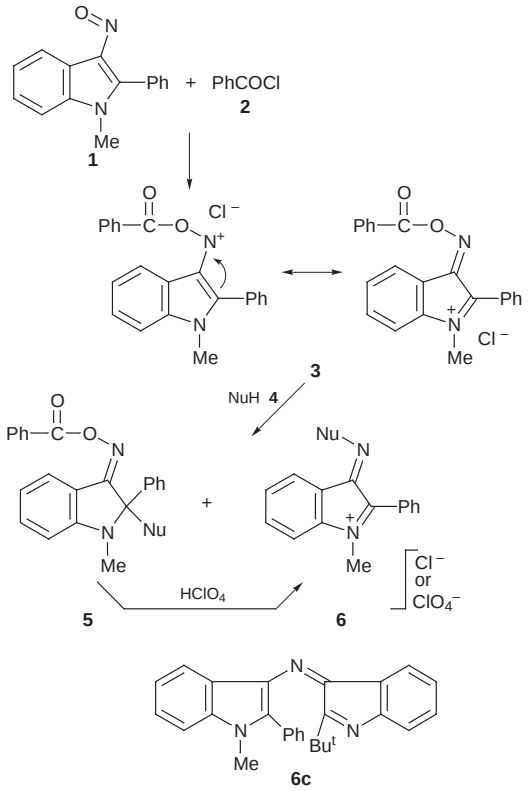
J. Chem. Research (S), 1999, 362–363
J. Chem. Research (M), 1999, 1634–1644

Monica Rossetti,[a] Pierluigi Stipa,[a] Rita Petrucci[b] and Lucedio Greci*[a]

[a] *Dipartimento di Scienze dei Materiali e della Terra, Università, Via Brecce Bianche, I-60131 Ancona, Italy*
[b] *Dipartimento di Ingegneria Chimica, dei Materiali, delle Materie Prime e Metallurgiche, Università "La Sapienza", Via del Castro Laurentiano 7, I-00161 Roma, Italy*

2-Phenyl-3-nitrosoindole activated with PhCOCl reacts with indoles and indolizines (NuH) affording products of 1,2-addiction which undergo 1,3-nucleophilic migration in acid media.

1-Methyl-2-phenyl-3-nitrosoindole reacts with benzoyl chloride affording the adduct **3**, which mainly shows an iminium structure as has been recently demonstrated.[1] This adduct undergoes nucleophilic attack at C-2 as observed in many other indolenine structures.[2–4] However, nitrosoarenes including *N,N*-dimethyl-*p*-nitrosoaniline in the presence of benzoyl chloride[1] react at the nitrogen of the nitroso group as nitrenium ions forming a new carbon–nitrogen bond.[5–8]



Scheme 1 Nu = 1-methyl-2-phenylindol-3-yl (**a**); 1,2-dimethylindol-3-yl (**b**); 2-*tert*-butylindol-3-yl (**c**); indol-3-yl (**d**); 2-phenyl-3-acetylindolizin-1-yl (**e**); 2-phenylindolizin-3-yl (**f**); 1-methyl-2-phenylindolizin-3-yl (**g**); 2-phenyl-3-methylindolizin-1-yl (**h**); 1-methyl-2-(4-methylphenyl)indolizin-3-yl (**i**).

Here, we report the reaction of **3** with a series of indoles **4a–d** and indolizines **4e–i** with different nucleophilicity. The first step of the reaction is the nucleophilic attack at C-2 adduct **3** by the nucleophiles yielding the yellow adducts **5** [Scheme 1, Chart 1 (full text)] with elimination of hydrogen chloride.[5] The structures of compounds **5** were established by comparison of their spectroscopic data with those of a similar compound[9] the structure of which was elucidated by X-ray analysis. As a consequence, the stereochemistry of the C=N bond should show an *E* configuration with respect to the substituents at C-2. Compounds **5** are susceptible to proton attack at a variety of sites, one of which is the oxygen of the carbonyl group of the benzoyl moiety. Protonation at this site leads to the elimination of benzoic acid and the incipient formation of a nitrene which promotes 1,3-migration of the indolyl or the indolizinyl group from C-2 to N, affording salts **6** [Scheme 1, Chart 1 (full text)]. These compounds, always formed during the reaction, were also obtained by acid treatment of pure adducts **5**.[1] For nucleophiles **4b**, **4d** and **4e** transposition products **6b**, **6d** and **6e** and were not observed.

Compounds **6**, formed in the reaction medium as chlorides, were isolated as perchlorates, this counter ion leading to formation readily isolable pure green crystals. However for **6d**, **6d** and **6e** such purification failed and only a viscous green mass was obtained. For 2-*tert*-butylindole, the transposition product **6c** is a neutral compound, owing to deprotonation at the indole nitrogen. Concerning the stereochemistry of the C=N bond in **6c**, no crystallographic data is available even though compounds showing an indolenine structure have been known since the beginning of this century.[10] However, the crystal structure of 2-phenyl-3-phenylimino-3*H*-indole-1-oxide shows an *E* configuration for the exocyclic nitrogen with respect to the substituent at C-2.[11] A similar configuration was also observed for adduct **3**.[1] The structures of perchlorates **6a**, **6b**, **6d** and **6e** were previously demonstrated by reduction of similar compounds to the corresponding secondary amines[12,13] and, more recently, by X-ray analysis of the salt obtained in the reaction of **3** with 1-ethyl-2-phenylindole.[14] The yields of the isolated products are reported in Table 1.

The attainment of adducts **5** depends on the nucleophilicity of the indoles and indolizines involved in the reaction; the higher the nucleophilicity of the nucleophile, the easier the 1,3-migration to form compounds **6**. Because the nucleophilicity of substrates increases with decrease of their oxidation potentials, the tendency to migration for the studied nucleophiles can be correlated with their oxidation potentials.

The studied indoles show E_{pa} (*vs.* NHE) which vary from 1.10 V for 2-*tert*-butylindole **4c** to 1.49 V for the unsubstituted indole **4d**;[8,15,16] the anodic $E_{1/2}$ (*vs.* NHE)

* To receive any correspondence (*e-mail*: greci@popcsi.unian.it).

Table 1 Yields of products isolated in the reactions of activated nitrosoindole **3** with nucleophiles **4a–i**

Reagents	Products (% Yield)	
3+**4a**	**5a** (30)	**6a** (35)
3+**4b**	**5b** (24)	
3+**4c**		**6c** (73)
3+**4d**	**5d** (77)	
3+**4e**	**5e** (53)	
3+**4f**		**6f** (86)
3+**4g**		**6g** (65)
3+**4h**		**6h** (70)
3+**4i**		**6i** (75)

of indolizines range from 0.75 V for indolizines **4g–i** to 1.2 V for indolizine **4e**.[15] From the oxidation potentials it can be deduced that indolizines possess a nucleophilicity higher than that of indoles and thus a lower stability for the adducts **5** could be expected. These suppositions are confirmed by the experimental data; in fact, adducts **5** were isolated for all the studied indoles, whereas in the case of indolizines this type of adduct was obtained only for indolizine **4e** which shows an oxidation potential similar to those of the studied indoles.

Thanks are due to the Italian MURST and to Ancona University for financial support.

Techniques used: IR, ^{1}H NMR, mass spectrometry

References: 17

Chart 1: Nucleophiles **4a–i** and isolated products **5** and **6**

Received, 1st February 1999; Accepted, 19th March 1999
Paper E/9/00849G

References cited in this synopsis

1 L. Greci, M. Rossetti, R Galeazzi, P. Sgarabotto and P. Cozzini, *J. Chem. Soc., Perkin Trans. 2*, 1998, 2683.
2 H. Takeuchi and K. Takano, *J. Chem. Soc., Perkin Trans. 1*, 1986, 611.
3 G. Kohnstmam, W. A. Pecth and L. H. William, *J. Chem. Soc., Perkin Trans. 2*, 1984, 423.
4 T. Sone, K. Hamamoto, Y. Sciji, S. Shinkai and O. Manabe, *J. Chem. Soc., Perkin Trans. 2*, 1981, 1596.
5 M. Colonna, L. Greci and L. Marchetti, *Gazz. Chim. Ital.*, 1974, **104**, 385.
6 L. Cardellini, P. Carloni, E. Damiani, L. Greci, P. Stipa, C. Rizzoli and P. Sgarabotto, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1589.
7 P. Carloni, L. Greci, M. Iacussi, M. Rossetti, C. Rizzoli and P. Sgarabotto, *J. Chem. Res.*, 1996, (*S*) 350; (*M*) 1924.
8 P. Carloni, L. Greci, M. Iacussi, M. Rossetti, P. Cozzini and P. Sgarabotto, *J. Chem. Res.*, 1998, (*S*) 232; (*M*) 1121.
9 E. Foresti Serantoni, R. Mongiorgi, M. Colonna, L. Greci, L. Marchetti and G. D. Andreetti, *Gazz. Chim. Ital.*, 1974, **104**, 1217.
10 W. J. Houlihan, *Indoles, Part II*, Wiley Interscience, New York, 1972, p. 599.
11 C. Rizzoli, P. Sgarabotto, F. Ugozzoli, P. Carloni, E. Damiani, L. Greci and P. Stipa, *J. Heterocycl. Chem.*, 1993, **30**, 637.
12 M. Colonna, L. Greci and L. Marchetti, *Ann. Chim. (Rome)*, 1973, **63**, 785.
13 P. Bruni, M. Colonna and L. Greci, *Tetrahedron*, 1971, **27**, 5893.
14 L. Greci, unpublished results.
15 M. Colonna, L. Greci, M. Poloni, F. P. Colonna and G. Distefano, *J. Chem. Soc., Perkin Trans. 2*, 1986, 1229.
16 R. J. Waltman, A. F. Diaz and J. Bargon, *J. Phys. Chem.*, 1984, **88**, 4343.