A New Procedure for the Synthesis of 2-(2-Indolyl)pyrroles, 2,3′-Bi-indolyls, and 2-(3-Indolyl)-3-(2-indolyl)indoles

Vittorio Bocchi* and Gerardo Palla

Istituto di Chimica Organica dell'Università, 43100 Parma, Italy

The 3-bromoindoles were found to react with pyrroles and indoles, in the presence of protic or Lewis acids, to give 2-(2-indolyl)pyrroles, 2,3′-bi-indolyls, and trimeric products such as 2-(3-indolyl)-3-(2-indolyl)indoles.

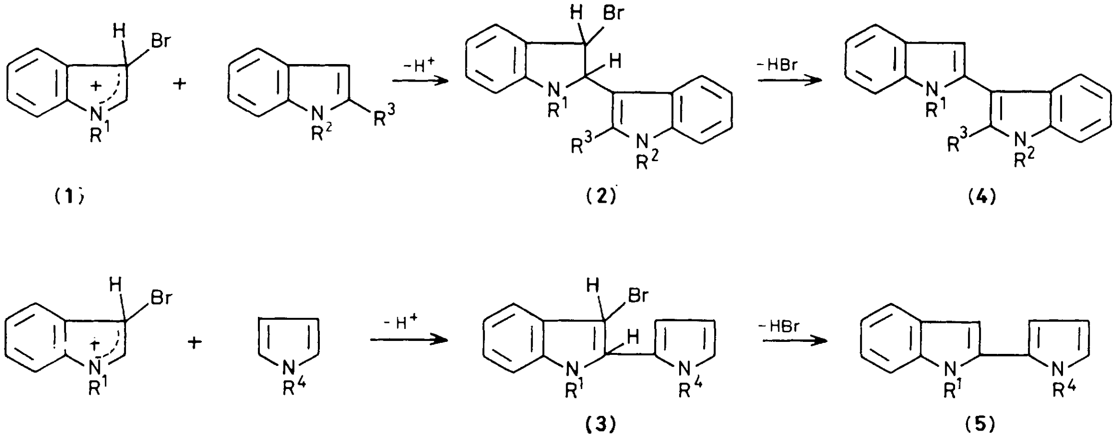
Convenient syntheses of dimeric indoles have been recently reported for 2,2′-bi-indolyls[1,2] but no general synthetic method exists for the 2,3′-bi-indolyls, even though dimers of indole[3] and *N*-methylindole[1,4] are known.

Recently we reported a high yield selective synthesis of the 3-bromoindoles[5] that we now prove to be convenient reagents for the synthesis of indolylpyrroles, 2,3′-bi-indolyls, and also trimeric products. The reaction is carried out in dry organic

Table 1. Synthesis of 2,3′-bi-indolyls, 2-(2-indolyl)pyrroles and 2-(3-indolyl)-3-(2-indolyl)indoles by acid promoted reaction of 3-bromoindoles with indoles and pyrroles.

Bromoindole [a]	Substrate	Acid [b]	Product[c]	% Yield[d]	M.p./°C
A	Pyrrole	D	2-(2-Indolyl)pyrrole	83	223—225
A	*N*-Methylpyrrole	D	*N*-Methyl-2-(2-indolyl)pyrrole	76	91—92
A	Indole	D	2,3′-Bi-indolyl	85	203—205[e]
A	2-Methylindole	D	2′-Methyl-2,3′-bi-indolyl	92	155—156
A	*N*-Methylindole	D	*N*′-Methyl-2,3′-bi-indolyl	70	142—144
A	2,3′-Bi-indolyl	D	2-(3-Indolyl)-3-(2-indolyl)indole	43	239—243
A	3-Methylindole	$SnCl_4$	3-Methyl-2,3′-bi-indolyl	64	154—156
B	3-Methylindole	$SnCl_4$	2′,3-Dimethyl-2,3′-bi-indolyl	91	[f]
C	2-Methylindole	D	*N*,2′-Dimethyl-2,3′-bi-indolyl	86	194—196
C	*N*-Methylindole	D	*N*,*N*′-Dimethyl-2,3′-bi-indolyl	73	135—137[g]
C	*N*,*N*′-Dimethyl-2,3′-bi-indolyl	D	*N*,*N*′,*N*″-trimethyl-2-(3-indolyl)-3-(2-indolyl)indole	58	199—201[h]

[a] A: 3-bromoindole; B: 3-bromo-2-methylindole; C: *N*-methyl-3-bromoindole. [b] D: trifluoroacetic acid. [c] Compounds were identified by their elemental analyses and spectra. [d] Yields are based on isolated products after silica gel column chromatography, [e] Lit.[3] 203.5—205 °C. [f] The product retains solvent. [g] Lit.[1] 137—138 °C. [h] Lit.[7] 201—203 °C.



Scheme 1. R^1, R^2, R^4 = H, Me; R^3 = H, Me, 3-indolyl.

solvents, in the presence of protic or Lewis acids, mixing equimolecular amounts of bromoindole and indole or pyrrole. The indolinium cation (**1**) is probably the active species leading to the intermediate (**2**) or (**3**) that easily aromatizes to give the final product (**4**) or (**5**), losing hydrogen bromide (Scheme 1).

The dimeric indolyls (**4**) and (**5**) when treated further with 3-bromoindole gave trimeric products. Tetramers and pentamers of *N*-alkylindoles have also been detected. The reaction is catalysed by both protic or Lewis acids; trifluoroacetic acid is superior for indole and pyrrole, and Lewis acids ($SnCl_4$, $TiCl_4$) are better for *N*-substituted indoles. Partially saturated dimers have also been detected as secondary products,[6] together with unusual trimeric products.

Moreover we found that 3-substituted-2,3′-bi-indolyls can be obtained in good yields, under similar conditions, by the reaction of 3-bromoindoles with 3-substituted indoles in the presence of equimolecular amounts of $SnCl_4$. In this way the 2′,3-dimethyl-2,3′-bi-indolyl was obtained from 3-bromo-2-methylindole and skatole in 90% yield. We can therefore consider the following method general for the synthesis of 2,3′-bi-indolyls: trifluoroacetic acid (0.2 mmol) was added to a solution of 3-bromoindole (1 mmol) and indole (1 mmol) in dry methylene dichloride (10 ml), and the mixture stirred at room temperature for 20 min. The mixture was then made basic with aqueous ammonia and evaporated to dryness. The 2,3′-bi-indolyl was recovered with ethyl acetate and purified by column chromatography on silica gel with hexane–ethyl acetate (8:2, v/v) as eluant: yield 85%, m.p. 203—205 °C.

This research was supported by M.P.I. (Ministero della Pubblica Istruzione).

Received, 6th June 1983; Com. 731

References

1 J. Bergman and N. Eklund, *Tetrahedron*, 1980, 1439.
2 I. Saito, T. Morii, S. Matsugo, and T. Matsuura, *J. Chem. Soc., Chem. Commun.*, 1982, 977.
3 J. Bergman, *J. Heterocycl. Chem.*, 1973, **10**, 121.
4 M. Kunori, *Nippon Kagaku Zasshi*, 1962, **83**, 836; *Chem. Abstr.*, 1963, **59**, 1573c; M. Kunori, *Nippon Kagaku Zasshi*, 1962, **83**, 839; *Chem. Abstr.*, 1963, **59**, 1573e.
5 V. Bocchi and G. Palla, *Synthesis*, 1982, 1096.
6 W. A. Remers in 'Indoles, I,' ed. W. J. Haulihan, Wiley Interscience, New York, 1972, p. 66.
7 J. Bergman and N. Eklund, *Tetrahedron*, 1980, 1445.