Monatshefte für Chemie 115, 1101—1106 (1984)

Monatshefte für Chemie
Chemical Monthly

1,3-Dipolar Cycloaddition Reactions of Benzo[h]naphthyridinium N-Phenacylides

Barbara Bachowska and **Wanda Śliwa***

Institute of Chemistry, Pedagogical University, PL-42-201 Częstochowa, Poland

(Received 24 January 1984. Accepted 29 February 1984)

The 1,3-dipolar cycloaddition reactions of 1,5- and 1,6-benzo[h]naphthyridinium N-phenacylides, formed *in situ* from the appropriate quaternary bromides in basic medium, with acrylonitrile, ethyl acrylate and dimethyl acetylenedicarboxylate were investigated.

(Keywords: Aza-aromatic N-ylides; Cycloaddition, 1,3-dipolar)

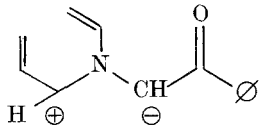
1,3-Dipolare Cycloadditionsreaktionen von Benzo[h]naphthyridinium-N-phenacyliden

Es wurden die 1,3-dipolaren Cycloadditionsreaktionen von 1,5- und 1,6-Benzo[h]naphthyridinium-N-phenacyliden untersucht, die *in situ* aus den entsprechenden quaternären Bromiden in Gegenwart von Alkali dargestellt wurden. Als Dipolarophile wurden Acrylnitril, Ethylacrylat und Acetylendicarbonsäuredimethylester eingesetzt.

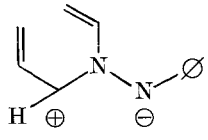
Introduction

The present paper deals with recent results of our research concerning benzo[h]naphthyridines, being of interest with respect to their biological properties[1—3].

Cycloaddition reactions of azaaromatics, e.g. those of unsubstituted systems, as well as of their N-methylides (e.g. **A**) and N-iminoylides (e.g. **B**), reacting as 1,3-dipoles, are a useful synthetic approach to condensed heterocycles[4—9].



A



B

In former studies we have described the cycloaddition reaction of 1,5- and 1,6-benzo[h]naphthyridines (*bn*) and dimethyl acetylene dicarboxylate (*DMAD*)[10], the present work is dealing with 1,3-dipolar cycloaddition of their N-methylides; for this purpose we chose 1,5- and 1,6-*bn* N-phenacylides.

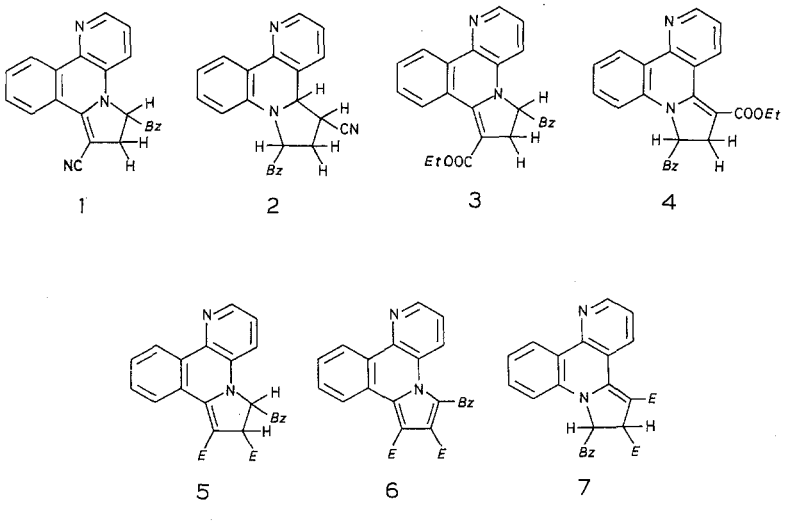
In the cycloadditions, N-ylides may react either as the isolated species, or, usually, they are formed *in situ*; in this case the quaternary salts of azaaromatics, especially bromides, are treated with dipolarophiles in basic medium; in our work we employed the latter method.

The starting materials were 1,5- and 1,6-*bn* phenacyl bromides, obtained by the reaction of benzo[h]naphthyridines with phenacyl bromide[11]. The isomeric 1,5- and 1,6-benzo[h]naphthyridines were accessible from 4-aminoquinoline and 4-aminoisoquinoline, respectively, by the *Skraup* procedure, using arsenic pentoxide as oxidizing agent[2].

The quaternary salts were treated with dipolarophiles—acrylonitrile, ethyl acrylate and *DMAD* in the presence of triethylamine. The reaction of 1,5- and 1,6-*bn* phenacyl bromides with acrylonitrile was performed in *DMF*, while in the case of ethyl acrylate and *DMAD* the reaction accomplished in benzene proved to be more convenient.

Formulae of the obtained cycloadducts **1–7** are shown in Scheme 1.

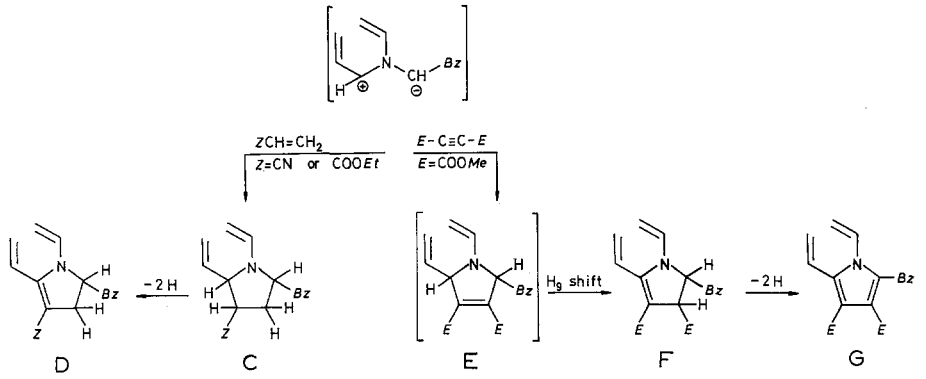
Scheme 1



Results and Discussion

According to a possible mechanism of the cycloaddition reaction of *bn* N-ylides with acrylonitrile and ethyl acrylate in the first step adducts of the type **C** are formed: They are either the end products or they can undergo a dehydrogenation to give the cycloadducts **D** (Scheme 2).

Scheme 2



The cycloaddition of the above ylides with *DMAD* affords as the primary products the unstable compounds of the type **E** leading immediately by a H_9-shift to **F** which may be dehydrogenated to give **G**.

The proposed mechanism of the investigated 1,3-dipolar cycloaddition reactions as shown in Scheme 2, is in accordance with literature data for similar 1,3-dipolar cycloaddition reactions of azaaromatics[12—20], as well as with unpublished results from our laboratory concerning cycloadditions of *bn* N-carboethoxymethylides.

The structures of all compounds obtained were confirmed by ^{1}H-NMR and IR spectroscopy, as well as by MS and elemental analysis data, and are compatible with those of cycloadducts obtained from *bn* N-carboethoxymethylides.

The reaction of 1,5-*bn* N-ylide with acrylonitrile affords a cycloadduct of the type **D**, i.e. 6*H*,7*H*-6-benzoyl-8-cyano-1,5-diazapyrroline[1,2—*f*]phenanthrene (**1**).

For this compound, the structure with a 7,8-double bond can be excluded because of the absence of the H9 singlet. The H6 is coupled with two geminal H7 protons, excluding also the system with a 6,7-double bond; therefore the only acceptable structure is **1**.

The reactions of 1,5- and 1,6-*bn* N-ylides with ethyl acrylate proceed in a similar way, yielding 6*H*,7*H*-6-benzoyl-8-carboethoxy-1,5-

diazapyrroline[1,2—*f*]phenanthrene (**3**) and 7*H*,8*H*-6-carboethoxy-8-benzoyl-1,9-diazapyrroline[2,1—*f*]phenanthrene (**4**).

The coupling constants of H6 in **1** and **3** and those of H8 in **4** are somewhat higher than expected from the *Carplus* curve probably due to the influence of the benzoyl group.

Compounds of the type **1**, **3**, and **4** were formed in cycloaddition reactions of analogous azaaromatic N-ylides as products[12—14], or as intermediates[15,16].

On the other hand, the reaction of 1,6-*bn* N-ylide with acrylonitrile—although carried out under the same conditions as for the isomeric 1,5-*bn* N-ylide—resulted in a product of the type **C**, 6-cyano-8-benzoyl-1,9-diazapyrrolidine[2,1—*f*]phenanthrene (**2**), a similar adduct being formed in the 1,3-dipolar cycloaddition reaction of pyridinium N-phenacylide with this dipolarophile[17].

Cycloaddition reaction with *DMAD* afforded in the case of 1,6-*bn* N-ylide the product of type **F**, 7*H*,8*H*-8-benzoyl-6,7-dicarbomethoxy-1,9-diazapyrroline[2,1—*f*]phenanthrene (**7**), while 1,5-*bn* N-ylide yielded besides the major cycloadduct 6*H*,7*H*-6-benzoyl-7,8-dicarbomethoxy-1,5-diazapyrroline[1,2—*f*]phenanthrene (**5**) also the compound of type **G**, with the probable structure **6** (6-benzoyl-7,8-dicarbomethoxy-1,5-diazapyrrolo[1,2—*f*]phenanthrene), however only in trace amount.

The poor yield of **6** allowed the determination of its structure only on the basis on elemental analysis and MS and IR spectroscopy data.

Compounds analogous to **5** and **7** were formed in 1,3-dipolar cycloaddition reactions of phthalazinium N-methylides with *DMAD*[18], and compounds of the type **6** are products of such cycloadditions of a number of azaaromatic N-ylides[16,19,20].

Experimental Part

Preparative chromatography was performed on 60 G silica gel (Merck) 20 cm × 20 cm plates, and tlc on 60 F 254 silica gel (Merck) precoated DC aluminium sheets. In the column chromatography 100–200 mesh silica gel (POCh Gliwice) was used.

^{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 spectraon a LKB-2091 mass spectrometer. Melting points determined on a *Boëtius* apparatus are uncorrected.

General procedure of the 1,3-dipolar cycloaddition reaction of 1,5- and 1,6-*bn* N-phenacylides with acrylonitrile, ethyl acrylate and *DMAD*.

1,5- or 1,6-*bn* N-phenacyl bromide (379 mg; 1 mmol) in *DMF* (5 ml) or in benzene (15 ml) was treated under anhydrous conditions with dipolarophile—acrylonitrile (106 mg, 0.13 ml; 2 mmol, ethyl acrylate (150 mg, 0.16 ml;

1.5 mmol) or *DMAD* (213 mg, 0.18 ml; 1.5 mmol), and triethylamine (101 mg, 0.14 ml; 1 mmol in the case of *DMF*, or 141 mg, 0.19 ml; 1.4 mmol in the case of benzene.

The mixture was stirred (in DMF at 0°, in benzene at room temperature) for 2 h, and allowed to stand for 12 h; then the formed triethylammonium bromide was filtered off.

In the reaction with acrylonitrile the solution was poured onto water (25 ml), and the precipitated solid was separated and recrystallized.

In the reaction with ethyl acrylate and *DMAD* the solution was treated with *n*-hexane to precipitate the crude product which was filtered off and purified.

All synthesized cycloadducts were obtained in the form of yellow crystals.

1: M.p. 225–226° (from acetone); yield 45%; tlc eluent: benzene—diethyl ether 6/4; IR (cm^{-1}): 2180 (CN), 1680 (CO), 1220 (C—O—C); ^{1}H-NMR (δ, ppm); 8.87 (dd, 1 H, $J_{13,12}$ = 7.5 Hz; $J_{13,11}$ = 2.5 Hz; H13); 8.65 (dd, 1 H, $J_{4,3}$ = 7.5 Hz; $J_{4,2}$ = 2 Hz; H4); 8.43 (d, 1 H, $J_{2,3}$ = 4.5 Hz; H2); 8.25 (d, 2 H, $J_{o,m}$ = 7.5 Hz; 2 Ho); 8.10–7.63 (m, 5 H; 2 Hm, Hp, H11, H12); 7.43 (dd, 1 H, $J_{3,4}$ = 7.5 Hz; $J_{3,2}$ = 4,5 Hz; H3); 6.67 (dd, 1 H, $J_{6,7b}$ = 15 Hz; $J_{6,7a}$ = 5 Hz; H6); 4.12–3.60 (m, 1 H, H7a); 3.30–2.78 (m, 1 H, H7b); MS (M^+): 349 (69%); elem. anal. for $C_{23}H_{15}N_3O$ (349.38): calc. C 79.06; H 4.33; N 12.03; found C 78.89; H 4.16; N 12.07.

2: M.p. 174–175°, purified by dissolving the crude product in *DMF* at room temp. and precipitated with diethyl ether; yield 37%; tlc eluent: chloroform; IR (cm^{-1}): 2240 (CN), 1680 (CO), 1215 (C—O—C); ^{1}H-NMR (δ, ppm): 8.75 (d, 1 H, $J_{2,3}$ = 4.5 Hz; H2); 8.50–8.22 (m, 3 H, 2 Ho, H13); 8.00–7.60 (m, 4 H; 2 Hm, Hp, H4); 7.52 (dd, 1 H, $J_{3,4}$ = 7.5 Hz; $J_{3,2}$ = 4.5 Hz; H3; 7.25 (t, 1 H, $J_{11,10}$ = $J_{11,12}$ = 7.5 Hz; H11); 6.87 (t, 1 H, $J_{12,11}$ = $J_{12,13}$ = 7.5 Hz; H12); 6.25 (d, 1 H, $J_{10,11}$ = 7.5 Hz; H10; 6.10–5.82 (m, 1 H, H8); 5.55 (d, 1 H, $J_{5,6}$ = 4.5 Hz, H5); 4.52–4.20 (m, 1 H, H6); 3.22–3.02 (m, 1 H, H7a); 2.50–2.20 (m, 1 H, H7b); MS (M^+): 351 (9%); elem. anal. for $C_{23}H_{17}N_3O$ (351.40): calc. C 78.61; H 4.88; N 11.96; found C 78.80; H 5.02; N 12.00

3: M.p. 199–200° (from acetone); yield 51%; tlc eluent: benzene—diethyl ether 4/1; IR (cm^{-1}): 1690 (CO), 1660 (COO*Et*), 1275, 1200 (C—O—C); ^{1}H-NMR (δ, ppm): 9.78 (d, 1 H, $J_{13,12}$ = 7.5 Hz; H13); 8.90 (d, 1 H, $J_{4,3}$ = 7.5 Hz; H4); 8.42 (d, 1 H, $J_{2,3}$ = 4.5 Hz; H2); 8.28 (d, 2 H, $J_{o,m}$ = 7.5 Hz; 2Ho); 8.15–7.62 (m, 5 H; 2 Hm, Hp, H11, H12); 7.42 (dd, 1 H, $J_{3,4}$ = 7.5 Hz; $J_{3,2}$ = 4.5 Hz; H3); 7.20 (d, 1 H, $J_{10,11}$ = 7.5 Hz; H 10); 6.55 (dd, 1 H, $J_{6,7b}$ = 15 Hz; $J_{6,7a}$ = 5 Hz; H6; 4.20 (q, 2 H, J = 7.5 Hz; CH_2); 4.10–ca. 3.50 (m, 1 H; H7a; overlapping with H_2O); 3.22–ca. 2.70 (m, 1 H; H7b; overlapping with *DMSO*); 1.32 (t, 3 H, J = 7.5 Hz; CH_3); MS (M^+): 396 (100%); elem. anal. for $C_{25}H_{20}N_2O_3$ (396.43): calc. C 75.74; H 5.08; N 7.07; found C 75.62; H 4.90; N 6.99.

4: M.p. 184–185° (from benzene or acetone), yield 28%; tlc eluent: benzene—methanol 95/5 or benzene—diethyl ether 9/1; IR (cm^{-1}): 1690 (CO); 1650 (COO*Et*); 1270, 1220 (C—O—C); ^{1}H-NMR (δ, ppm): 10.25 (d, 1 H, $J_{13,12}$ = 7.5 Hz; H13); 9.05 (d, 1 H, $J_{2,3}$ = 4.5 Hz; H2); 8.72 (dd, 1 H, $J_{4,3}$ = 8 Hz; $J_{4,2}$ = 2 Hz; H4); 8.3 (d, 2 H, $J_{o,m}$ = 7.5 Hz; 2 Ho); 8.00–7.42 (m, 5 H; 2 Hm, Hp, H3, H11); 7.25 (t, 1 H, $J_{12,11}$ = $J_{12,13}$ = 7.5 Hz; H12); 6.82 (dd, 1 H, $J_{10,11}$ = 7.5 Hz; $J_{10,12}$ = 2 Hz; H10); 6.60 (dd, 1 H, $J_{8,7b}$ = 15 Hz; $J_{8,7a}$ = 5 Hz; H8); 4.22 (q, 2 H, J = 7.5 Hz; CH_2); 4.00–ca. 3.50 (m, 1 H, H7a; overlapping with H_2O); 3.20–2.72 (m, 1 H, H7b); 1.30 (t, 3 H, J = 7.5 Hz; CH_3); MS (M^+): 396 (36%); elem. anal. for $C_{25}H_{20}N_2O_3$ (396,43): calc. C 75.74; H 5.08; N 7.07; found C 75.69; H 4.92; N 7.07.

5 and **6**: the crude product was separated by preparative chromatography (chloroform as eluent).

5: M.p. 224–225° (from benzene); yield 30.5%; tlc eluent: chloroform; IR (cm^{-1}): 1730 (CO), 1660 (COO*Me*), 1240, 1210 (C—O—C); ^{1}H-NMR (δ, ppm); 10.00 (d, 1H, $J_{13,12}$ = 7.5 Hz; H13); 9.05 (dd, 1H, $J_{4,3}$ = 7.5 Hz; $J_{4,2}$ = 2 Hz; H4); 8.72–8.30 (m, 3H; 2Ho, H2); 8.20–7.72 (m, 5H; 2Hm, Hp, H11, H12); 7.70–7.41 (m, 2H; H3, H10); 6.95 (d, 1H, $J_{6,7}$ = 2.5 Hz; H6); 4.13 (d, 1H, $J_{7,6}$ = 2.5 Hz; H7); 3.92 (s, 3H; CH_3); 3.70 (s, 3H; CH_3).

6: M.p. 259–260° (from benzene); yield 1.7%; tlc eluent: chloroform; IR (cm^{-1}): 1730 (CO), 1670 (COO*Me*), 1260, 1220 (C—O—C); MS (M^+): 438 (100%); elem. anal. for $C_{26}H_{18}N_2O_5$ (438.44): calc. C 71.22; H 4.14; N 6.39; found C 70.99; H 4.03; N 6.35.

7: M.p. 114–115°; the crude product was column chromatographed (with chloroform as eluent), and then purified by preparative chromatography (with benzene—ether 9/1 as eluent), followed by recrystallisation from benzene; yield 24.5%; tlc eluent: chloroform; IR (cm^{-1}): 1720 (CO), 1670 (COO*Me*), 1260, 1220 (C—O—C); ^{1}H-NMR (δ, ppm): 10.30 (d, 1H, $J_{13,12}$ = 8 Hz; H13); 9.12 (d, 1H, $J_{2,3}$ = 5 Hz; H2); 8.80 (d, 1H, $J_{4,3}$ = 8 Hz; H4); 8.43 (d, 2H, $J_{o,m}$ = 5 Hz; 2Ho); 8.00–7.40 (m, 6H; 2Hm, Hp, H3, H11, H12); 7.22–6.90 (m, 2H; H8, H10); 4.05 (d, 1H, $J_{7,8}$ = 2.5 Hz; H7); 3.90 (s, 3H; CH_3); 3.68 (s, 3H; CH_3); MS (M^+): 440 (25,5%); elem. anal. for $C_{26}H_{20}N_2O_5$ (440.44): calc. C 70.90; H 4.58; N 6.36; found C 70.72; H 4.67; N 6.16.

References

[1] *Śliwa W.*, Pol. J. Chem. **52**, 271 (1978).
[2] *Śliwa W.*, Prace Nauk. Inst. Chem. Org. i Fiz. Politech. Wrocł., 1978, 13, Stud. i Mat., No. 8.
[3] *Śliwa W., Zamarlik H.*, Heterocycles **12**, 529 (1979).
[4] *Huisgen R., Gambra F. P.*, Chem. Ber. **115**, 2242 (1982).
[5] *Acheson R. M., Elmore N. F.*, Adv. Het. Chem., Vol. 23, 263. New York: Academic Press. 1978.
[6] *Abramovitch R. A., Grims G., Rogers R. B., Shinkai J.*, J. Amer. Chem. Soc. **98**, 5671 (1976).
[7] *Katritzky A. R., Dennis N., Sabongi G. J., Turker L.*, J. Chem. Soc., Perkin 1 **1979**, 1525.
[8] *Śliwa W.*, Heterocycles **14**, 1793 (1980).
[9] *Śliwa W.*, Wiad. Chem. **35**, 833 (1981); **36**, 231, 631 (1982).
[10] *Śliwa W., Postawka A.*, J. prakt. Chem. **325**, 157 (1983).
[11] *Śliwa W.*, Pol. J. Chem. **55**, 2199 (1981).
[12] *Kato T., Chiba T., Tanaka S.*, J. Het. Chem. **13**, 461 (1976).
[13] *Kato T., Chiba T., Tanaka S., Sasaki T.*, Heterocycles, **11** Spec., 227 (1978).
[14] *Zugravescu I., Constantinescu M., Surpateanu G., Leblanche-Combier A., Devos L.*, Rev. Roum. Chim. **24**, 1089 (1978).
[15] *Terientiev P. B., Vinogradova S. M., Kost A.*, Chim. Giet. Sojed. **1980**, 651.
[16] *Sasaki T., Kanematsu K., Kakehi A., Ito G.*, Tetrahedron **28**, 4947 (1972).
[17] *Fröhlich J., Kröhnke F.*, Chem. Ber. **104**, 1621 (1971).
[18] *Petrovanu M., Caprosu M., Stefanescu E., Stavri N.*, Rev. Med.-Chir. **86**, 141 (1982).
[19] *Linn W. J., Webster O. W., Benson R. E.*, J. Amer. Chem. Soc. **87**, 3651 (1965).
[20] *Sasaki T., Kanematsu K., Yukimoto Y., Ochiai S.*, J. Org. Chem. **36**, 813 (1971).