# Synthesis of Unsymmetrically Substituted 6,12-Diaryldibenzo[*b*,*f*][1,5]diazocines and Their Precursor Schiff Bases

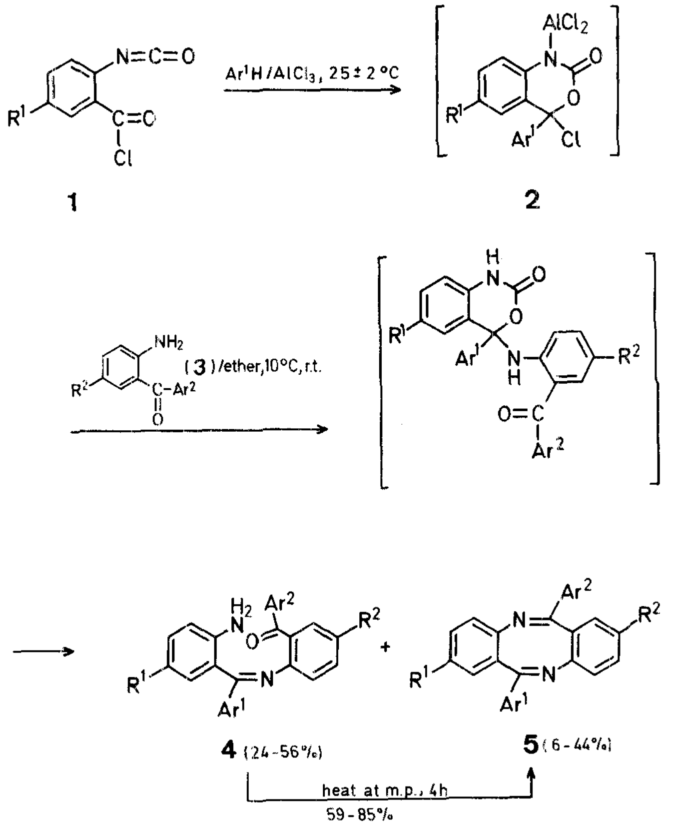
Baman P. Acharya, Y. Ramachandra Rao*

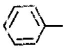
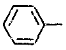
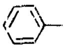
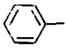
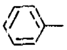
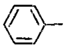
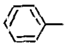
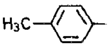
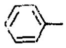
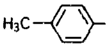
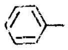
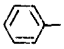
Regional Research Laboratory, Bhubaneswar-751 013, India

A new route for the preparation of some unsymmetrically substituted 6,12-diaryldibenzo[*b*,*f*][1,5]diazocines **5** and their precursor Schiff bases **4** from 2-isocyanatobenzoyl chloride and its 5-chloro derivative are described.

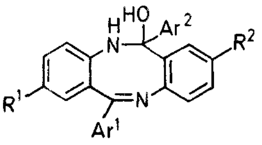
6,12-Diaryldibenzo[*b*,*f*][1,5]diazocines **(5)** are known to possess antigonadotropic, hypotensive, blood cholesterol-lowering, and estrogenic activities[1]. They are obtained by the self-condensation of 2-aminophenylarylmethanones[1,2], photoirradiation of 2,1-benzisothiazoles[3], dimerisation of ring contracted benzazetes[4], and by reacting 3-aryl-2,1-benzoxazoles with Lawesson reagent[5]. All these methods afford symmetrically substituted dibenzodiazocines only. We now report a new route from 2-isocyanatobenzoyl chlorides **(1)** that affords a facile method for their preparation and also of unsymmetrically substituted 6,12-diaryldibenzo[*b*,*f*][1,5]diazocines not reported so far.

Friedel-Crafts acylation of some arenes with 2-isocyanatobenzoyl chloride **(1)** has been reported[6] to give symmetrically substituted **5** as minor products. Their formation was postulated in acid medium by the action of 2-aminophenylarylmethanones **(3)** on the cyclic intermediate complex **2** during decomposition with water. However, the Friedel-Crafts acylation complex obtained with **1** ($R^1$ = H) and benzene, when reacted with **3** ($R^2$ = H), gave only 20% of **5a**. Understandably, this is due to the decreased nucleophilicity of the added 2-aminobenzophenone in the presence of aluminium chloride. Addition of ether prior to that of **3** removed the Lewis acid and the reaction proceeded smoothly to afford the new Schiff bases **4** and the dibenzodiazocines **5**. The latter were also obtained by pyrolysis of **4**.

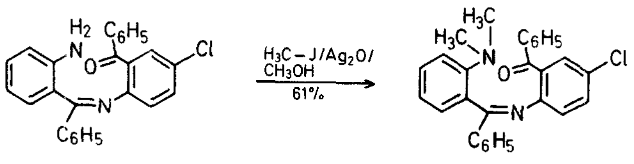


| **4,5** | $R^1$ | $R^2$ | $Ar^1$ | $Ar^2$ |
|---|---|---|---|---|
| **a** | H | H |  |  |
| **b** | H | Cl |  |  |
| **c** | Cl | H |  |  |
| **d** | H | H |  |  H3C |
| **e** | Cl | H |  |  H3C |
| **f** | Cl | Cl |  |  |

The Schiff bases 4 were quite labile and underwent facile hydrolysis at room temperature in 95% methanol containing a trace of mineral acid to the corresponding 2-aminophenylarylmethanones 3. The hydrolysis took place even on silica gel and the compounds could be isolated by short path column chromatography over basic alumina. Because of their absorption in the infrared spectra at 3450 and 3350$^{-1}$, with the former twice as intense as the latter, we suspected these compounds to be the isomers 6. However, methylation of **4b** in methanol with methyl iodide and silver oxide gave only the *N*,*N*-dimethyl derivative 7, confirming the assigned structure. All the spectral data of the Schiff's bases and the dibenzodiazocines are in accordance with their structures (Table).

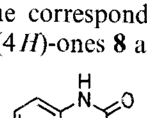


**6**



**4b** **7**

Other compounds isolated from the reaction mixture were the corresponding 4,4-diaryl-1,2-dihydro-3,1-benzoxazine-2(4*H*)-ones **8** and 2-aminophenylarylmethanones **3**.



**8**

2-Isocyanatobenzoyl chloride (**1**; $R^1$ = H) was prepared from isatoic anhydride[7]. Its 5-chloro derivative was obtained by chlorination[8] of **1** ($R^1$ = H) in dichloroethane. 2-Aminophenylarylmethanones **3** were obtained[9] by Friedel-Crafts acylation of appropriate aromatic substrates with **1** ($R^1$ = H or Cl).

**6,12-Diaryldibenzo[*b*,*f*][1,5]diazocines 5; General Procedure:**
To a stirred suspension of aluminium chloride (3.95 g, 0.03 mol) in benzene (30 ml) is added during 15 min a solution of **1** (0.01 mol), while maintaining the temperature at 25 ± 2 °C. After an additional 45 min stirring to ensure complete formation of the complex, the mixture is cooled to 9–10 °C, dry ether (4 ml) in benzene (20 ml) is added dropwise over 10 min and the mixture stirred at this temperature for 10 min. To the resulting clear solution, is then added the desired 2-aminophenylarylmethanone **3** (0.01 mol) and the stirring is continued at room temperature for 3 h. The mixture is poured into ice-cold water (250 ml), the organic layer separated and the aqueous phase extracted with benzene (2 × 50 ml). The combined organic phase is washed with water (2 × 100 ml), dried with magnesium sulfate, and concentrated in vacuo to a small volume. The residue is then applied to a column of basic alumina and eluted successively with hexane/benzene mixtures (1:1, 1:3) and benzene and compounds **5**, **3**, and **4** are isolated respectively in the order of elution. Compound is **8** eluted out with benzene/ethyl acetate (19:1). All the compounds are further purified by recrystallisation from methanol and are homogeneous by T.L.C. (Table).

Pyrolysis of Schiff Bases 4; General Procedure:
The Schiff base **4** (100 mg) is pyrolysed at its melting point under vacuo for 4 h. The residue obtained on cooling is crystallised from methanol, except **5b** (90% aqueous methanol) (Table).

**Methylation of 4b:**
To a stirred suspension of the Schiff base **4b** (250 mg, 0.6 mmol) and silver oxide (1.0 g) in methanol (25 ml) at room temperature is added methyl iodide (0.5 g, 3.5 mmol) in methanol (10 ml) over 5 min. The stirring is continued and the progress of the reaction is followed by T.L.C. After 24 h, the mixture is filtered, the filtrate concentrated, and chromatographed on basic alumina. The dimethyl derivative **7** is separated from unreacted **4b** and purified by crystallisation from methanol; yield: 160 mg, (61%); m.p. 92 °C.

**Table.** 6,12-Diaryldibenzo[*b*,*f*][1,5]diazocines **4** and their Precursor Schiff Bases **5** prepared

| Product No. | Yield[a] [%] | m.p.[b] [°C] | Molecular Formula[c] or Lit. m.p. [°C] | I.R. (Nujol)[d] $\nu$ [cm$^{-1}$] | $^1$H-N.M.R. (CDCl$_3$/TMS)[e] $\delta$ [ppm] | M.S.[f] $m/e$ (M$^+$) |
|---|---|---|---|---|---|---|
| **4a** | 24 | 119° | $C_{26}H_{20}N_2O$ (376.5) | 3450, 3350, 1650, 1610 | 5.66–6.1 (br. s, 2H); 6.33–7.7 (m, 18H$_{arom}$) | 376 |
| **4b** | 56 | 155° | $C_{26}H_{19}ClN_2O$ (410.9) | 3445, 3250, 1655, 1605 | 5.6–6.1 (br. s, 2H); 6.2–7.8 (m, 17H$_{arom}$) | 410, 412 (M$^+$ + 2) |
| **4c** | 42 | 61° | $C_{26}H_{19}ClN_2O$ (410.9) | 3450, 3355, 1645, 1600 | 6.0–6.3 (br. s, 2H); 6.55–7.7 (m, 17H$_{arom}$) | 410, 412 (M$^+$ + 2) |
| **4d** | 33 | 143° | $C_{27}H_{22}N_2O$ (390.5) | 3460, 3340, 1625, 1600 | 2.34 (s, 3H, CH$_3$); 6.2 (br. s, 2H); 6.44–7.8 (m, 17H$_{arom}$) | 390 |
| **4e** | 33 | 118° | $C_{27}H_{21}ClN_2O$ (424.9) | 3440, 3345, 1635, 1610 | 2.4 (s, 3H, CH$_3$); 6.4 (br. s, 2H); 6.6–8.0 (m, 16H$_{arom}$) | 424, 426 (M$^+$ + 2) |
| **5a** | 44 (85) | 188° | 186°[6] | 1615, 1590 | – | – |
| **5b** | 27 (66) | 162° | $C_{26}H_{17}ClN_2$ (392.9) | 1615, 1585 | – | – |
| **5c** | 9 (74) | 162° | $C_{26}H_{17}ClN_2$ (392.9) | 1615, 1585 | – | 392, 394 (M$^+$ + 2) |
| **5d** | 6 (59) | 165° | $C_{27}H_{20}N_2$ (372.5) | 1615, 1595 | – | – |
| **5f** | 31 | 216° | 214°[10] | 1610, 1565 | – | – |

[a] Yields given are after crystallisation. The yield of **5** obtained from pyrolysis of **4** is given in parenthesis.
[b] Melting points are not corrected.
[c] Satisfactory microanalyses obtained C ±0.4, H ±0.12, N ±0.25.
[d] Recorded on Perkin Elmer 297 spectrometer.
[e] Recorded on Varian EM 390 spectrometer.
[f] Recorded on AEI-MS 3074 spectrometer.

| | | | | |
|---|---|---|---|---|
| $C_{28}H_{23}ClN_2O$ | calc. | C 76.59 | H 5.28 | N 6.38 |
| (438.7) | found | 76.72 | 5.24 | 6.25 |

I.R. (Nujol): $\nu$ = 1650, 1602 cm$^{-1}$.

$^1$H-N.M.R. (CDCl$_3$/TMS): $\delta$ = 2.4 (s, 6H, 2 CH$_3$); 6.55–7.77 ppm (m, 17 H$_{arom}$).

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[1] Wakankar, D.M., Hosangadi, B.D. *Indian J. Chem.* **1980**, *19B*, 703 and references cited therein.

[2] Misra, B.K. *Ph. D. Thesis*, Utkal University, Bhubaneswar, 1981.

[3] Ohashi, M., Ezaki, A., Yonezawa, T. *J. Chem. Soc. Chem. Commun.* **1974**, 617.

[4] Rees, C.W., Storr, R.C., Whittle, P.J. *J. Chem. Soc. Chem. Commun.* **1976**, 411.

[5] Konwar, D., Barua, R.C., Sandhu, J.S., Barua, J.N. *Indian J. Chem.* **1982**, *21B*, 899.

[6] Misra, B.K., Rao, Y.R., Mahapatra, S.N. *Indian J. Chem.* **1983**, *22B*, 1132.

[7] Iwakura, Y., Uno, K., Kang, S. *J. Org. Chem.* **1966**, *31*, 142.

[8] Misra, B.K., Rao, Y.R., Mahapatra, S.N. *Org. Prep. Proced. Int.* **1981**, *13*, 363.

[9] Misra, B.K., Rao, Y.R., Mahapatra, S.N. *Indian J. Chem.* **1979**, *18B*, 19.

[10] Sternbach, L.H., Frier, R.I., Metlesics, W., Sach, G., Stempal, E. *J. Org. Chem.* **1962**, *27*, 3781.