A new approach to functionalized naphthyridines: synthesis of 5-cyano-2,7-naphthyridin-1-one derivatives from ethyl acetoacetate and benzoylacetonitrile

V. A. Dorokhov, A. Yu. Yagodkin, V. S. Bogdanov, and S. V. Baranin*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: 007 (095) 135 5328. E-mail: vador@ioc.ac.ru

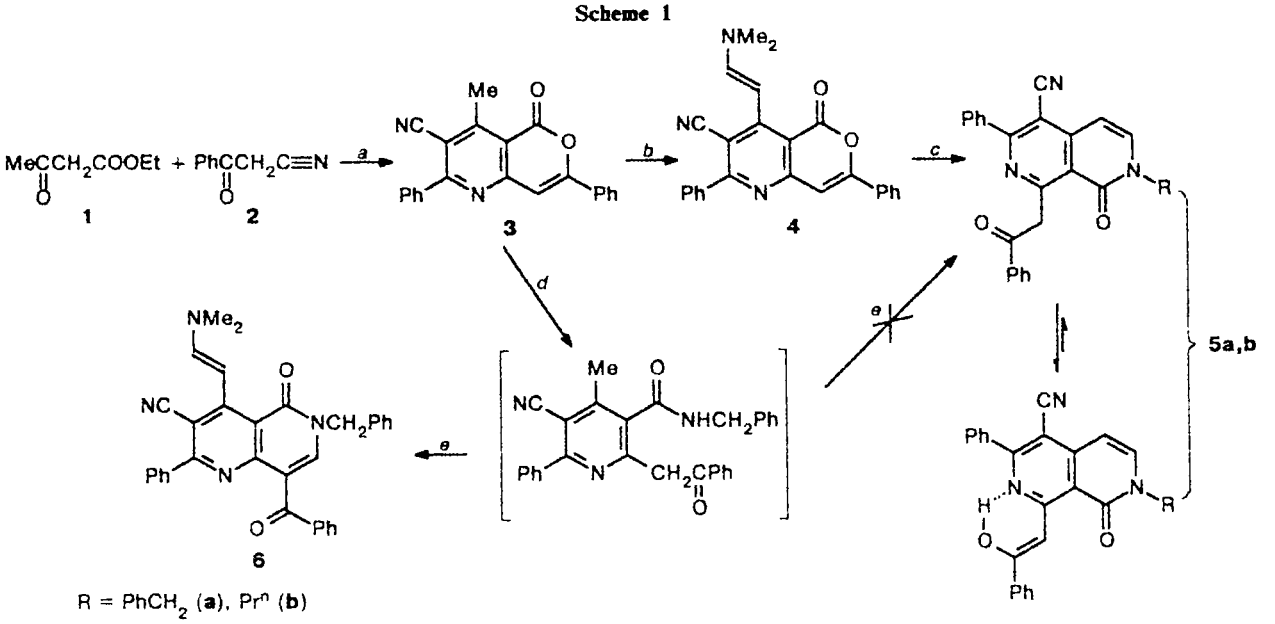
Recently[1] we found that ethyl acetoacetate (**1**) reacts with benzoylacetonitrile (**2**) in the presence of a catalytic amount of nickel acetylacetonate to give substituted 3-cyanopyrano[4,3-*b*]pyridin-5-one (**3**). Based on this reaction, we developed a new scheme for building the 2,7-naphthyridine system: condensation of compound **3** with dimethylformamide dimethyl acetal (DMF DMA) gave enamine **4**; when the latter is treated with primary amines, it undergoes recyclization to yield 2-alkyl-5-cyano-8-phenacyl-6-phenyl-2,7-naphthyridin-1-ones **5a,b** (Scheme 1). According to the data of ^{1}H NMR spectroscopy (in $CDCl_3$), the phenacyl group exists by more than 90% in the enol form stabilized by the formation of the intramolecular O—H...N hydrogen bond.

If the order in which the reagents are added to pyranopyridine **3** is changed, *i.e.*, if it is first treated with benzylamine and then introduced in the condensation with DMF DMA, a representative of 1,6-naphthyridines, carbonitrile **6**, is formed instead of 2,7-naphthyridine **5a**. Compound **6**, whose structure has been proved by X-ray diffraction analysis,* is formed with participation of 2 equivalents of DMF DMA.

3-Cyano-4-(2-dimethylaminovinyl)-2,7-diphenylpyrano-[4,3-*b*]pyridin-5-one (4). A mixture of compound **3** (0.4 g, 1.2 mmol) and DMF DMA (0.3 g, 2.5 mmol) in 5 mL of *o*-xylene was refluxed for 4 h. The precipitate formed was filtered off, washed with MeOH (2×5 mL), and dried in air for 12 h to give 0.3 g (65%) of enamine **4**, m.p. 238—239 °C. MS (EI, 70 eV), *m/z*: 393 $[M]^+$. IR (KBr), ν/cm^{-1}: 2205 (C≡N);

* The X-ray diffraction analysis was carried out by O. V. Shishkin (A. N. Nesmeyanov Institute of Organoelement Compounds of the RAS).

Scheme 1



Reagents and conditions: *a*. See Ref. 1; *b*. Xylene, DMF DMA, Δ, 4 h; *c*. Py, RNH_2, Δ, 5 h; *d*. EtOH, $PhCH_2NH_2$, Δ, 5 h; *e*. C_6H_6, DMF DMA, Δ, 20 h.

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 5, pp. 1079—1080, May, 1997.

1066-5285/97/4605-1041 $18.00

1720 (C=O); 1610, 1520. ^{1}H NMR ($CDCl_3$), δ: 3.18 (s, 6 H, Me_2N); 7.00 (d, 1 H, CH=, J = 13.5 Hz); 7.12 (s, 1 H, CH=); 7.50—7.90 (m, 10 H, 2 Ph); 8.30 (d, 1 H, NCH=).

2-Benzyl-5-cyano-8-phenacyl-6-phenyl-2,7-naphthyridin-1-one (5a). A mixture of enamine **4** (0.22 g, 0.5 mmol) and benzylamine (0.20 g, 1.8 mmol) in 3 mL of pyridine was refluxed for 5 h. The precipitate was filtered off, washed with MeOH (5 mL) and ether (2×5 mL), and dried *in vacuo* (10 Torr, 50 °C) to give 0.15 g (50%) of 2,7-naphthyridine **5a**, m.p. 277—278 °C. MS (EI, 70 eV), m/z: 455 $[M]^+$. IR (KBr), ν/cm^{-1}: 2210 (C≡N); 1660, 1612, 1550 (C=C, C=O). ^{1}H NMR ($CDCl_3$), δ: 5.30 (s, 2 H, CH_2); 6.78 (d, 1 H, CH=); 7.40—8.10 (m, 15 H, 3 Ph + 1 H, CH=); 8.53 (s, 1 H, CH=); 16.63 (br.s, 1 H, OH).

5-Cyano-8-phenacyl-6-phenyl-2-propyl-2,7-naphthyridin-1-one (5b) was prepared similarly to compound **5a**. The yield of 2,7-naphthyridine **5b** was 58%, m.p. 258—260 °C. MS (EI, 70 eV), m/z: 407 $[M]^+$. ^{1}H NMR ($CDCl_3$), δ: 1.08 (t, 3 H, Me); 1.88 (m, 2 H, CH_2); 4.00 (t, 2 H, NCH_2); 6.70 (d, 1 H,CH=); 7.49—8.00 (m, 10 H, 2 Ph + 1 H, CH=); 8.46 (s, 1 H, CH=); 16.63 (s, 1 H, OH).

8-Benzoyl-6-benzyl-3-cyano-4-(2-dimethylaminovinyl)-2-phenyl-1,6-naphthyridin-5-one (6). A mixture of compound **3** (0.3 g, 0.88 mmol) and benzylamine (0.5 g, 4.6 mmol) in 3 mL of EtOH was refluxed for 5 h. The precipitate was filtered off, washed with EtOH (3 mL) and ether (2 mL), and dried *in vacuo*. Benzene (5 mL) and DMF DMA (0.2 g, 1.7 mmol) were added, and the mixture was refluxed for 20 h. The precipitate was filtered off, washed with ether (2×5 mL), and dried *in vacuo* (10 Torr, 50 °C) to give 0.2 g (74%) of 1,6-naphthyridine **6**, m.p. 238—239 °C. MS (EI, 70 eV), m/z: 510 $[M]^+$. IR (KBr), ν/cm^{-1}: 2205 (C≡N); 1663, 1630, 1605, 1500 (C=C, C=O). ^{1}H NMR ($CDCl_3$), δ: 3.15 (s, 6 H, Me_2N); 5.23 (s, 2 H, NCH_2); 7.22—7.88 (m, 15 H, 3 Ph + 1 H, CH= + 1 H, CH=); 8.00 (d, 1 H, CH=).

The results of elemental analysis of compounds **4**, **5a,b**, and **6** correspond to the results of calculations.

References

1. V. A. Dorokhov, S. V. Baranin, A. Yu. Yagodkin, V. S. Bogdanov, and Z. K. Dem'yanets, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 2295 [*Russ. Chem. Bull.*, 1995, **44**, 2201 (Engl. Transl.)].

Received February 17, 1997

A new approach to synthesis of 1-aryl-2-nitrozodiazene 1-*N*-oxides

A. M. Churakov, S. E. Semenov, S. L. Ioffe, Yu. A. Strelenko, and V. A. Tartakovsky*

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 47 Leninsky prosp., 117913 Moscow, Russian Federation. Fax: 007 (095) 135 5328. E-mail: churakov@ioc.ac.ru

We recently obtained 1-aryl-2-nitrodiazene 1-oxides (NDO) by nitration of 1-aryl-2-acetyldiazene 1-oxides[1]; however, the imperfection of the method of their synthesis due to thermal and chemical instability of the starting compounds hinders investigation of this new class of compounds.

This publication investigates the possibility of NDO synthesis (Scheme 1) by substitutive nitration of stable 1-aryldiazene 1-oxides **2** that include *tert*-butyl (**2a—c**), *tert*-butoxycarbonyl (**2d**), and carbamoyl (**2e**) groups at the distal N atom.

In nitration with nitronium tetrafluoroborate in MeCN, the best results were obtained for *tert*-butyldiazene oxides **2a—c**; the yields of corresponding NDO **3a—c** were ≥75% (Table 1). Apparently, this reaction proceeds *via* formation of intermediate **5** with subsequent elimination of the *tert*-butyl cation.

Nitrodiazene oxide **3a** is also produced in good yield from carbamoyldiazene oxide **2e**, but the reaction rate in this case is substantially slower. The most easily substituted group is the *tert*-butoxycarbonyl group in

Table 1. Synthesis of 1-aryl-2-nitrodiazene 1-oxides **3a—c** (see Scheme 1)

Reaction	T/°C (t/h)	Yield of product **3** (%)
2a → **3a**	20 (0.7)	91
2b → **3b**	1) −20 (0.5), 2) −20 → +10 (0.2)	81
2c → **3c**	20 (6)	75
2d → **3a**	−20 → +20 (0.2)	45
2e → **3a**	20 (7)	85

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 5, pp. 1081—1082, May, 1997.

1066-5285/97/4605-1042 $18.00