Arynic Synthesis of Substituted Indoles

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Summary Halogenoanils are converted into indoles in good yields by arynic reactions.

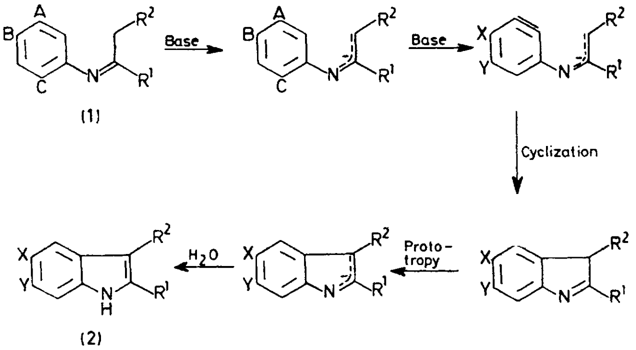
Within the framework of our studies on arynic reactions in aprotic solvent,[1] a part of our programme is devoted to synthesis of heterocyclic compounds.[2] We report a new method of synthesis of indoles by arynic cyclization[3,4] (Scheme and Table).

Table

Run	A	B	C	R¹	R²	X	Y	(2) %[a]	m.p. (°C)	Ref.
1	Br	H	H	Ph	H	H	H	72	188—189	5
2	Cl	Cl	H	Ph	H	Cl	H	57	198	6
3	OMe	H	Cl	Ph	H	H	OMe	61	176	[b]
4	Br	H	H	$-[CH_2]_4-$		H	H	70	119·5	5
5	Cl	Cl	H	$-[CH_2]_4-$		Cl	H	45	147	7

[a] Yields given after isolation of (**2**) by chromatography on silica.
[b] New product.

The halogenoanils (**1**) are readily obtained from the corresponding halogenoanilines[8] and ketones.[9] Except run **3** (Table) all the runs were carried out for 24 h at room temperature in tetrahydrofuran (THF) with $NaNH_2$–Bu^tONa[1] as enolization and elimination reagent. Run **3** was carried out in hexamethylphosphoramide–THF (1 : 4) mixture for 72 h at 60 °C. In this case, a S_NAr mechanism could be applicable. The presence of the aromatic ring on the nitrogen atom of the anils (**1**) and strong basic media explain the enolization, usually difficult in the case of imines.[10]



Scheme

Most of the isolated indoles have been reported previously (Table). Analytical and spectral data of all products compared well with the reported values.[5] The importance of this reaction is in its good selectivity hardly achieved by classical methods.[11]

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