SYNTHESIS OF ALKYL 1,2-DICYANOPYRROLIDINO[1,2-*f*]-PHENANTHRIDINE-3-CARBOXYLATES

Milan POTACEK[a], Tomas TOPINKA[a], Jiri DOSTAL[b] and Otakar HUMPA[a]

[a] *Department of Organic Chemistry, Masaryk University, 611 37 Brno, Czech Republic*
[b] *Department of Biochemistry, Masaryk University, 662 43 Brno, Czech Republic*

Received June 8, 1995
Accepted June 22, 1995

Dedicated to Professor Otakar Cervinka on the occasion of his 70th birthday.

Alkyl 1,2-dicyanopyrrolidino[1,2-*f*]phenanthridine-3-carboxylates *II* were prepared from 5-(alkoxycarbonylmethyl)phenanthridinium bromides *I* and fumaronitrile in the presence of triethylamine. The products *II* underwent spontaneous dehydrogenation to give pyrrolino[1,2-*f*]phenanthridines *III*. The structures of the products were determined by spectral methods (IR, NMR, MS).

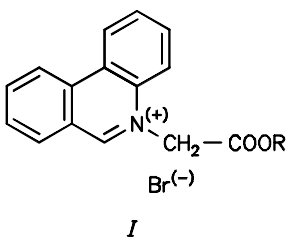
Synthesis of five-membered nitrogen heterocycles is often based on 1,3-dipolar cycloadditions with azomethine ylides[1]. Azomethine ylides have a carbanion attached to a positively charged nitrogen atom and can react as 1,3-dipoles with suitable dipolarophiles[2–5]. In this paper continuing our research[6,7] we describe cycloadditions of phenanthridinium-based azomethine ylides with fumaronitrile.

Quaternary phenanthridinium salts *Ia*, *Ib* were used as 1,3-dipole precursors in cycloaddition reactions with fumaronitrile as a dipolarophile. The compounds *I* were prepared from phenanthridine and alkyl bromoacetate as described earlier[6]. Azomethine ylides were generated by anhydrous triethylamine in the presence of fumaronitrile.

Reaction of *Ia* with fumaronitrile afforded two diastereoisomeric cycloadducts *IIa* and *IIb*. The IR and MS spectra of compounds *IIa*, *IIb* were almost identical. ^{1}H and ^{13}C NMR spectra proved the structures of the isolated compounds being expected pyrrolidinophenanthridines. Diastereoisomers *IIa*, *IIb* were separated by flash column chromatography on silica gel (eluent chloroform). The configuration of the products *II* was solved by ^{1}H NMR spectra comparing them with the spectra of compounds *III* and using our knowledge of the behaviour of the ylide used. Our earlier experiments namely showed that the azomethine ylide reacts at the given conditions always with the retention of the dipolarophile configuration so confirming concerted mechanism. Therefore configuration at C-1 and C-2 was considered to be *trans* according to the

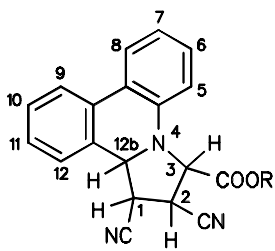
starting fumaronitrile. The hydrogen atoms H-3 and H-12b in *IIa* showed doublets with coupling constants 9.4 Hz and 4.7 Hz, respectively. Their configuration was assigned conformably to the papers[6,8] as 2,3-*cis* and 1,12b-*trans*. The other of the isolated isomers *IIb* (less polar fraction) was not stable enough to afford an elemental analysis with good results. In its spectrum the coupling constants were $^3J(2,3)$ = 3.6 Hz and $^3J(1,12b)$ = 8.7 Hz which indicated the 2,3-*trans* and 1,12b-*cis* configuration. Pyrrolidinophenanthridine *IIb* spontaneously oxidized when exposed to air to give *IIIa*. The dehydrogenated derivative *IIIa* displayed two bands of two CN groups in its IR spectrum. The weak band at 2 240 cm^{-1} corresponded to the cyano group at C-2 atom, the strong band (2 180 cm^{-1}) was caused by the CN group at C-1 conjugated with C=C bond of the pyrroline ring. In the NMR spectrum of *IIIa* appeared two doublets of H-2 and H-3 atoms with a typical *trans* coupling constant 3.4 Hz. The ^1H NMR spectrum of a crude reaction mixture showed the cycloadducts *IIa* and *IIb* present at the ratio of 1 : 3. Similar observations were made during the reaction of methyl analog *Ib*. Products so prepared were compounds *IIc*, *IId* and *IIIb*.

We can conclude that azomethine ylides from quaternary phenanthridinium salts *Ia* and *Ib* afforded in the reaction with fumaronitrile pyrrolidinophenanthridines *IIa–IId*.

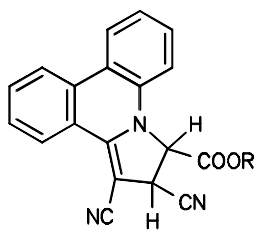


I

Ia, R = C_2H_5
Ib, R = CH_3



II



III

	R	Configuration 1,2	2,3	1,12b
IIa	C_2H_5	*trans*	*cis*	*trans*
IIb	C_2H_5	*trans*	*trans*	*cis*
IIc	CH_3	*trans*	*cis*	*trans*
IId	CH_3	*trans*	*trans*	*cis*
IIIa	C_2H_5	—	*trans*	—
IIIb	CH_3	—	*trans*	—

Those with the *cis* configuration at C-1 and C-12 underwent easy dehydrogenation to products *IIIa*, *IIIb*, although the stability of the other ones is also limited to weeks and their very slow transformation was observed by TLC. The dehydrogenation of compounds *IIIa*, *IIIb* to fully aromatic pyrrolophenanthridines proceeded with a negligible conversion probably due to electron-withdrawing properties of two cyano groups present.

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage Rapido 79-2106 and are uncorrected. Elemental analyses of the stable compounds were performed with an elemental analysator Perkin–Elmer 2400. IR spectra (wavenumbers in cm^{-1}) were recorded on a Unicam SP 1000 spectrophotometer. ^1H and ^{13}C NMR spectra (δ, ppm; *J*, Hz) were recorded on a Tesla BS 587 A (80/20 MHz) instrument with TMS as an internal standard. Mass spectra were obtained with a Varian Mat 445 spectrometer. TLC was carried out on Silufol plates (Kavalier, Czech Republic) in dichloromethane–ether 20 : 1 and detected in UV light (254 nm), column chromatography on silica gel 40–63 μm (Merck). Fumaronitrile was product of Janssen Chimica.

Reaction of *Ia* with Fumaronitrile

Fumaronitrile (0.44 g, 5.8 mmol) and triethylamine (0.8 g, 8 mmol) were added to a suspension of 5-(ethoxycarbonylmethyl)phenanthridinium bromide (*Ia*) (2 g, 5.8 mmol) in dichloromethane under nitrogen atmosphere. The mixture was allowed to stand at room temperature. After 3 h the mixture was concentrated in vacuo and the residue was extracted with benzene. The benzene filtrate after concentration gave a mixture of two isomers *IIa* and *IIb* (0.6 g, 31%). Fractional crystallization from benzene–cyclohexane afforded 0.1 g (5%) of the compound *IIa* and 0.25 g (13%) of *IIb*.

Ethyl 1,2-trans-2,3-cis-1,12b-trans-1,2-dicyanopyrrolidino[1,2-f]phenanthridine-3-carboxylate (IIa); m.p. 178–180 °C. For $C_{21}H_{17}N_3O_2$ (343.4) calculated: 73.45% C, 4.99% H, 12.24% N; found: 72.54% C, 4.86% H, 12.09% N. IR spectrum (KBr): 3 050, 3 010, 2 960, 2 230 (m, CN); 1 750 (s, CO); 1 600, 1 495, 1 445, 1 380, 1 300, 1 280, 1 200, 1 180, 1 150, 1 130, 1 060, 1 020, 730. ^1H NMR spectrum ($CDCl_3$): 1.34 t, 3 H, *J* = 7.2 (CMe); 4.36 q, 2 H, *J* = 7.2 (CH_2); 5.71 d, 1 H, *J* = 4.7 (H-12b); 4.86 d, 1 H, *J* = 9.4 (H-3); 3.90–4.05 m, 2 H (H-1 and H-2); 6.38 dd, 1 H, *J* = 8, *J* = 1.3 and 6.80–7.91 m, 7 H (arom). ^{13}C NMR spectrum ($CDCl_3$): 14.16 (CMe); 62.77 (CH_2); 34.65, 40.57 (C-1 and C-2); 61.45, 61.87 (C-3 and C-12b); 115.89, 116.61 (2 × CN); 112.05, 120.28, 122.96, 123.75, 12.86, 128.21, 129.28, 129.71 (8 × C–H); 120.65, 128.78, 130.85, 140.38 (4 × Cq); 168.75 (CO). Mass spectrum (electron impact), *m/z* (%): 343 (M^+, 22), 314 (4), 270 (11), 265 (37), 243 (7), 218 (19), 193 (100), 179 (12), 165 (12).

Ethyl 1,2-trans-2,3-trans-1,12b-cis-1,2-dicyanopyrrolidino[1,2-f]phenanthridine-3-carboxylate (IIb); m.p. 161–163 °C. IR spectrum (KBr): 3 050, 3 010, 2 980, 2 920, 2 240 (w, CN), 1 740 (s, CO), 1 600, 1 500, 1 450, 1 380, 1 300, 1 200, 1 185, 1 030, 755. ^1H NMR spectrum ($CDCl_3$): 1.34 t, 3 H, *J* = 7.1 (CMe); 4.33 q, 2 H, *J* = 7.1 (CH_2); 3.40–3.85 m, 2 H (H-1 and H-2); 4.85 dd, 1 H, *J* = 3.6, *J* = 0.5 (H-3); 5.23 d, 1 H, *J* = 8.7 (H-12b); 6.67 d, 1 H, *J* = 7.8 and 6.96–7.90 m, 7 H (arom). ^{13}C NMR spectrum ($CDCl_3$): 14.17 (CMe); 62.99 (CH_2); 34.65, 39.74 (C-1 and C-2); 62.99, 64.25 (C-3 and C-12b); 117.15, 117.54 (2 × CN); 112.97, 120.84, 122.97, 123.75, 125.01, 128.36, 129.33, 129.81 (8 × C–H); 120.84, 128.79, 130.11, 140.54 (4 × Cq); 169.07 (CO). Mass spectrum (electron impact), *m/z* (%): 343 (M^+, 22), 314 (4), 270 (13), 265 (34), 243 (5), 218 (10), 193 (100), 179 (19), 165 (12).

Ethyl 2,3-*trans*-1,2-Dicyano-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-3-carboxylate (*IIIa*)

The compound *IIb* (0.5 g, 1.52 mmol) was dissolved in acetone and the solution was allowed to stand at room temperature exposed to air. After 30 days the solvent was evaporated and the residue was chromatographed on a column of silica gel in chloroform. The product was crystallized from acetone–ethanol. Yield 0.05 g (10%), m.p. 223–224 °C. For $C_{21}H_{15}N_3O_2$ (341.4) calculated: 73.96% C, 4.39% H, 12.31% N; found: 73.75% C, 4.46% H, 12.09% N. IR spectrum (Nujol): 2 240 (w, C(2)**CN**), 2 180 (s, C(1)**CN**, conjugated), 1 755 (s, CO), 1 600, 1 570, 1 400, 1 315, 1 280, 1 205, 1 165, 750, 715. ^{1}H NMR spectrum ($CDCl_3$): 1.25 t, 3 H, J = 7.1 (CMe); 4.28 q, 2 H, J = 7.1 (CH_2); 4.30 d, 1 H, J = 3.4 (H-2); 5.34 d, 1 H, J = 3.4 (H-3); 6.76–8.79 m, 8 H (arom).

Reaction of *Ib* with Fumaronitrile

Fumaronitrile (0.12 g, 1.5 mmol) and triethylamine (0.2 g, 2 mmol) were added to a suspension of 5-(methoxycarbonylmethyl)phenanthridinium bromide (*Ib*) (0.5 g, 1.5 mmol). The treatment of the mixture was the same as for *Ia*. The yield of the mixture of *IIc* and *IId* was 0.25 g (51%). Compounds were separated by a column chromatography on silica gel, eluent chloroform.

Methyl 1,2-trans-2,3-cis-1,12b-trans-1,2-dicyanopyrrolidino[1,2-f]phenanthridine-3-carboxylate (IIc); m.p. 209–211 °C. For $C_{20}H_{15}N_3O_2$ (329.4) calculated: 72.94% C, 4.59% H, 12.76% N; found: 73.35% C, 4.50% H, 12.55% N. IR spectrum (KBr): 3 020, 2 950, 2 840, 2 240 (m, CN); 1 755 (s, CO); 1 605, 1 500, 1 445, 1 385, 1 330, 1 290, 1 215, 1 180, 740. ^{1}H NMR spectrum ($CDCl_3$): 3.88 s, 3 H (OMe); 3.92–4.07 m, 2 H (H-1 and H-2); 4.92 d, 1 H, J = 8.5 (H-3); 5.72 d, 1 H, J = 4.5 (H-12b); 6.37 dd, 1 H, (J = 7.9, J = 1.4) and 6.80–7.92 m, 7 H (arom). ^{13}C NMR spectrum (CD_3SOCD_3): 33.26 (C-1 and C-2); 52.60 (Me); 60.62, 61.52 (C-3 and C-12b); 117.15, 117.68 (2 × CN); 111.76, 119.14, 122.39, 123.47, 127.92, 128.85, 129.03, 130.06 (8 × C–H); 119.43, 126.64, 129.63, 140.41 (4 × Cq); 169.53 (CO). Mass spectrum (chemical ionization), *m/z* (%): 330 (MH^+, 63), 251 (8), 214 (8), 180 (13), 143 (7), 123 (26), 99 (10), 89 (45), 85 (8), 59 (100), 57 (32).

Methyl 1,2-trans-2,3-trans-1,12b-cis-1,2-dicyanopyrrolidino[1,2-f]phenanthridine-3-carboxylate (IId); m.p. 180–182 °C. IR spectrum (KBr): 3 060, 3 020, 2 960, 2 940, 2 860, 2 260 (w, CN); 1 750 (s, CO); 1 605, 1 500, 1 450, 1 385, 1 300, 1 210, 1 180, 740. ^{1}H NMR spectrum ($CDCl_3$): 3.38–3.82 m, 2 H (H-1 and H-2); 3.87 s, 3 H (OMe); 4.86 d, 1 H, J = 3.5 (H-3); 5.22 d, 1 H, J = 8.7 (H-12b); 6.64–7.88 m, 8 H (arom). ^{13}C NMR spectrum ($CDCl_3$): 34.43, 39.57 (C-1 and C-2); 53.34 (OMe); 62.80, 63.94 (C-3 and C-12b); 116.97, 117.36 (2 × CN); 112.75, 120.75, 122.89, 123.64, 124.99, 128.24, 129.28, 129.78 (8 × C–H); 120.60, 129.35, 129.92, 140.34 (4 × Cq); 169.53 (CO).

Methyl 2,3-*trans*-1,2-Dicyano-2,3-dihydropyrrolo[1,2-*f*]phenanthridine-3-carboxylate (*IIIb*)

Solution of compound *IId* (0.5 g, 1.28 mmol) in acetone was kept standing for several days in oxygen atmosphere. Then the reaction mixture was separated on a column of silica gel (chloroform). Yield 24.8 mg (5%), m.p. 199–200 °C. IR spectrum (Nujol): 2 240 (w, C(2)**CN**); 2 180 (s, C(1)**CN**, conjugated); 1 750 (s, CO); 1 600, 1 570, 1 400, 1 445, 1 320, 1 215 s, 1 170, 750, 715. ^{1}H NMR spectrum ($CDCl_3$): 3.83 s, 3 H (OMe); 4.32 d, 1 H, J = 3.3 (H-2); 5.38 d, 1 H, J = 3.3 (H-3); 6.75–8.80 m, 8 H (arom).

REFERENCES

1. Huisgen R.: *1,3-Dipolar Cycloaddition Chemistry*, Vol. 1. Wiley & Sons, New York 1984.
2. Stuckwish C. G.: Synthesis *1973*, 469.
3. Jones R. C. F., Nichols J. R., Cox M. T.: Tetrahedron Lett. *31*, 2333 (1990).

4. Huisgen R., Grashey R., Steingruber E.: Tetrahedron Lett. *1963*, 1441.
5. Bende Z., Toke L., Weber L., Toth G., Janke F., Csonka G.: Tetrahedron *40*, 369 (1984).
6. Dostal J., Potacek M., Humpa O., Marek J.: Bull. Soc. Chim. Belg. *103*, 343 (1994).
7. Potacek M., Topinka T., Dostal J., Marek J.: Collect. Czech. Chem. Commun. *59*, 2641 (1994).
8. Woller P. B., Cromwell N. H.: J. Org. Chem. *35*, 888 (1970).