Application of Phase-Transfer Catalysis to the Synthesis of 3-Diazo-3*H*-indoles

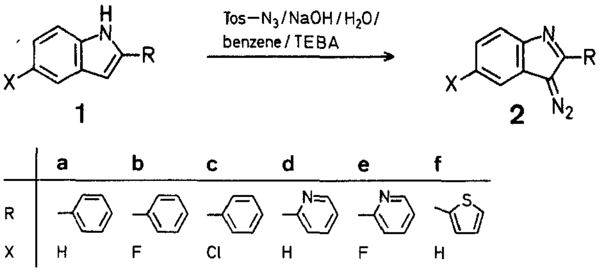
Asensio GONZÁLEZ, Carmen GÁLVEZ*

Departamento de Química Orgánica de la Facultad de Química de la Universidad de Barcelona, Spain

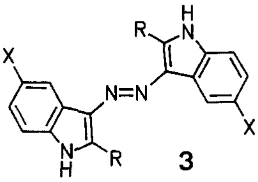
Conventional methods for the synthesis of diazo compounds[1] are based upon two principles: either the diazo function is built up in a stepwise fashion (diazotization of amines, the Forster reaction) or by modification of functional groups containing two neighbouring N-atoms (dehydration of hydrazones, the Bamford-Stevens reaction, deacylation of *N*-nitrosocarboxamides). A third general possibility consists of the introduction of both N-atoms, i.e. the entire diazo group in a single reaction step (diazo-group transfer). The latter method is carried out in the presence of a suitable base and to date, tosyl azide has been used almost exclusively as diazo-group transfer reagent.

In the synthesis of diazoindoles, the above-mentioned possibilities are practically limited to the conventional method of diazotization of aminoindoles. These latter compounds are obtained from the reduction of nitrosoindoles[2] or azo compounds of the indole series[3].

We report here that 2-aryl(heteroaryl)indoles (**1**) can be converted into the corresponding 3-diazo-3*H*-indoles (**2**) in good yields via diazo-group transfer using tosyl azide in an aqueous-organic two-phase system containing sodium hydroxide and catalytic amounts of triethylbenzylammonium chloride. The diazo compounds **2** thus obtained are stable.



In preliminary experiments we noticed that on performance of the reaction in homogeneous phase and in the absence of the ammonium salt, bis[3-indolyl]-diazenes (3,3′-azoindoles, **3**) were formed whereas 3-diazo-3*H*-indoles (**2**) could not be detected in the reaction products[5,7].



The 2-aryl(heteroaryl)indoles **1a**[8], **1b**[9], **1c**[10], **1d**[11], and **1f**[12] were prepared following the procedure described for **1e**.

5-Fluoro-2-(2-pyridyl)-indole (1e):

2-Acetylpyridine 4-fluorophenylhydrazone is prepared from 2-acetylpyridine and 4-fluorophenylhydrazine[13]. A mixture of the hydrazone (22.9 g, 0.1 mol) and polyphosphoric acid (100 g) is heated at 160 °C (oil bath) for 15 min. The mixture is then hydrolyzed and neutralized with aqueous sodium hydroxide. The precipitate formed is isolated by suction and purified by column chromatography on alumina using chloroform as eluent; yield 14.4 g (68%); m.p. 145 °C.

$C_{13}H_9FN_2$	calc.	C 73.57	H 4.27	N 13.20	F 8.96
(220.2)	found	73.54	4.19	13.16	8.91

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 7-8$ (complex signal, 8 H); 8.5 ppm (m, 1 H, 6-H of pyridine ring).

2-Aryl(heteroaryl)-3-diazo-3*H*-indoles (2); General Procedure:

A aqueous 40% solution (3 ml) of sodium hydroxide is added dropwise to a vigorously stirred mixture of the indole **1** (5.2 mmol), tosyl

Table. 2-Aryl(heteroaryl)-3-diazo-3*H*-indoles (**2**)

2	Yield[a] [%]	Reported Yield [%]	m.p. [°C]	Molecular formula[b] or m.p. [°C] reported	I.R. (KBr)[c] $\nu_{C=N_2}$ [cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS)[f] δ [ppm] (complex signals)
a	75	—[2]; 58.5[d,4]; 38[e,5]	107–108°	107–108°[2]	2110	7.2–7.9
b	87		124–125°	$C_{14}H_8FN_3$ (237.2)	2095	7.2–7.9
c	90		149–150°	$C_{14}H_8ClN_3$ (253.7)	2100	7.0–7.8
d	87	43[e,6]	97–98°	97–98°[6]	2120	7.0–8.5
e	80		138–139°	$C_{13}H_7FN_4$ (238.2)	2110	
f	83		96°	$C_{12}H_7N_3S$ (225.2)	2100	7.0–7.9

[a] Yield of isolated pure product.

[b] The microanalyses were in good agreement with the calculated values: C, ±0.22; H, ±0.19; N, ±0.10; Cl, ±0.10; F, ±0.12; S, ±0.15.

[c] Pye-Unicam SP 1100.

[d] Yield based on 2-phenyl-3-phenylazoindole.

[e] Yield based on **1**.

[f] Recorded at 60 MHz on a Hitachi-Perkin-Elmer Spectrometer R-12B.

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azide (1.024 g, 5.2 mmol), and triethylbenzylammonium chloride (30 mg, 0.13 mmol) in benzene (40 ml). The mixture is protected from light, stirred at room temperature for 18 h, and then extracted with water (3 × 30 ml). The organic layer is dried with sodium sulfate, the benzene removed by distillation, and the residual product chromatographed on alumina using benzene as eluent.

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* Address for correspondence.

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