Preparation of Hexa-, Penta- and Tetraphenyl-2,6- and -2,7-naphthyridines

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Received December 23, 1982

Di- and triphenyldibenzoylpyridines (**1**) were prepared by the condensation reaction of 3,4-dibenzoyl-2,5-diphenylthiophene (**2**) with methylamine derivatives **3** and by the subsequent oxidative ring cleavage of the resultant thieno[3,4-*c*]pyridines **4**. The reaction of **1** with **3** afforded polyphenyl-2,6- (**5**) and -2,7-naphthyridines (**6**).

J. Heterocyclic Chem., **20**, 971 (1983).

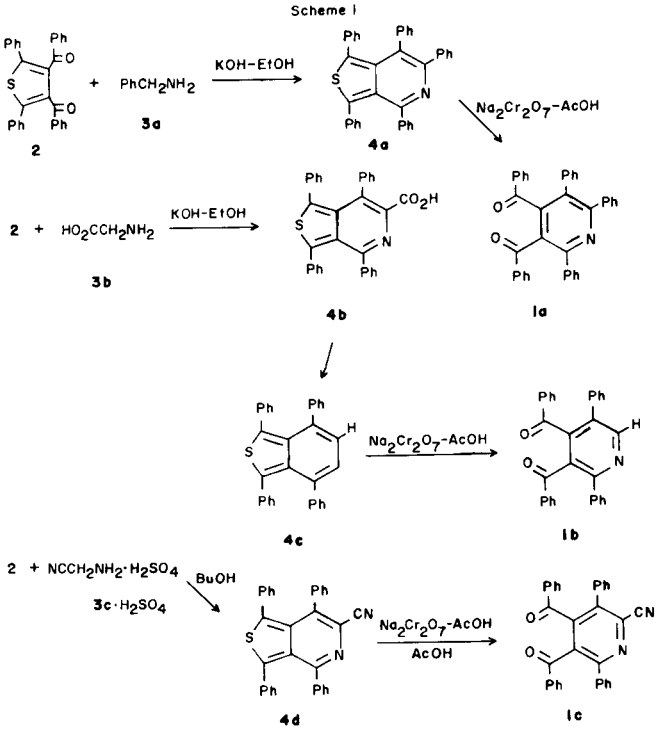
Recently, we have reported (1-3) the condensation reaction of vicinally diaroyl-substituted five-membered heterocycles with methylamines, giving a variety of pyridine-fused heterocyclic compounds. Condensation of *o*-dibenzoylbenzene affording 1,4-diphenylisoquinolines was also reported by the authors (4). As a continuation of the above, we now report the preparation of hexa-, penta- and tetraphenyl-2,6- and -2,7-naphthyridines by the reaction of dibenzoylpyridines with methylamines.

Results and Discussion.

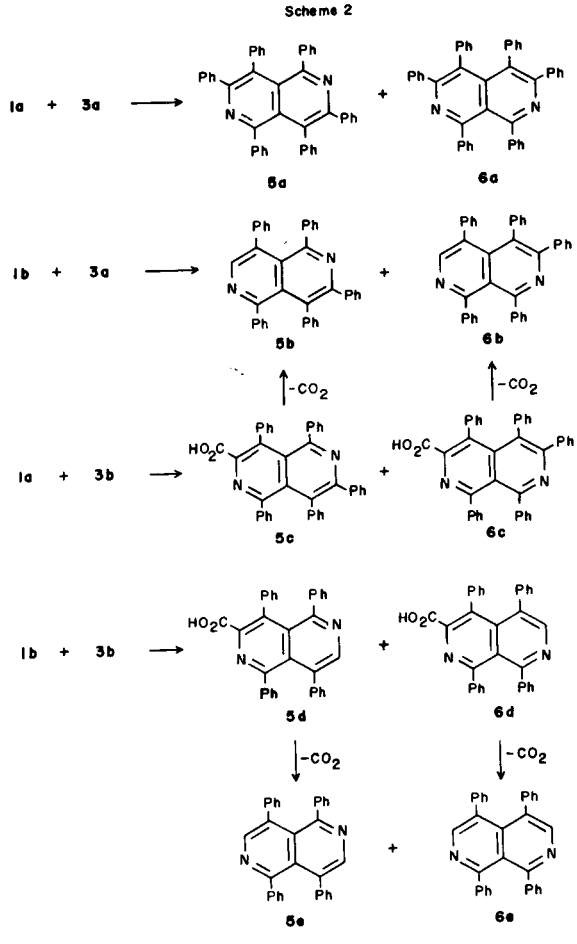
Dibenzoylpyridines **1** were prepared according to Scheme 1. Dibenzoylthiophene (**2**) (5) reacted with **3a** and **3b** in refluxing ethanolic potassium hydroxide to give corresponding thieno[3,4-*c*]pyridines, **4a** and **4b**, in 87 and 81% yields, respectively. Compound **4b** was decarboxylated at 240° to give **4c** in 86% yield. Condensation reaction of **2** with **3c** sulfate was carried out in refluxing butanol because of the lability of the free **3c**. The expected **4d** was obtained in only a poor yield and **2** was recovered in 77% yield. The oxidative cleavage of the thiophene ring of **4a** and **4c** by sodium dichromate in acetic acid afforded the desired dibenzoylpyridines, **1a** and **1b**, in 80 and 88% yields, respectively. Thiophene-ring cleavage of **4d** also gave the desired **1c** in a satisfactory yield, however, as mentioned above, reaction of **2** with **3c** sulfate afforded **4d** in only discouraging yield and the reaction of **1c** with **3c** was not investigated.

Condensation reaction of **1a** and **1b** with **3** was carried

Scheme 1



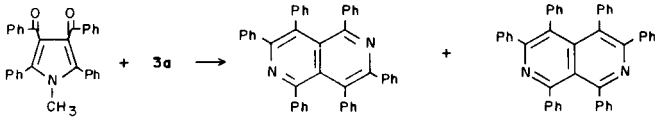
Scheme 2



out and the results are summarized in Scheme 2 and Table. In the reaction of **1a** or **1b** with **3a**, the expected naphthyridines, **5a** and **6a**, or **5b** and **6b**, were obtained. Formation of 2,7-naphthylidines was favored in reactions with **3a**. Reaction of **1a** or **1b** with **3b** afforded a mixture of the corresponding naphthyridinecarboxylic acid, **5c** and **6c**, or **5d** and **6d**. As the separation of the naphthyridine carboxylic acid was unsuccessful, the mixture was subjected to decarboxylation at 240°, affording a mixture of the corresponding naphthyridines (**5b** and **6b**, and **5e** and **6e**). Pure samples of **5** and **6** were obtained by chromatography. Contrary to the condensation reaction with **3a**, 2,6- and 2,7-naphthyridines were formed in almost equal amounts in the reaction with **3b**. The reason is unknown.

Structural assignment of the above obtained hexa-**5a** and **6a**, penta-**5b** and **6b** and tetraphenylnaphthyridines **5e** and **6e** was done on the basis of analysis and spectral data. As shown in the Figure, electronic spectra of **5b**, **5e**, **6b** and **6e** are in a good agreement with the reported those (7) of the parent 2,6- and 2,7-naphthyridines. Although the shape of the spectra of two hexaphenylnaphthyridines **5a** and **6a** are alike, we assigned the one **5a**, having absorption maximum at longer wave length as 2,6-naphthyridine and the other, **6a**, as 2,7-naphthyridine.

Previously, we reported (3) that the reaction of 3,4-dibenzoyl-1-methyl-2,5-diphenylpyrrole (**7**) with **3c** gave 6-cyano-2-methyl-1,3,4,7-tetraphenylpyrrolo[3,4-*c*]pyridine in 62% yield, while the reaction with **3a** did not give the corresponding pyrrolo[3,4-*c*]pyridine under strongly basic conditions (in the presence of DBU in refluxing toluene or potassium *t*-butoxide in refluxing *t*-butyl alcohol). Recently, we re-investigated the reaction of **7** with **3a** without solvent at 140-150° in the presence of DBU for 96 hours, and interestingly, found the formation of a 2:1 mixture of **5a** and **6a** instead of the expected pyrrolo[3,4-*c*]pyridine. The pathway of the formation of naphthyridines **5a** and **6a** in the above reaction is obscure.



7 **5a** **6a**

Table

Preparation of Naphthylidines

Pyridine	Methylamine	2,6-Naphthylidine (Yield)	2,7-Naphthylidine (Yield)
1a	**3a**	**5a** (29%)	**6a** (41%)
	3b	**5b** (30%)	**6b** (30%)
1b	**3a**	**5b** (21%)	**6b** (55%)
	3b	**5c** (33%)	**6c** (29%)

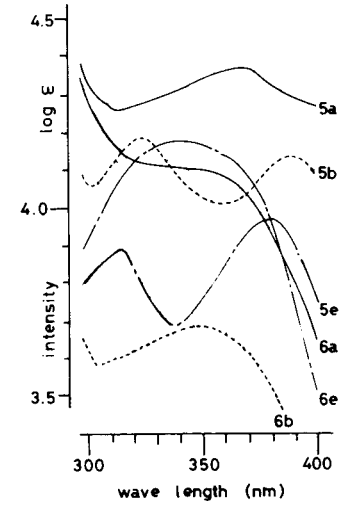


Figure. Electronic spectra of 2,6- **5** and 2,7-naphthylidines **6**.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra were measured on a Nippon Bunko A-102 spectrophotometer as potassium bromide pellets. The ^{1}H-nmr determined at 100 MHz on a Nippon Denshi JEOL FT-100 in deuteriochloroform using TMS as an internal standard. Mass spectra were obtained on a Nippon Denshi JMS-OISG-2 mass spectrometer at 75 eV using a direct inlet system. Electronic spectra were measured on a Shimazu UV-240 in chloroform.

Reaction of **2** with **3a**.

A mixture of **2** (2.00 g) and **3a** (4 ml) in 10% ethanolic potassium hydroxide (50 ml) was refluxed for one hour and poured into 1*N*-hydrochloric acid (200 ml). Precipitates were collected by filtration to give 2.02 g of **4a** (87%).

1,3,4,6,7-Pentaphenylthieno[3,4-*c*]pyridine (**4a**).

This compound was obtained as yellow needles (ethanol), mp 247-249°; ms: m/e (relative intensity) 515 (100), 429 (22), 121 (4), 77 (4).

Anal. Calcd. for $C_{37}H_{25}NS$: C, 86.18; H, 4.89; N, 2.72. Found: C, 85.88; H, 4.93; N, 2.67.

Reaction of **2** with **3b**.

A mixture of **2** (1.00 g) and **3b** (3.00 g) in 10% ethanolic potassium hydroxide (50 ml) was refluxed for one hour, poured into 1*N* hydrochloric acid (200 ml) and extracted with benzene (70 ml × 2). Benzene-extract was dried over sodium sulfate and evaporated *in vacuo* to leave the residue which was column chromatographed on silica gel (Wako C-300) using benzene as an eluent to give 0.88 g of **4b** (81%).

1,3,4,7-Tetraphenylthieno[3,4-*c*]pyridine-6-carboxylic Acid (**4b**).

This compound was obtained as yellow prisms (a 1:1-mixture of hexane and benzene), mp 212-213°; ir: ν CO 1760, 1720 cm^{-1}; ms: m/e (relative intensity) 483 (21), 439 (100), 406 (47).

Anal. Calcd. for $C_{32}H_{21}NO_2S$: C, 79.41; H, 4.38; N, 2.90. Found: C, 79.81; H, 4.83; N, 3.25.

Decarboxylation of **4b**.

Carboxylic acid **4b** (200 mg) was heated at 240° in silicone bath for 20 minutes and recrystallized from a 2:1 mixture of benzene and hexane to give 157 mg of **4c** (86%).

1,3,4,7-Tetraphenylthieno[3,4-*c*]pyridine (**4c**).

This compounds was obtained as pale green needles, mp 278-279°; ms:

m/e (relative intensity) 439 (100), 406 (14).

Anal. Calcd. for $C_{31}H_{21}NS$: C, 84.70; H, 4.82; N, 3.19. Found: C, 84.40; H, 4.82; N, 3.19.

Reaction of **2** with **3c** Sulfate.

A mixture of **2** (500 mg) and **3c** sulfate (1 g) in butanol (30 ml) was refluxed for 40 hours and evaporated *in vacuo* to leave the residue which was column chromatographed on silica gel (Wako C-300). Unreacted **2** (385 mg) was eluted with a 1:2 mixture of hexane and benzene, and 16 mg of **4d** (3%) was eluted with benzene.

6-Cyano-1,3,4,7-tetraphenylthieno[3,4-*c*]pyridine (**4d**).

This compound was obtained as pale green needles (hexane), mp 238-239°; ir: ν CN 2230 cm^{-1}; ms: m/e (relative intensity) 464 (100), 77 (5).

Anal. Calcd. for $C_{32}H_{20}N_2S$: C, 82.72; H, 4.34; N, 6.03. Found: C, 82.39; H, 4.32; N, 6.01.

Oxidation of **4a**.

A mixture of **4a** (300 mg) and sodium dichromate (500 mg) in acetic acid (10 ml) was refluxed for one hour and poured into water (100 ml) to give 241 mg of **1a** (80%).

3,4-Dibenzoyl-2,5,6-triphenylpyridine (**1a**).

This compound was obtained as pale yellow particles (hexane) mp 190-192°; ir: ν CO 1670, 1655 cm^{-1}; ms: m/e (relative intensity) 515 (43), 105 (100), 77 (84).

Anal. Calcd. for $C_{37}H_{25}NO_2$: C, 86.19; H, 4.89; N, 2.72. Found: C, 86.24; H, 4.96; N, 2.74.

Oxidation of **4c**.

A mixture of **4c** (480 mg) and sodium dichromate (500 mg) in acetic acid (30 ml) was refluxed for 30 minutes and treated as described above to afford 420 mg of **1b** (88%).

3,4-Dibenzoyl-2,5-diphenylpyridine (**1b**).

This compound was obtained as colorless plates (hexane), mp 169-170°; ir: ν CO 1650 cm^{-1}; ms: m/e (relative intensity) 439 (18), 334 (15), 202 (25), 105 (71), 77 (100).

Anal. Calcd. for $C_{31}H_{21}NO_2$: C, 84.72; H, 4.82; N, 3.19. Found: C, 84.57; H, 4.84; N, 3.14.

Oxidation of **4d**.

A mixture of **4d** (15 mg) and sodium dichromate (20 mg) in acetic acid (30 ml) was refluxed for 30 minutes and treated as described above to give 11 mg of **1c** (73%).

2-Cyano-4,5-dibenzoyl-3,6-diphenylpyridine (**1c**).

This compound was obtained as pale yellow prisms (hexane), mp 222-223°; ir: ν CN 2250, ν CO 1665 cm^{-1}; ms: m/e (relative intensity) 464 (100), 387 (33).

Anal. Calcd. for $C_{32}H_{20}N_2O_2$: C, 82.74; H, 4.34; N, 6.03. Found: C, 82.56; H, 4.35; N, 5.96.

Preparation of Hexaphenylnaphthylidines **5a** and **6a**.

After a mixture of **1a** (100 mg) and **3a** (500 mg) in 10% ethanolic potassium hydroxide (30 ml) was refluxed for 2 hours, it was poured into a large excess of water and extracted with benzene (50 ml × 2). Benzene-extract was dried over sodium sulfate and evaporated *in vacuo* to leave the residue which was column chromatographed on silica gel using benzene as an eluent. The benzene eluent was condensed to 1.5 ml and column chromatographed on C.I.G. prepacked column (silica gel, CPS-153, Kusano Scientific Co.) using benzene and chloroform as eluents to give **5a** (33 mg) and **6a** (46 mg).

1,3,4,5,7,8-Hexaphenyl-2,6-naphthyridine (**5a**).

This compound was obtained as pale green needles (hexane-benzene 10:1), mp 287-288°; ms: m/e (relative intensity) 586 (M^+, 100), 509 (10). ^1H nmr: δ 6.68-7.62 (m, 30H).

Anal. Calcd. for $C_{44}H_{30}N_2$: C, 90.07; H, 5.15; N, 4.77. Found: C, 89.90; H, 5.20; N, 4.78.

1,3,4,5,6,8-Hexaphenyl-2,7-naphthyridine (**6a**).

This compound was obtained as somewhat green needles (hexane-benzene 10:1), mp 321-322°; ms: m/e (relative intensity) 586 (M^+, 100), 509 (53); ^1H nmr: δ 6.72 (s, 10H), 7.01-7.17 (m, 12H), 7.20-7.35 (m, 4H), 7.48-7.61 (m, 4H).

Anal. Calcd. for $C_{44}H_{30}N_2$: C, 90.07; H, 5.15; N, 4.77. Found: C, 90.19; H, 5.26; N, 4.65.

Preparation of Pentaphenylnaphthylidines **5b** and **6b**.

(i) By the Reaction of **1b** With **3a**.

A mixture of **1b** (100 mg) and **3a** (500 mg) in 10% ethanolic potassium hydroxide (30 ml) was refluxed for 2 hours and treated as described above to give **5b** (24 mg) and **6b** (65 mg).

1,3,4,5,8-Pentaphenyl-2,6-naphthyridine (**5b**).

This compound was obtained as pale green needles (hexane), mp 262°; ms: m/e (relative intensity) 510 (M^+, 100), 509 (M^+-H, 37); ^1H nmr: δ 6.72-7.50 (m, 25H), 8.59 (s, 1H).

Anal. Calcd. for $C_{38}H_{26}N_2$: C, 89.38; H, 5.13; N, 5.49. Found: C, 88.94; H, 5.28; N, 5.53.

1,3,4,5,8-Pentaphenyl-2,7-naphthyridine (**6b**).

This compound was obtained as somewhat green prisms (hexane), mp 221-222°; ms: m/e (relative intensity) 510 (M^+, 100). 509 (M^+-H, 61); ^1H nmr: δ 6.79 (s, 5H), 6.93 (s, 5H), 6.98-7.18 (m, 9H), 7.26-7.54 (m, 6H), 8.52 (s, 1H).

Anal. Calcd. for $C_{38}H_{26}N_2$: c, 89.38; H, 5.13; N, 5.49. Found: C, 89.26; H, 5.13; N, 5.56.

(ii) By the Reaction of **1a** With **3b** and the Subsequent Decarboxylation.

After a mixture of **1a** (100 mg) and **3b** (500 mg) in 10% ethanolic potassium hydroxide (30 ml) was heated at reflux for 2 hours, it was poured into a large excess of water. White precipitates formed were filtered and heated at 270° for 20 minutes. Compounds **5b** (30 mg) and **6b** (30 mg) were isolated as described above.

Preparation of Tetraphenylnaphthylidines **5c** and **6c**.

Compounds **5c** (33 mg) and **6c** (29 mg) were obtained from starting **1b** (100 mg) and **3b** (500 mg) by the procedure described above.

1,4,5,8-Tetraphenyl-2,6-naphthyridine (**5e**).

This compound was obtained as pale yellow needles (hexane), mp 285-286°; ms: m/e (relative intensity) 434 (M^+, 100), 433 (M^+-1, 30), 330 (M^+-PhCNH, 18); ^1H nmr: δ 6.97-7.12 (m, 16H), 7.18-7.23 (m, 4H), 8.64 (s, 2H).

Anal. Calcd. for $C_{32}H_{22}N_2$: C, 88.45; H, 5.10; N, 6.45. Found: C, 88.02; H, 5.12; N, 6.43.

1,4,5,8-Tetraphenyl-2,7-naphthyridine (**6e**).

This compound was obtained as pale yellow needles; ms: m/e (relative intensity) 434 (M^+, 100), 433 (M^+-1, 42), 357 (M^+-Ph, 16), 330 (M^+-PhCNH, 10); ^1H nmr: δ 6.95-7.13 (m, 16H), 7.32-7.46 (m, 4H), 8.63 (s, 2H).

Anal. Calcd. for $C_{32}H_{22}N_2$: C, 88.45; H, 5.10; N, 6.45. Found: C, 88.20; H, 5.17; N, 6.42.

Reaction of **7** With **3a** in the Presence of DBU.

After **7** (100 ml) was heated in **3a** (7 mg) and DBU (1 ml) at 140-150° for 4 days, it was poured into an excess of 1*N* hydrochloric acid and extracted with benzene. Benzene extract was dried over sodium sulfate and evaporated *in vacuo* to give a 2:1 mixture (68 mg) of **5a** and **6a**.

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