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Studies in Benzonaphthyridines: Synthesis of Benzoimidazonaphthyridines

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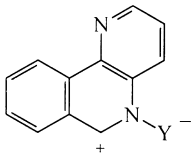
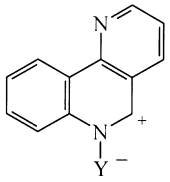
Quaternary salts of azaaromatics have been intensively studied for both theoretical and practical points of view,[1–2] e.g. they are useful in solar energy conversion and storage,[3–8] and therefore the chemistry of *N*-substituted benzonaphthyridines is of interest.

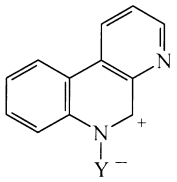
In our former work concerning the properties of quaternary benzonaphthyridinium salts, 1,3-dipolar cycloaddition reactions of benzo[*c*]-1,5-, benzo[*h*]-1,6-, and benzo[*f*]-1,7-naphthyridine phenacylides, ethoxycarbonylmethylides and dichloromethylides (1)–(3) have been investigated.[9–14]



(1a) Y= CHCOPh
(1b) Y= CHCOOEt
(1c) Y= CCl_2

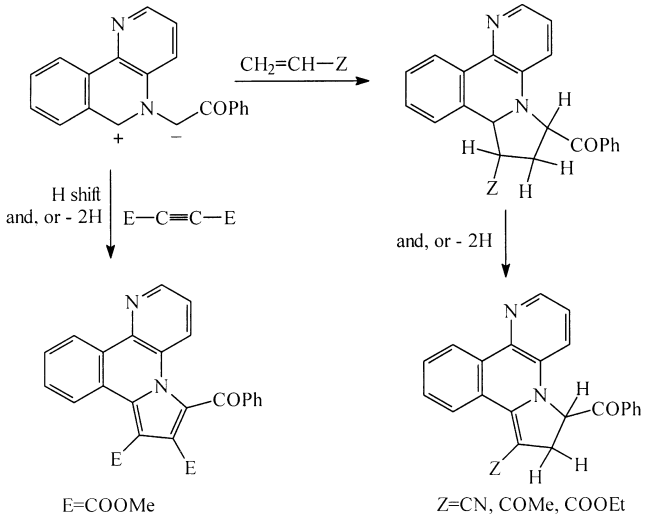


(2a) Y= CHCOPh
(2b) Y= CHCOOEt
(2c) Y= CCl_2



(3a) Y= CHCOPh
(3b) Y= CHCOOEt
(3c) Y= CCl_2

Tetracyclic cycloadducts: substituted benzopyrrolo-, benzopyrroline-, or benzopyrrolidine-naphthyridines, resulted from our synthetic work (see Scheme 1).



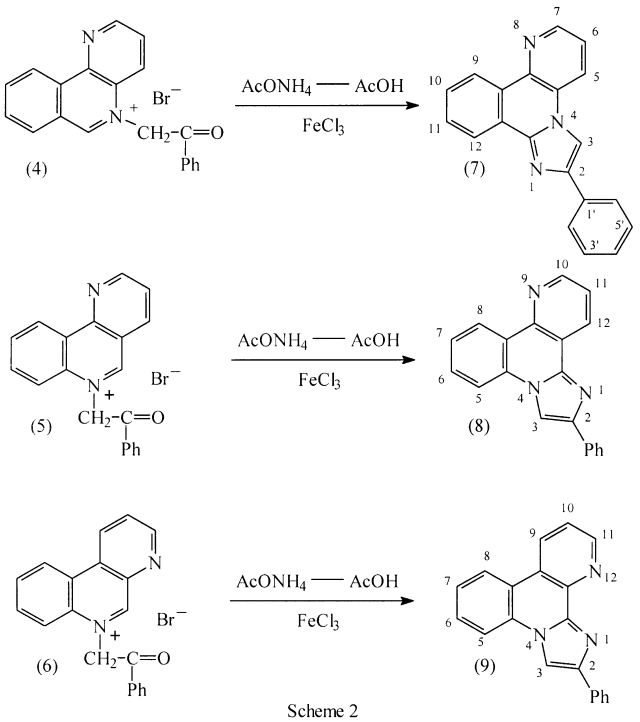
Scheme 1

In the present work we describe the cyclization reactions of 5-phenacylbenzo[*c*]-1,5-, 6-phenacylbenzo[*h*]-1,6-, and 6-phenacylbenzo[*f*]-1,7-naphthyridinium bromides (4)–(6) with ammonium acetate.

The starting materials (4)–(6) were prepared from benzo[*c*]-1,5-, benzo[*h*]-1,6- and benzo[*f*]-1,7-naphthyridines by reaction with phenacyl bromide.[15]

We have observed that the reactions of (4)–(6) with ammonium acetate in the presence of the oxidant ferric chloride in acetic acid led to cyclization products (7)–(9), namely 2-phenylbenzo[*c*]imidazo[1,2-*a*]-1,5-naphthyridine (7), 2-phenylbenzo[*h*]imidazo[2,1-*f*]-1,6-, naphthyridine (8), are 2-phenylbenzo[*f*]imidazo[1,2-*h*]-1,7-naphthyridine (9) (see Scheme 2).

Earlier Toja et al.[16] reported a similar procedure for isoquinolinium phenacyl bromides. Their products, arylimidazo[2,1-*a*]isoquinolines, were shown to exhibit pregnancy-terminating activity in both hamsters and rats. Accordingly we anticipate similar interesting applications



Scheme 2

 10.1071/CH00127 0004-9425/01/020105

for our imidazole analogues. The imidazole derivatives (7)–(9) complete the series of fused, four-ring cyclic derivatives of benzonaphthyridines which we obtained previously.[9–14]

The structures of the compounds obtained were confirmed by ^{1}H nuclear magnetic resonance (NMR) and mass spectroscopic data, as well as by elemental analysis. The ^{1}H NMR spectra of the cyclized products (7)–(9) showed 13 aromatic protons, including five protons from the phenyl group, and were compared with those of cycloadducts obtained from the reaction of benzonaphthyridinium *N*-phenacylides (1a)–(3a) and respective dipolarophiles. In the ^{1}H NMR spectrum of (7) the H 12 signal is shifted downfield strongly, compared with that of the respective benzopyrrolonaphthyridine; this observation is probaby due to the influence of the additional nitrogen in the imidazole ring. However, no significant influence of the nitrogen on the chemical shift of H 12 in the ^{1}H NMR spectrum of (8) was observed. The singlets of H 3 at δ 9.21 in the spectrum of (7), at δ 9.08 in the spectrum of (8), and at δ 8.12 in the spectrum of (9) are very characteristic.

These results illustrate the interesting reactivity of quaternary benzonaphthyridinium salts, especially that reactions of cyclization can readily lead to novel tetracyclic, fused heterocycles. The biological activity of (7)–(9) will be investigated.

Experimental

Melting points (m.p.) of the synthesized compounds were determined on a Boëtius apparatus and are uncorrected. Thin-layer chromatography was performed on $60F_{254}$ silica gel (Merck) precoated DC aluminium sheets. ^{1}H NMR spectra were recorded on a 200 MHz Bruker spectrometer in $(CD_3)_2SO$ with $SiMe_4$ as internal standard, and mass spectra on an AMD–604 mass spectrometer.

General Procedure for Synthesis of (7)–(9)

A mixture of (4), (5) or (6) (2 g, 5.3 mmol), ammonium acetate (2.7 g, 36.3 mmol), anhydrous ferric chloride (3 g, 18.4 mmol) in acetic acid (15 cm^3) was heated in an autoclave at 150°C for 6 h. After cooling to room temperature, the precipitated solid was filtered, washed with acetic acid (10 cm^3), water, and then taken up with methylene chloride (40 cm^3) and 37% aqueous ammonia. Evaporation of the solvent and recrystallization of the solid residue from ethyl acetate gave products (7), (8), and (9), respectively.

All synthesized *products* were obtained as small pale-grey crystals. Their melting points (m.p.), yields, elemental analyses, ^{1}H NMR and mass spectroscopic data are shown below.

Compound (7): m.p. 189–190°C; yield 48% (Found: C, 81.1; H, 4.2; N, 14.0 $C_{20}H_{13}N_3$ requires C, 81.3; H, 4.4; N, 14.2%). ^{1}H NMR δ 9.21, s, 1H, H 3; 8.62, dd, $J_{12,11}$ 7.35, $J_{12,10}$ 1.21 Hz, 1H, H 12; 8.51, dd, $J_{7,6}$ 4.54, $J_{7,5}$ 1.53 Hz, 1H, H 7; 8.22, dd, $J_{9,10}$ 7.45, $J_{9,11}$ 1.68 Hz, 1H, H 9; 8.01–8.12, m, 2H, H 2′,6′; 7.78, dd, $J_{6,7}$ 4.54, $J_{6,5}$ 8.38 Hz, 1H, H 6; 7.66, dd, $J_{10,9}$ 7.45, $J_{10,11}$ 7.15 Hz, 1H, H 10; 7.46–7.61, m, 3H, H 3′,5′,11; 7.38, dd, $J_{4',3'} = J_{4',5'}$ 7.09, $J_{4',2'} = J_{4,6}$ 1.23 Hz, 1H, H4′; 7.23, dd, $J_{5,6}$ 8.38, $J_{5,7}$ 1.53 Hz, 1H, H 5. Mass spectrum: *m/z* 295 (M$^+$, 100%).

Compound (8): m.p. 195–196.5°C; yield 41% (Found: C, 81.0; H, 4.3; N, 14.1. $C_{20}H_{13}N_3$ requires C, 81.3; H, 4.4; N, 14.2%). ^{1}H NMR δ 9.08, s, 1H, H 3; 8.72, dd, $J_{10,11}$ 4.93, $J_{10,12}$ 1.48 Hz, 1H, H 10; 7.94–8.10, m, 5H, H 2′,6′,11,8,12; 7.79, dd, $J_{6,5}$ 7.78, $J_{6,7}$ 7.28 Hz, 1H, H 6; 7.51, dd, $J_{3',2'} = J_{5',6'}$ 7.81, $J_{3',4'} = J_{5',4'}$ 7.08 Hz, 2H, H 3′,5′; 7.42, dd, $J_{7,8}$ 7.94, $J_{7,6}$ 7.28 Hz, 1H, H 7; 7.32, dd, $J_{4',3'} = J_{4',5'}$ 7.08, $J_{4',2'} = J_{4',6'}$ 1.21 Hz, 1H, H 4′; 7.21, dd, $J_{5,6}$ 7.78, $J_{5,7}$ 1.23 Hz, 1H, H 5. Mass spectrum: *m/z* 295 (M$^+$, 100%).

Compound (9): m.p. 185–186°C; yield 38% (Found: C, 81.1; H, 4.5; N, 14.4. $C_{20}H_{13}N_3$ requires C, 81.3; H, 4.4; N, 14.2%). ^{1}H NMR δ 8.96, dd, $J_{11,10}$ 5.13, $J_{11,9}$ 1.2 Hz, 1H, H 11; 8.24, dd, $J_{8,7}$ 7.82, $J_{8,6}$ 1.56 Hz, 1H, H 8; 8.12, s, 1H, H 3; 8.06, dd, $J_{2',3'} = J_{6',5'}$ 7.91, $J_{2',4'} = J_{4',6'}$ 1.25 Hz, 2H, H 2′,6′; 7.89, dd, $J_{6,5}$ 7.85, $J_{6,7}$ 7.34 Hz, 1H, H 6; 7.73, dd, $J_{9,10}$ 8.10, $J_{9,11}$ 1.2 Hz, 1H, H 9; 7.62, dd, $J_{10,9}$ 8.10, $J_{10,11}$ 5.13 Hz, 1H, H 10; 7.51–7.58, m, 3H, H 7,3′,5′; 7.37, dd, $J_{4',3'} = J_{4',5'}$ 7.12, $J_{4',2'} = J_{4',6'}$ 1.25 Hz, 1H, H 4′; 7.24, dd, $J_{5,6}$ 7.85, $J_{5,7}$ 1.27 Hz, 1H, H 5. Mass spectrum: *m/z* 295 (M$^+$, 100%).

References

[1] W. Śliwa, *Heterocycles* **1986**, *24*, 181.
[2] W. Śliwa, B. Mianowska, *Heterocycles* **1989**, *29*, 557.
[3] A. Slama-Schwok, J. J. Rabani, *J. Phys. Chem.* **1987**, *91*, 4394.
[4] J. Olmsted III, Th. J. Meyer, *J. Phys. Chem.* **1987**, *91*, 1649.
[5] D. Doizi, J. C. Mialocg, *J. Phys. Chem.* **1987**, *91*, 3524.
[6] A. Harriman, G. R. Millward, P. Neta, M. C. Richoux, J. M. Thomas, *J. Phys. Chem.* **1988**, *92*, 1286.
[7] J. Rabani, R. W. Fessenden, R. E. Sassoon, *J. Phys. Chem.* **1988**, *92*, 2379.
[8] M. P. Lenoir, R. L. Sassoon, J. J. Kozak, *J. Phys. Chem.* **1988**, *92*, 2526.
[9] B. Bachowska, W. Śliwa, *Monatsch. Chem.* **1984**, *115*, 1101.
[10] B. Bachowska, W. Śliwa, *Acta Chim. Hung.* **1988**, *125*, 491.
[11] B. W. Bachowska, *Monatsch. Chem.* **1995**, *126*, 227.
[12] T. Radzikowska, W. Śliwa, *J. Prakt. Chem.* **1985**, *327*, 689.
[13] T. Radzikowska, W. Śliwa, *J. Prakt. Chem.* **1987**, *329*, 529.
[14] T. Girek, T. Zujewska, W. Śliwa, *Acta Chim. Hung.* **1990**, *127*, 711.
[15] W. Śliwa, *Pol. J. Chem.* **1981**, *55*, 2199.
[16] E. Toja, A. Omodei-Salé, D. Favara, C. Cattaneo, L. Gallico, G. Galliani, *Arzneim-Forsch/Drug Res.* **1983**, *33 (II)*, 1222.