A directive effect of heterofunctions in cyclocondensation reactions of acetylenylquinones with hydrazine

Igor I. Barabanov, Irina D. Ivanchikova and Mark S. Shvartsberg*

Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation. Fax: +7 3832 34 2350; e-mail: shvarts@kinetics.nsc.ru

10.1070/MC2000v010n05ABEH001353

The heterocycle formed in the cyclocondensation reactions of 2-acetylenyl-1-chloro-9,10-anthraquinones or 5-acetylenyl-3-diethylamino-1,4-naphthoquinones with NH_2NH_2 is influenced by the presence of a heterofunction, *e.g.* a hydroxyl group, in the acetylenic substituent; this directive effect was used for the synthesis of naphtho[2,3-*h*]cinnoline-4,7,12-trione and 4*H*-naphtho[1,8-*cd*]-1,2-diazepin-8-one derivatives.

Acetylenic derivatives of cinnoline and benzene with a labile chlorine atom at the *ortho* position react with hydrazine to close a pyrazole ring.[1–3] When continuing our studies of the heterocyclization of acetylenylquinones,[4–9] we carried out this condensation in the anthraquinone series.

In 2-acetylenyl-1-chloro-9,10-anthraquinones **1**, the halogen atom is readily substituted by nucleophilic groups,[10] and the triple bond activated by the quinone nucleus is efficiently attacked by N-nucleophiles.[11] This attack is directed onto the β-C atom of the triple bond. Therefore, we supposed that the cyclocondensation of **1** with NH_2NH_2 will result in the formation of a six-membered diazine ring rather than a five-membered diazole ring as in the above reactions.[1–3] In addition, competitive heterocyclization with the participation of the *peri*-carbonyl group can play a noticeable role.

We found that anthraquinones **1** easily condense with NH_2NH_2 (pyridine, 90–115 °C). Compounds **1a**,**b** with no heteroatomic groups in their acetylenic substituents are transformed to only pyrazole derivatives. Compound **1a** gives a mixture of 3-phenylethynyldibenzo[*cd*,*g*]indazol-6-one **2a**† and 3-benzylnaphtho-[2,3-*g*]indazole-6,11-dione **3a**† (~2:1) in 66% yield. The main product obtained from **1b** is pyrazoloanthrone **2b**† (45% yield).

However, the reaction route is changed when starting quinone **1** has a hydroxyl group at the γ-C atom of its side chain. The condensation product of **1c** was found to be 1,2-dihydro-3-(1-hydroxy-1-methylethyl)naphtho[2,3-*h*]cinnoline-7,12-dione **4c**. This compound is reactive and can undergo transformations in the course of its isolation and purification.

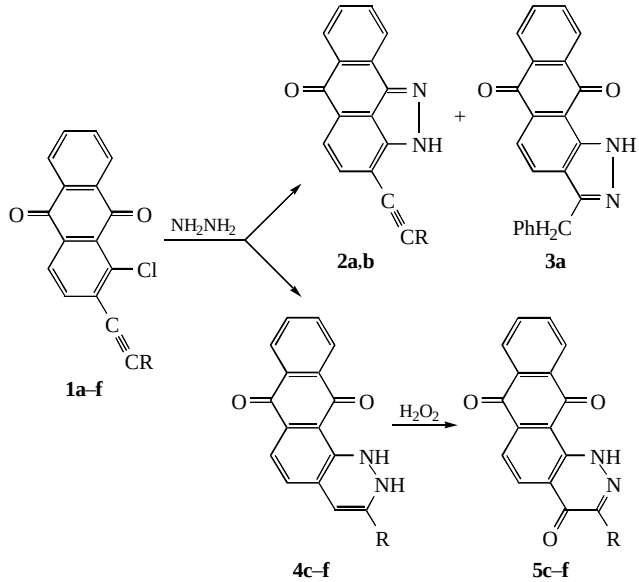
We found that H_2O_2 readily oxidises **4c** to naphthocinnoline-trione **5c** (possibly, *via* the tautomeric 4*H*-form) and developed the one-pot synthesis of **5c** starting from **1c** (85% yield). This procedure was applied to the heterocyclization of ether **1d** and alcohols **1e**,**f**. The formation of **4d**–**f** was monitored by TLC. The routes of reactions are the same as for **1c** and lead to anthraquinones fused with a pyridazine ring **5d**–**f**.†

Thus, heterofunctions (a hydroxyl or alkoxy group) at the γ-C atom of the acetylenic substituents facilitate the participation of the triple bond in the formation of a heterocycle and the attack on the β-C atom of this substituent by the nucleophile.

A similar specific effect of heterofunctions has been observed in another reaction, the cyclocondensation of *peri*-acetylenylquinones with NH_2NH_2.

Recently, we reported the cyclocondensation of 3-diethylamino-5-phenylethynyl-1,4-naphthoquinone **6a** with hydrazine.[9] This reaction results in the closure of a six-membered pyridazine ring and affords **7a**. Unlike **6a**, *peri*-acetylenyl-9,10-anthraquinones with NH_2NH_2 form a seven-membered diazepine ring to give 4*H*-anthra[9,1-*cd*]-1,2-diazepin-8-ones **8**.[4]

To prepare previously unknown interesting heterocyclic system of 4*H*-naphtho[1,8-*cd*]-1,2-diazepin-8-one, we attempted to change the direction of the cyclocondensation of 5-acetylenyl-3-diethylamino-1,4-naphthoquinones **6** with the use of orienting heterofunctions. Quinones **6b**–**d** (hydroxyacetylenyl analogues



Scheme 1

† All new compounds gave satisfactory microanalytical and spectroscopic data.

2a: mp 281–283 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 7.40–7.50 (m, 3H, Ph), 7.50–7.75 (m, 4H, Ph, H^{8,9}), 7.80 (d, 1H, H$^{4(5)}$, *J* 7.5 Hz), 8.05 (d, 1H, H$^{5(4)}$, *J* 7.5 Hz), 8.27 (d, 1H, H$^{7(10)}$, *J* 7.6 Hz), 8.46 (d, 2H, H$^{10(7)}$, *J* 8.1 Hz).

2b: mp 170.5–171 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.90 (t, 3H, Me, *J* 6.8 Hz), 1.20–1.55 (m, 4H, MeCH_2CH_2), 1.60–1.75 (m, 2H, $CH_2CH_2C\equiv$), 2.52 (t, 2H, $CH_2C\equiv$, *J* 7.0 Hz), 7.59 (d, 1H, H$^{4(5)}$, *J* 7.4 Hz), 7.50–7.80 (m, 2H, H^{8,9}), 7.98 (d, 1H, H$^{5(4)}$, *J* 7.4 Hz), 8.26 (d, 1H, H$^{7(10)}$, *J* 7.2 Hz), 8.48 (d, 1H, H$^{10(7)}$, *J* 8.1 Hz).

3a: mp 224–225 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 4.41 (s, 2H, CH_2), 7.30–7.35 (m, 5H, Ph), 7.75–7.85 (m, 2H, H^{8,9}), 7.86 (d, 1H, H$^{4(5)}$, *J* 8.6 Hz), 7.97 (d, 1H, H$^{5(4)}$, *J* 8.6 Hz), 8.25–8.40 (m, 2H, H^{7,10}), 11.70 (br. s, 1H, NH).

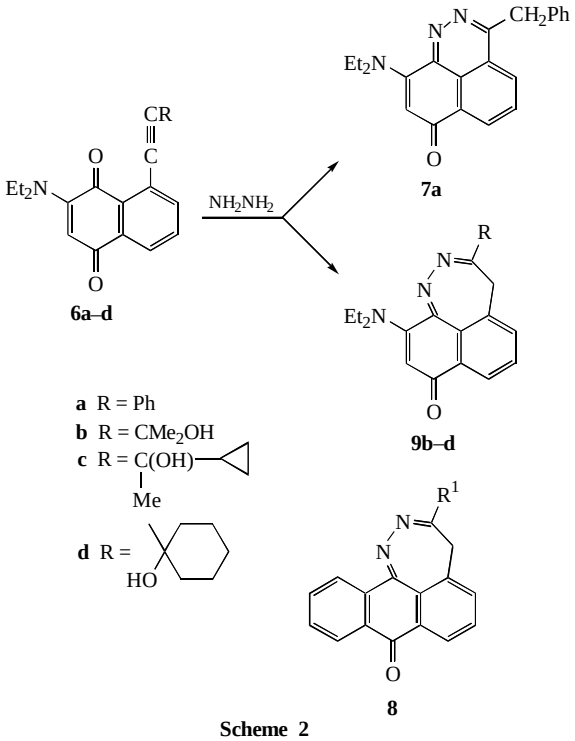
4c: mp 216.5–218.5 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.83 (s, 6H, Me), 7.80–7.95 (m, 3H, H$^{5(6),9,10}$), 8.12 (s, 1H, H^4), 8.22 (d, 1H, NH$^{1(2)}$, *J* 8.6 Hz), 8.25–8.45 (m, 3H, H$^{6(5),8,11}$), 8.65 (d, 1H, NH$^{2(1)}$, *J* 8.6 Hz).

5c: yield 85.2%, mp 209–211 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.70 (s, 6H, Me), 7.80–7.95 (m, 2H, H^{9,10}), 8.28 (d, 1H, H$^{5(6)}$, *J* 8.3 Hz), 8.25–8.40 (m, 2H, H^{8,11}), 8.73 (d, 1H, H$^{6(5)}$, *J* 8.3 Hz), 13.70 (br. s, 1H, NH).

5d: yield 53.5%, mp 224–226 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 1.72 (s, 6H, Me), 3.30 (s, 3H, OMe), 7.75–7.95 (m, 2H, H^{9,10}), 8.24 (d, 1H, H$^{5(6)}$, *J* 8.3 Hz), 8.15–8.40 (m, 2H, H^{8,11}), 8.71 (d, 1H, H$^{6(5)}$, *J* 8.3 Hz), 13.61 (br. s, 1H, NH).

5e: yield 46.7%, mp 227–228.5 °C. ^{1}H NMR (250 MHz, $CDCl_3$) δ: 0.99 (d, 3H, Me, *J* 6.7 Hz), 1.01 (d, 3H, Me, *J* 6.7 Hz), 2.36 (m, 1H, C*H*Me$_2$), 2.77 (br. s, 1H, OH), 4.69 (d, 1H, OCH, *J* 6.0 Hz), 7.70–8.10 (m, 2H, H^{9,10}), 8.27 (d, 1H, H$^{5(6)}$, *J* 8.4 Hz), 8.15–8.55 (m, 2H, H^{8,11}), 8.69 (d, 1H, H$^{6(5)}$, *J* 8.4 Hz), 13.74 (br. s, 1H, NH).

5f: yield 38.8%, mp >275 °C (decomp.). ^{1}H NMR (250 MHz, $CDCl_3$) δ: 4.88 (s, 2H, CH_2), 7.85–7.95 (m, 2H, H^{9,10}), 8.29 (d, 1H, H$^{5(6)}$, *J* 8.4 Hz), 8.25–8.40 (m, 2H, H^{8,11}), 8.72 (d, 1H, H$^{6(5)}$, *J* 8.4 Hz), 13.78 (br. s, 1H, NH).



Scheme 2

of **6a**) were condensed with NH_2NH_2 under the same conditions as in the cyclization of **6a** (pyridine, 115 °C). Hydroxyacetylenylquinones **6b**–**d** were found to yield 3-substituted naphthodiazepinones **9b**–**d**.‡ The reaction was accompanied by the formation of by-products and resins. Nevertheless, the yields of purified **9b**–**d** were 53–56%.

‡ **9b**: mp 88–89 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.28 (t, 6H, *Me*CH_2, *J* 7.0 Hz), 1.43 (s, 3H, Me), 1.55 (s, 3H, Me), 2.78 (d, 1H, H^4_a, *J* 12.7 Hz), 3.91 (d, 1H, H^4_b, *J* 12.7 Hz), 3.45–3.65 (m, 4H, NCH_2), 3.85 (br. s, 1H, OH), 5.69 (s, 1H, H^9), 7.32 (d, 1H, H^5, *J* 7.6 Hz), 7.56 (t, 1H, H^6, *J* 7.6 Hz), 7.92 (d, 1H, H^7, *J* 7.6 Hz).

9c: mp 156–157 °C (a mixture of diastereomers). ^{1}H NMR (200 MHz, $CDCl_3$) δ: –0.20–0.15, 0.30–0.70 and 0.80–1.00 (3m, 5H, cyclopropyl), 1.20–1.40 and 1.54 (m and s, 9H, *Me*CH_2, *Me*COH), 2.90 (d, 1H, H^4_a, *J* 12.6 Hz), 3.91 (d, 1H, H^4_b, *J* 12.6 Hz), 3.45–3.65 (m, 4H, NCH_2), 3.73 (br. s, 1H, OH), 5.74 (s, 1H, H^9), 7.31 and 7.35 (2d, 1H, H^5), 7.58 and 7.62 (2t, 1H, H^6), 8.03 and 8.06 (2d, 1H, H^7).

9d: mp 123–125 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.29 (t, 6H, Me, *J* 7.0 Hz), 1.40–2.00 (m, 10H, cyclohexyl), 2.73 (d, 1H, H^4_a, *J* 12.7 Hz), 3.95 (d, 1H, H^4_b, *J* 12.7 Hz), 3.30 (br. s, 1H, OH), 3.40–3.65 (m, 4H, NCH_2), 5.72 (s, 1H, H^9), 7.35 (d, 1H, H^5, *J* 7.5 Hz), 7.59 (t, 1H, H^6, *J* 7.5 Hz), 8.00 (d, 1H, H^7, *J* 7.5 Hz).

Thus, in the cyclocondensation of *peri*-acetylenyl-1,4-naphthoquinones **6** as well as in the above reaction of 2-acetylenyl-1-chloro-9,10-anthraquinones **1** with NH_2NH_2, the hydroxyl group of a substituent directs the attack of the N-nucleophile onto the β-C of this substituent.

It is well known that the regio- or stereoselectivity of reactions such as the lithiation of aromatic compounds and the epoxidation of allyl alcohols is determined by the association of a substrate with a reagent.[12,13]

We suppose that the directive effect of heterofunctions in the hydrazine cyclocondensations also belongs to this range of phenomena and can be explained by the association of the function with NH_2NH_2 by hydrogen bonds.

Note that the reactions considered offer ways for the synthesis of new condensed heterocyclic systems.

This work was supported by the Russian Foundation for Basic Research (grant no. 98-03-32945).

References

1 D. E. Ames and D. Bull, *Tetrahedron*, 1982, **38**, 383.
2 S. F. Vasilevsky and T. A. Prikhod'ko, *Mendeleev Commun*., 1996, 98.
3 T. A. Prikhod'ko and S. F. Vasilevsky, *Mendeleev Commun*., 1998, 149.
4 M. S. Shvartsberg, I. D. Ivanchikova and S. F. Vasilevsky, *Tetrahedron Lett*., 1994, **35**, 2077.
5 M. S. Shvartsberg, I. D. Ivanchikova and L. G. Fedenok, *Tetrahedron Lett*., 1994, **35**, 6749.
6 A. V. Piskunov and M. S. Shvartsberg, *Mendeleev Commun*., 1995, 155.
7 M. S. Shvartsberg, I. I. Barabanov and L. G. Fedenok, *Mendeleev Commun*., 1997, 98.
8 L. G. Fedenok, I. I. Barabanov and I. D. Ivanchikova, *Tetrahedron Lett.*, 1999, **40**, 805.
9 M. S. Shvartsberg and I. D. Ivanchikova, *Tetrahedron Lett*., 2000, **41**, 771.
10 M. V. Gorelik, *Khimiya antrakhinona i ego proizvodnykh* (*Chemistry of Anthraquinones and their Derivatives*), Khimiya, Moscow, 1983, p. 203 (in Russian).
11 A. V. Piskunov, A. A. Moroz and M. S. Shvartsberg, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1986, 864 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1986, **35**, 785).
12 E. N. Prilezhaeva, *Reaktsiya Prilezhaeva. Elektrofil'noe okislenie* (*The Prilezhaev Reaction. Electrophilic Oxidation*), Nauka, Moscow, 1974, p. 167 (in Russian).
13 L. Brandsma and H. D. Verkruijsse, *Preparative Polar Organometallic Chemistry*, Springer–Verlag, Berlin, 1987, vol. 1, p. 186.

Received: 30th June 2000; Com. 00/1679