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Cycloaddition Reactions of 1,5-, 1,6- and 4,6-Benzo[*h*]naphthyridinium N-Dichloromethylides with Dimethyl Acetylenedicarboxylate

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Summary. Cycloaddition reactions of 1,5-, 1,6-, and 4,6-benzo[*h*]naphthyridinium N-dichloromethylides with dimethyl acetylenedicarboxylate are reported. Ylides were formed *in situ* from corresponding benzo[*h*]naphthyridines and dichlorocarbene.

Keywords. Azaaromatic N-ylide; Cycloaddition; Dichlorocarbene.

Cycloadditionsreaktionen von 1,5-, 1,6- und 4,6-Benzo[*h*]naphthyridinium-N-dichloromethyliden mit Acetylendicarbonsäuredimethylester

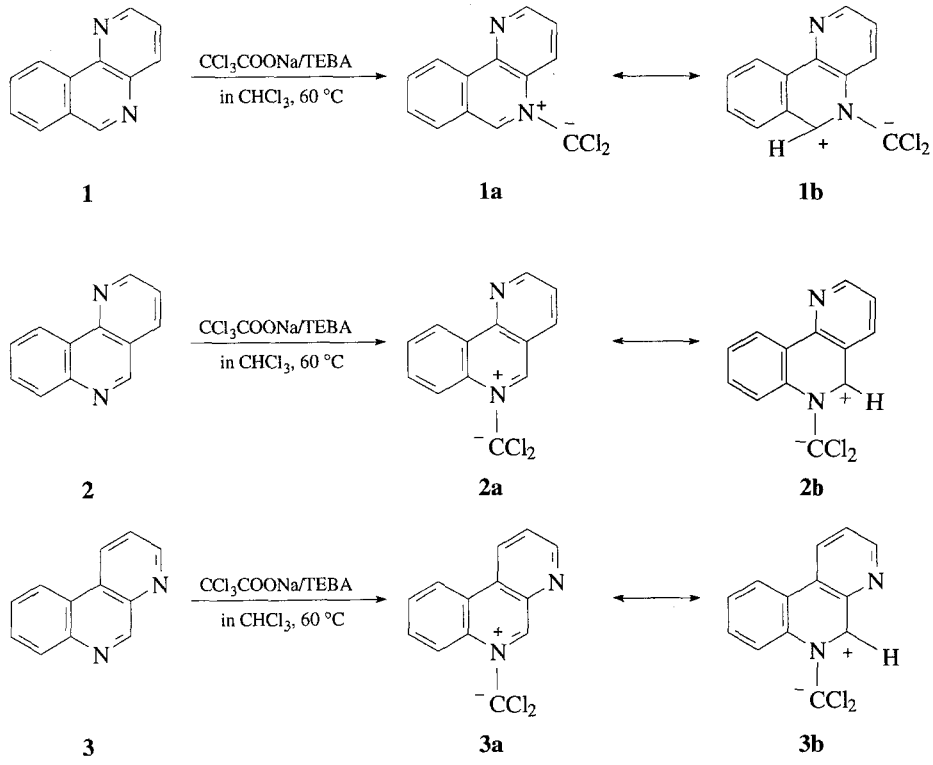
Zusammenfassung. Es wurden Cycloadditionsreaktionen von 1,5-, 1,6- und 4,6-Benzo[*h*]naphthyridinium-N-dichloromethyliden mit Acetylendicarbonsäuredimethylester untersucht. Die Ylide werden *in situ* aus den entsprechenden Benzo[*h*]naphthyridinen und Dichlorcarben erhalten.

Introduction

Cycloaddition reactions of azaaromatics as well as of their N-methylides reacting as 1,3-dipoles provide a useful synthetic approach to condensed heterocycles [1–5]. In former studies, we have described the 1,3-dipolar cycloaddition reactions of 1,5- and 1,6-benzo[*h*]naphthyridinium N-phenacylides with dipolarophiles [6, 7]. The present work deals with cycloaddition reactions of benzo[*h*]naphthyridinium N-dichloromethylides with dimethyl acetylenedicarboxylate (*DMAD*).

The title N-dichloromethylides were formed in situ from 1,5-, 1,6-, and 4,6-benzo[*h*]naphthyridines (*BN*) and dichlorocarbene which was generated by thermal decomposition of sodium trichloroacetate in chloroform in the presence of benzyltriethylammonium chloride (*TEBA*).

The formation of 1,5-, 1,6- and 4,6-*BN*-N-dichloromethylides is shown in Scheme 1.



Scheme 1

Results and Discussion

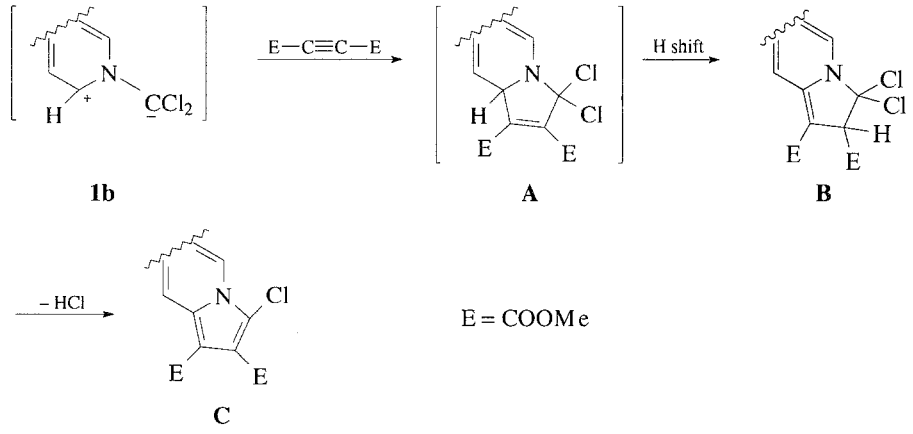
A proposed mechanism for the considered reactions of *BN*–N-dichloromethylides as 1,3-dipoles with *DMAD* as dipolarophile is shown in Scheme 2.

The reaction of **1b**, **2b**, or **3b** with *DMAD* is supposed to start with the formation of an unstable product of type **A**, followed by a H shift leading immediately to **B** which undergoes a dehydrohalogenation to give the cycloadduct **C**.

The proposed course of the reactions is in accordance with literature data for similar 1,3-dipolar cycloaddition reactions of ylides from pyridine and quinoline systems and dichlorocarbene [8] as well as with results from our laboratory concerning the cycloaddition of *BN*-N-phenacylides and *BN*-N-carboethoxymethylides [6, 7, 9–12].

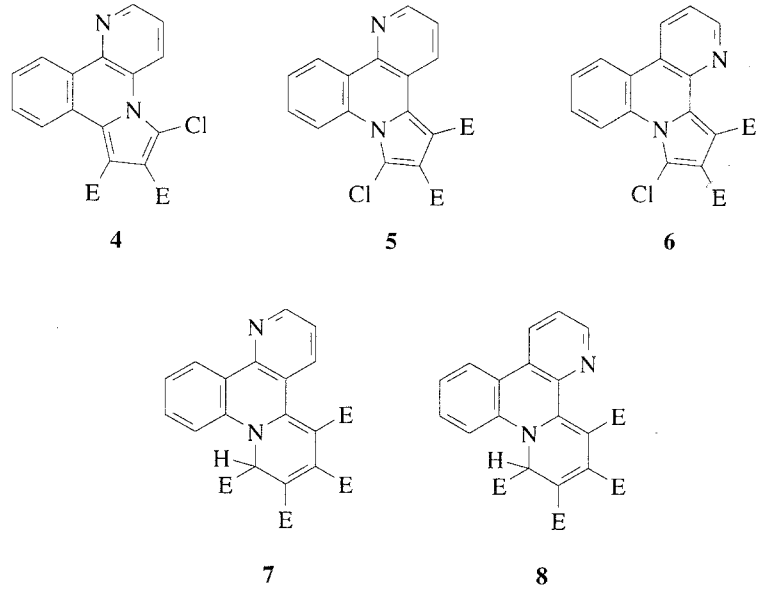
The cycloadducts of type **C** were separated from the mixture of compounds. In the reaction of 1,6- and 4,6-*BN* with *DMAD* in the presence of dichlorocarbene, additional products were separated from the mixtures: tetramethyl-9*H*-1,10-diazapyrido(2,1-*f*)phenanthrene-6,7,8,9-tetracarboxylate (**7**) from the reaction of 1,6-*BN* and tetramethyl-9*H*-4,10-diazapyrido(2,1-*f*)phenanthrene-6,7,8,9-tetracarboxylate (**8**) from the reaction of 4,6-*BN*, respectively. The cycloadducts **4**–**8** are shown in Scheme 3.

Products **7** and **8** were formed without participation of dichlorocarbene, similarly as in the case of cycloaddition reactions of 1,5- and 1,6-benzo[*h*]naphthyridines with *DMAD*, reported in previous work from our laboratory [13].



1b **A** **B** **C**

Scheme 2



4 **5** **6** **7** **8**

Scheme 3

Cycloaddition reactions of *BN*-N-dichloromethylides with *DMAD* proceed at lower yield than those of corresponding *BN*-N-carboethoxymethylides and *BN*-N-phenacylides; the aim of our present work, however, was the synthesis of cycloadducts for comparison with other compounds of this type prepared previously in our laboratory.

The starting 1,5- 1,6-, and 4,6-benzo[*h*]naphthyridines were synthesized from 4-aminoquinoline, 4-aminoisoquinoline, and 3-aminoquinoline, respectively, by the *Skraup* procedure [14]. Elemental analyses of the obtained products are satisfactory; their structures were confirmed by mass, as well as by ^{1}H NMR spectra.

Experimental

Preparative TLC was performed on 60G silica gel (Merck) 20 × 20 cm plates, TLC on 60F 254 silica gel (Merck) precoated DC aluminum sheets. ^{1}H NMR spectra were recorded on a 200 MHz Bruker

spectrometer in $CDCl_3$ using TMS as internal standard, MS spectra on a AMD-604 mass spectrometer at a nominal energy 70 eV. Melting points were determined on a Boëtius apparatus and are uncorrected.

General procedure of cycloaddition reactions of **1**, **2** and **3** *with DMAD in the presence of dichlorocarbene*

1,5-, 1,6-, or 4,6-*BN* (2.16 g, 12 mmol) in C_2H_5OH-free $CHCl_3$ (80 ml) was treated with *DMAD* (2.2 ml, 18 mmol), *TEBA* (2.04, 9 mmol), and sodium trichloroacetate (4 g, 21.5 mmol) under anhydrous conditions and an N_2 atmosphere portionswise during 0.5 h. The mixture was refluxed for 4 h; during this time, the starting material disappeared from the mixture of products. After cooling to room temperature, the solvent was removed; from the black residue, the main products were extracted with benzene in a *Soxhlet* extractor. Evaporation of the solvent gave a mixture of products which were separated by preparative chromatography (silica gel) using the eluent indicated below and recrystallized from hexane:benzene = 1:1 (**4**, **5**, **6**) and acetone (**7**, **8**). All products were obtained in the form of yellow crystals.

6-Chloro-7,8-dicarbomethoxy-1,5-diazapyrroline(1,2-f)phenanthrene (**4**)

M.p., 215–219 °C; TLC eluent, benzene–methanol 9/1; yield, 5,3%; ^{1}H NMR (δ, ppm): 9.10 (dd, 1H, $J_{13,12} = 8.0$ Hz, $J_{13,11} = 1.38$ Hz, H13), 9.0 (d, 1H, $J_{2,3} = 4.5$ Hz, H2), 8.40 (dd, 1H, $J_{4,3} = 7.5$ Hz, $J_{4,2} = 1.5$ Hz, H4), 7.97 (dd, 1H, $J_{3,4} = 7.5$ Hz, $J_{3,2} = 4.5$ Hz, H3), 7.8–7.73 (m, 3H, H10, H11, H12), 4.10 (s, 3H, CH_3), 3.95 (s, 3H, CH_3); MS (*m/e*): 368 (M^+, 100%). Anal. for $C_{19}H_{13}N_2ClO_4$ (368.5): calc., C 61.88, H 3.50, N 7.59; found, C 61.61, H 3.07, N 7.75%.

8-Chloro-6,7-dicarbomethoxy-1,9-diazapyrroline(2,1-f)phenanthrene (**5**)

M.p., 209–211 °C; TLC eluent, chloroform-methanol 95/5; yield, 4.4%; ^{1}H NMR (δ, ppm): 9.07 (dd, 1H, $J_{13,12} = 8$ Hz, $J_{13,11} = 1.5$ Hz, H13), 8.88 (dd, 1H, $J_{2,3} = 4$ Hz, $J_{2,4} = 1.5$ Hz, H2), 8.35 (dd, 1H, $J_{4,3} = 7.5$ Hz, $J_{4,2} = 1.5$ Hz, H4), 8.07 (dd, 1H, $J_{3,4} = 7.5$ Hz, $J_{3,2} = 4$ Hz, H3), 7.96 (ddd, 1H, $J_{12,13} = 8.1$ Hz, $J_{12,11} = 7.1$ Hz, $J_{12,10} = 1.3$ Hz, H12), 7.84 (ddd, 1H, $J_{11,10} = 7.7$ Hz, $J_{11,12} = 7.1$ Hz, $J_{11,13} = 1.5$ Hz, H11), 7.62 (dd, 1H, $J_{10,11} = 7.7$ Hz, $J_{10,12} = 1.3$ Hz, H10), 3.76 (s, 3H, CH_3), 3.68 (s, 3H, CH_3); MS (*m/e*): 368 (M^+, 100%). Anal. for $C_{19}H_{13}N_2ClO_4$ (368.5): calc., C 61.88, H 3.5, N 7.59; found, C 61.32, H 3.2, N 7.05%.

8-Chloro-6,7-dicarbomethoxy-4,9-diazapyrroline(2,1-f)phenanthrene (**6**)

M.p., 218–222 °C; TLC, eluent, benzene–acetone 6/4; yield, 7.3%; ^{1}H NMR (δ, ppm): 8.64 (dd, 1H, $J_{3,2} = 4.5$ Hz, $J_{3,1} = 1.6$ Hz, H3), 8.28 (dd, 1H, $J_{1,2} = 8.5$ Hz, $J_{1,3} = 1.6$ Hz, H1), 7.90 (dd, 1H, $J_{13,12} = 8.0$ Hz, $J_{13,11} = 1.4$ Hz, H13), 7.45 (dd, 1H, $J_{2,1} = 8.5$ Hz. $J_{2,3} = 4.5$ Hz, H2), 7.31 (ddd, 1H, $J_{11,12} = 7.3$ Hz, $J_{11,10} = 8.3$ Hz, $J_{11,13} = 1.4$ Hz, H11), 7.02 (ddd, 1H, $J_{12,11} = 7.3$ Hz, $J_{12,13} = 8.0$ Hz, $J_{12,10} = 1.02$ Hz, H12), 6.75 (dd, 1H, $J_{10,11} = 8.3$ Hz, $J_{10,12} = 1.02$ Hz, H10), 3.80 (s, 3H, CH_3), 3.77 (s, 3H, CH_3); MS (*m/e*): 368 (M^+, 100%). Anal. for $C_{19}H_{13}N_2ClO_4$ (368.5): calc., C 61.88, H 3.5, N 7.59; found, C 61.42, H 3.15, N 7.39%.

Tetramethyl-9H-1,10-diazapyrido(2,1-f)phenanthrene-6,7,8,9-tetracarboxylate (**7**)

M.p., 212–214 °C; TLC eluent, benzene–acetone 95/5; yield, 4.8%; ^{1}H NMR (δ, ppm): 8.65 (dd, 1H, $J_{2,3} = 4$ Hz, $J_{2,4} = 2$ Hz, H2), 8.35 (dd, 1H, $J_{14,13} = 8$ Hz, $J_{14,12} = 2$ Hz, H14), 7.53–7.47 (m, 2H, H4, H11), 7.45–7.38 (m, 2H, H12, H13), 7.25 (dd, 1H, $J_{3,4} = 6$ Hz, $J_{3,2} = 4$ Hz, H3), 5.90 (s, 1H, H9), 3.95, 3.75, 3.65, 3.48 (4s, 12H, $4CH_3$); MS (*m/e*): 464 (M^+, 12%). Anal. for $C_{24}H_{20}N_2O_8$ (464.20): calc., C 62.08, H 4.34, N 6.03; found, C 62.03, H 4.20, N 6.03%.

Tetramethyl-9H-4,10-diazapyrido(2,1-f)phenanthrene-6,7,8,9-tetracarboxylate (**8**)

M.p., 256–261 °C; TLC eluent, benzene-acetone 7/3; yield, 5.2%, ^{1}H NMR (δ, ppm): 8.53 (dd, 1H, $J_{3,2} = 4.9$ Hz, $J_{3,1} = 1.53$ Hz, H3), 8.03 (dd, 1H, $J_{1,2} = 7.87$ Hz, $J_{1,3} = 1.53$ Hz, H1) 7.79 (dd, 1H, $J_{14,13} = 7.66$ Hz, $J_{14,12} = 1.45$ Hz, H14), 7.51–7.4 (m, 2H, H2, H11), 7.39–7.3 (m, 2H, H12, H10), 5.9 (s, 1H, H9), 3.95, 3.73, 3.64, 3.55 (4s, 12H, 4CH_3); MS (*m/e*): 464 (M^+, 15%). Anal. for $C_{24}H_{20}N_2O_8$ (464.20): calc., C 62.08, H 4.34, N 6.03; found C 62.08, H 4.18, N 6.05%.

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