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1,3-Dipolar Cycloaddition Reactions of 4,6-Diazaphenanthrene 6-Phenacylide

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Summary. The 1,3-dipolar cycloaddition reactions of 4,6-diazaphenanthrene 6-phenacylide formed in situ from the appropriate quaternary bromide in basic medium were investigated; as dipolarophiles acrylonitrile, ethyl acrylate, *n*-butyl acrylate and diethyl maleate were used.

Keywords. Azaaromatic N-ylide; Cycloaddition; Diazaphenanthrene.

1,3-Dipolare Cycloadditionsreaktionen von 4,6-Diazaphenanthren-6-phenacylid

Zusammenfassung. Es wurden die 1,3-dipolaren Cycloadditionen von 4,6-Diazaphenanthren-6-phenacylid untersucht, welches in situ aus dem entsprechenden quaternären Bromid in Gegenwart von Alkali dargestellt wurde. Als Dipolarophile wurden Acrylnitril, Ethylacrylat, *n*-Buthylacrylat und Diethylmaleat eingesetzt.

Introduction

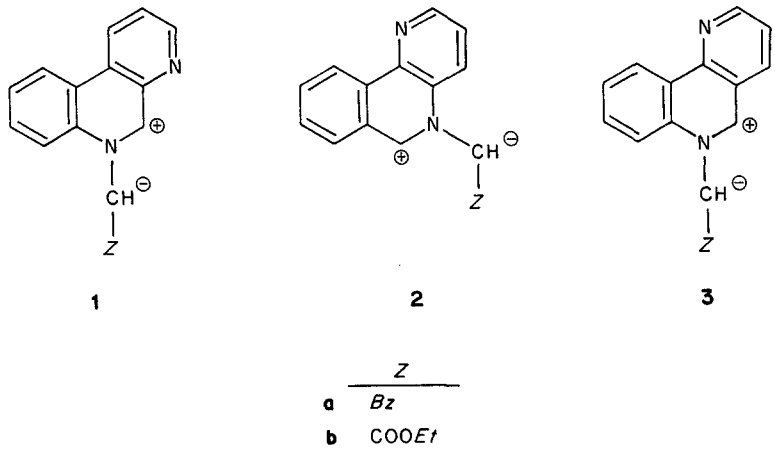
Cycloadditions of azaaromatics were intensively studied as synthetic approaches to compounds often difficult to obtain on other routes [1–3]; among these processes special attention was paid to 1,3-dipolar cycloaddition reactions [4–7]. Ylides, playing in these reactions the role of 1,3-dipoles, are formed from appropriate quaternary salts of azaaromatics, compounds which are of current interest in the chemistry of heterocycles [8–10].

Our research concerns the reactivity and UV spectra of diazaphenanthrenes (*dap*) [11, 12] along with their complexing properties [13, 14] having in view biological activities of these species [15, 16].

The present work dealing with 1,3-dipolar cycloadditions of 4,6-*dap*-4-phenacylide **1a** is a continuation of our former investigation of such reactions of isomeric compounds derived from 1,5- and 1,6-*daps* (**2a** and **3a**, respectively) [17–20], as well as their analogues, ethoxycarbonylmethylides **1b–3b** [21–24] (Scheme 1).

Results and Discussion

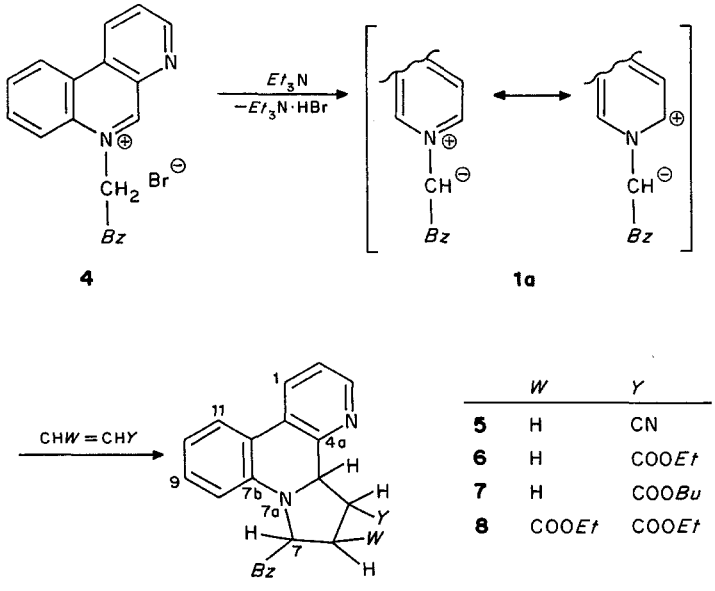
The quaternary salt of 4,6-*dap* with phenacyl bromide (**4**) was treated with Et_3N to form the ylide **1a**, which reacted in situ with dipolarophiles acrylonitrile,



Scheme 1

ethyl acrylate, *n*-butyl acrylate, and diethyl maleate affording 7-benzoyl-5-cyano-pyrido[2′,3′:3,4]pyrrolidine[1,2-a]quinoline (**5**), 7-benzoyl-5-ethoxycarbonylpyrido-[2′,3′:3,4]pyrrolidine[1,2-a]quinoline (**6**), 7-benzoyl-5-buthoxycarbonylpyrido[2′,3′:3,4]pyrrolidine[1,2-a]quinoline (**7**), and 7-benzoyl-5,6-diethoxycarbonylpyrido-[2′,3′:3,4]pyrrolidine[1,2-a]quinoline (**8**) (Scheme 2).

Quaternization of 4,6-*dap* with phenacyl bromide was performed at room temperature in *THF*, the cycloadditions were made at room temperature in *DMF* (for **5**) or in benzene (for **6**, **7**, and **8**). The starting 4,6-*dap* was synthesized from 3-aminoquinoline in the Skraup procedure, using arsenic pentoxide as oxidizing agent [23].



Scheme 2

In 1,3-dipolar cycloaddition reactions the primary products are either stable enough to be isolated or they undergo a dehydrogenation of the formed five-membered ring and a H shift. In our experiments for four dipolarophiles primary cycloadducts were obtained; this result is in accordance with that of a similar reaction of 1,5- and 1,6-*dap* isomers (**2a** and **3a**) with diethyl maleate [18].

Comparing this reactivity of **1a** with 4,6-*dap* ethoxycarbonylmethylide analogue **1b**, primary cycloadducts of **1b** were formed in the case of acrylonitrile, ethyl acrylate and diethyl maleate. Also in 1,3-dipolar cycloaddition reactions of 1,5- and 1,6-*dap* phenacylides **2a**, **3a**, and their analogues **2b**, **3b** with *DMAD* the primary cycloadducts are the main products [17] (*DMAD* = dimethyl acetylenedicarboxylate).

All investigated 1,3-dipolar cycloaddition reactions of **1a** and **1b** lead to stable, isolable primary cycloadducts, while in the case of 1,5- and 1,6-isomers beside primary compounds also dehydrogenated species are obtained, this fact being presumably due to the different positions of nitrogen atoms in the ylide **1a**.

In the ^{1}H NMR spectrum of **4** signals of all protons, and especially that of H5, are shifted downfield due to the positive charge of the nitrogen in position 6.

The influence of the five-membered ring in the cycloadducts is observed in an upfield shift of the aromatic protons of these compounds. Among the H8 signals of the cycloadducts, the largest upfield shift is found in the case of **6** and **8**.

Experimental Part

M.p.s. were determined on a Boetius apparatus and are uncorrected. TLC chromatography was performed on 60 F 254 silica gel (Merck) precoated DC aluminium sheets.

^{1}H NMR spectra were recorded on a 100 MHz Jeol spectrometer in *DMSO* using *TMS* as internal standard. IR spectra were taken in KBr discs on a Beckman 4240 spectrophotometer and MS spectra on a LKB-2091 mass spectrometer at a nominal energy 70 eV and 15 eV.

Quaternization of **4**, **6**-*dap into* **4**

The solution of 4,6-*dap* (1.8 g, 10 mmol) in *DMF* (12 ml) was treated under anhydrous conditions with phenacyl bromide (5.88 g, 20 mmol) and stirred at room temperature for 1–2 weeks. Every other day the formed solid was filtered off and the mixture completed by the addition of phenacyl bromide (2.99 g, 10 mmol).

The combined product was recrystallized from *Me*OH/*THF* (1:1), pale yellow crystals, m.p. 205–206°; tlc eluent: benzene-*Me*OH 5/1. IR (cm^{-1}): 1690 (CO), 1220 (O–C–O). ^{1}H NMR (δ, ppm): 10.59 (s, 1 H, H 5), 9.78 (d, 1 H, $J_{10,9} = 7.9$ Hz, H 10), 9.58 (dd, 1 H, $J_{3,2} = 4.3$ Hz, $J_{3,1} = 1.4$ Hz, H 3), 9.44–9.40 (m, 1 H, H 1), 8.69 (dd, 1 H, $J_{7,8} = 7.3$ Hz, $J_{7,9} = 2.7$ Hz, H 7), 8.53 (dd, 1 H, $J_{2,1} = 8.6$ Hz, $J_{2,3} = 4.3$ Hz, H 2), 8.38–8.26 (m, 5 H, 2 H_o, 2 H_m, H 8), 7.98–7.93 (m, 1 H, H 9), 7.82 (t, 1 H, $J_{p,m} = 7.9$ Hz, H_p), 7.31 (s, 2 H, CH_2). MS: no M^+, 180 (73%, 4,6-*dap*), 105 (100%, $C_6H_5CO^+$). Anal. for $C_{20}H_{15}N_2OBr$ (379.27): calc. C 63.33, H 3.99, N 7.39; found C 63.46, H 3.96, N 7.05.

General Procedure of the 1,3-Dipolar Cycloaddition Reaction of **1** *with Acrylonitrile, Ethyl Acrylate, N-Butyl Acrylate and Diethyl Maleate*

4 (379 mg, 1 mmol) in *DMF* (5 ml) in the case of **5** or in benzene (15 ml) in the case of **6**, **7** and **8** was treated under anhydrous conditions with the dipolarophile (acrylonitrile, 106 mg 0.13 ml, 2 mmol; ethyl acrylate 150 mg, 0.16 ml, 1.5 mmol; *n*-butyl acrylate, 192 mg, 0.21 ml, 1.5 mmol; or diethyl maleate 260 mg, 0.24 ml, 1.5 mmol) in the presence of triethylamine (141 mg, 0.19 ml, 1.4 mmol).

The mixture was stirred at room temperature for 2 h and allowed to stand for 24 h. The triethylammonium bromide was removed by filtration and the solution treated with *n*-hexane (in the case of **5** with water) to precipitate the crude product, which was filtered off and recrystallized.

5: M.p. 205 °C (from acetone); yield 46%; tlc eluent: benzene-methanol 5/1. IR (cm^{-1}): 2360 (CN), 1680 (CO), 1230 (C–O–C). ^{1}H NMR (δ, ppm): 8.60 (dd, 1 H, $J_{3,2} = 4.7$ Hz, $J_{3,1} = 1.2$ Hz, H 3), 8.44 (d, 1 H, $J_{11,10} = 7.5$ Hz, H 11), 8.28 (d, 2 H, $J_{o,m} = 7.5$ Hz, 2 H_o), 7.94 (d, 1 H, $J_{1,2} = 7.0$ Hz, H 1), 7.85 (d, 1 H, $J_{8,9} = 7.5$ Hz, H 8), 7.72 (t, 2H, $J_{m,o} = 7.5$ Hz, 2 H_m), 7.53 (dd, 1 H, $J_{2,1} = 7.0$ Hz, $J_{2,3} = 4.7$ Hz, H 2), 7.17 (t, 1 H, $J_{9,8} = J_{9,10} = 7.5$ Hz, H 9), 6.84 (t, 1 H, $J_{10,9} = J_{10,11} = 7.5$ Hz, H 10), 6.22 (d, 1 H, $J_{p,m} = 8.1$ Hz, H_p), 5.97–5.92 (m, 1 H, H 8), 5.39 (d, 1 H, $J_{4b,5} = 4.8$ Hz, H 4b), 4.18–4.14 (m, 1 H, H 5), 3.16–3.08 (m, 1 H, H 6a), 2.41–2.34 (m, 1H, H 6b). MS: 351 (13%, M^+). Anal. for $C_{23}H_{17}ON_3$ (351.43): calc. C 78.61, H 4.88, N 11.96; found C 78.37, H 4.50, N 11.78.

6: M.p. 133–136 °C (from ethanol); yield 37%; tlc eluent: benzene-ethanol 4/1. IR (cm^{-1}): 1720 (CO), 1245, 1200 (C–O–C). ^{1}H NMR (δ, ppm): 8.41 (d, 1 H, $J_{3,2} = 5.0$ Hz, H 3), 8.35–7.50 (m, 7 H, H 1, H 11, 2 H_o, 2 H_m, H_p), 7.38 (d, 1 H, $J_{8,9} = 7.5$ Hz, H 8), 7.10 (t, 1 H, $J_{9,10} = J_{9,8} = 7.5$ Hz, H 9), 6.74 (t, 1 H, $J_{10,11} = J_{10,9} = 7.5$ Hz, H 10), 6.10 (d, 1 H, $J_{2,1} = 7.5$ Hz, H2), 5.80–5.60 (m, 1 H, H 7), 5.49 (d, 1 H, $J_{4b,5} = 6.3$ Hz, H 4b), 4.03–3.58 (m, 3 H, CH_2, H 5), 3.50–3.10 (m, 1 H, H 6a, overlapping with H_2O), 3.10–2.50 (m, 1 H, H 6b, overlapping with *DMSO*), 0.93 (t, 3 H, $J = 7.5$ Hz, CH_3). MS: 398 (45.5%, M^+). Anal. for $C_{25}H_{22}O_3N_2$ (398.49): calc. C 75.35, H 5.55, N 7.03; found C 75.05, H 5.37, N 7.06.

7: M.p. 117–118 °C (from benzene-hexane 5/1); yield 28%; tlc eluent: benzene-methanol 5/1. IR (cm^{-1}): 1740 (CO), 1230 (C–O–C). ^{1}H NMR (δ, ppm): 8.32 (dd, 1 H, $J_{3,2} = 4.7$ Hz, $J_{3,1} = 1.5$ Hz, H 3), 8.20 (dd, 1 H, $J_{11,10} = 8.2$ Hz, $J_{11,9} = 1.5$ Hz, H 11), 8.16–8.12 (m, 2 H, H 1, H 8), 7.76–7.72 (m, 2 H, 2 H_o), 7.63–7.59 (m, 2 H, 2 H_m), 7.37–7.26 (m, 1 H, H 2), 7.00 (t, 1 H, $J_{9,8} = J_{9,10} = 8.2$ Hz, H 9), 6.64 (t, 1 H, $J_{10,9} = J_{10,11} = 8.2$ Hz, H 10), 6.03(d, 1 H, $J_{p,m} = 7.4$ Hz, H_p), 5.57–5.52 (m, 1 H, H 7), 5.39 (d, 1 H, $J_{4b,5} = 5.7$ Hz, H 4b), 3.78–3.65 (m, 3 H, H 5, CH_2), 2.77–2.70 (m,1 H, H 6a), 2.26–2.18 (m, 1 H, H 6b), 1.27–1.02 (m, 4 H, 2 CH_2), 0.72 (t, 3 H, $J = 7.3$ Hz, CH_3). MS: 426 (56%, M^+). Anal. for $C_{27}H_{26}O_3N_2$ (426.55): calc. C 76.09, H 6.15, N 6.56; found C 76.20, H 5.93, N 6.58.

8: M.p. 77–79 °C (from ethanol/water 1/1); yield 34%; tlc eluent: benzene-methanol 9/1. IR (cm^{-1}): 1720 (CO), 1660 (COOEt), 1240 (C–O–C). ^{1}H NMR (δ, ppm): 8.29 (d,1 H, $J_{3,2} = 5.0$ Hz, H 3), 8.06 (d, 1 H, $J_{11,10} = 7.0$ Hz, H 11), 7.88–7.40 (m, 6 H, H 1, 2 H_o, 2 H_m, H_p), 7.10–6.80 (m, 2 H, H 2, H 8), 6.55 (t, 1 H, $J_{9,10} = J_{9,8} = 7.0$ Hz, H 9), 6.08 (d, 1 H, $J_{10,11} = 7.0$ Hz, H 10), 5.73 (d, 1 H, $J_{7,6} = 6.0$ Hz, H 7), 5.53 (d, 1 H, $J_{4b,5} = 5.0$ Hz, H 4b), 4.10–3.40 (m, 6 H, 2 CH_2, H 5, H 6), 1.10–0.50 (m, 6 H, 2 CH_3). MS: 470 (8.4%, M^+). Anal. for $C_{28}H_{26}O_5N_2$ (470.53): calc. C 71.46, H 5.58, N 5.95; found C 71.44, H 5.31, N 6.10.

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