



Pergamon

Tetrahedron Letters 41 (2000) 5757–5760

TETRAHEDRON
LETTERS

An unusual heterocyclization of 2,3-diacetylenyl-1,4-naphthoquinones

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Received 26 October 1999; revised 26 May 2000; accepted 2 June 2000

Abstract

Cyclocondensation of 2,3-diacetylenyl-1,4-naphthoquinones with NH_2NH_2 affords 1,3-disubstituted 2*H*-*N*-aminobenzof[*f*]isoindole-4,9-diones. © 2000 Published by Elsevier Science Ltd.

Keywords: 2,3-diacetylenyl-1,4-naphthoquinones; hydrazine; reductive cyclocondensation; 1,3-disubstituted 2*H*-2-aminobenzof[*f*]isoindole-4,9-diones.

Acetylenic derivatives of quinones are synthons for a variety of fused quinonoid heterocycles.¹ The latter are of interest as potentially bioactive substances and components of new technical materials.

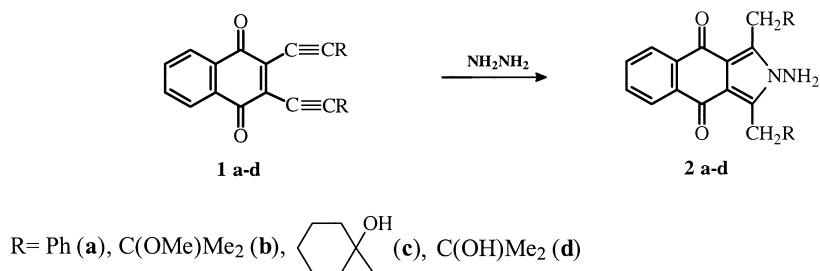
Acetylenylquinones were shown to undergo addition of *N*-nucleophiles to the triple bond.² This feature was used to construct *peri*-condensed polycyclic structures including 7- or 6-membered nitrogenous heterocycles by condensation of acetylenic derivatives of anthraquinone and naphthoquinone with NH_2NH_2 .³ In this paper a novel hydrazine cyclocondensation in the acetylenyl-naphthoquinone series is reported.

We have found that 2,3-diacetylenyl-1,4-naphthoquinones **1a–d** react with NH_2NH_2 (dioxane, 50–60°C, 30–60 min) to give 1,3-disubstituted 2*H*-*N*-aminobenzof[*f*]isoindole-4,9-diones **2a–d**⁴ in 53–80% yield (Scheme 1).

In ¹H NMR spectra of **2a–d** there are singlets at δ 3.28–4.57 ppm for the four protons of the two α -methylene groups of the symmetrically disposed side-chains and signals of doubled intensity for protons of the group R inserted into each of these chains. Singlets at δ 4.22–4.50 ppm as well as two absorption bands at 3280–3305 and 3365–3380 cm^{-1} in the IR spectra of **2** show that these compounds **2** have a primary amino group and therefore the *N*-aminopyrrole ring. The ¹³C NMR spectra contain signals at δ 115–118 and 135–137 ppm for the carbon atoms of the pyrrole ring and are in complete accordance with the structures of the products **2**.

The structure of 2*H*-2-amino-1,3-dibenzylbenzof[*f*]isoindole-4,9-dione **2a** was studied in more detail. The presence of the benzyl and amino substituents in **2a** was confirmed by its mass spectrum

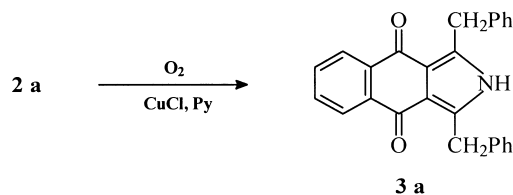
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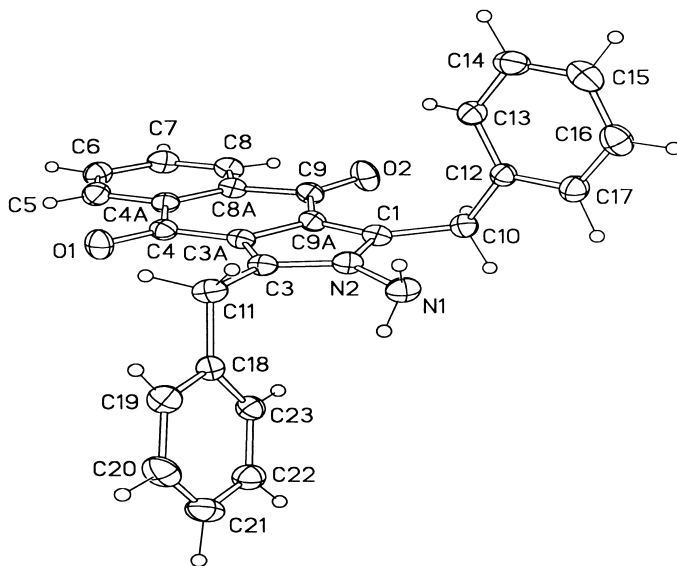
Scheme 1.

which contained intensive peaks corresponding to the ions PhCH₂ (91), [M–PhCH₂] (301) and [M–NH₂] (376).

In addition, the *N*-aminoisoindole **2a** was exposed to oxidative deamination under the conditions proposed for the deamination of *N*-aminolactams (O₂, pyridine, CuCl, 20°C).^{3c} The formation of 2*H*-1,3-dibenzylbenzo[*f*]isoindole-4,9-dione **3a**⁴ under these conditions in 35% yield witnesses to the fact that the products **2** do contain *N*-amino groups. The ¹H and ¹³C NMR spectra of **3a** are like those of **2a**, but the ¹H NMR spectrum includes, instead of the signal for NH₂, a broad singlet at 8.40 ppm for the NH group (Scheme 2).



Scheme 2.

Figure 1. X-Ray crystal structure of **2a**

An X-ray crystal structure analysis of **2a**⁵ unambiguously proved its chemical structure (Fig. 1). The 2*H*-benzoisindole-4,9-dione fragment of a molecule of **2a** is planar within $\pm 0.067(3)$ Å. Deviation of the amine N(1) atom from this plane is equal to 0.172(4) Å.

The cyclocondensation of diacetylenylquinones **1** with NH_2NH_2 is unusual. It results in the formation of bonds between the α -carbons of the acetylenic substituents and an N atom of NH_2NH_2 , whereas an attack of *N*-nucleophiles is directed, as a rule, at β -carbon of these substituents.² To explain this contradiction we propose that the reaction begins with reduction of the enediyne system of the starting compounds **1** and proceeds via intermediates of a type **4** (Fig. 2) which add NH_2NH_2 to give the products **2**.

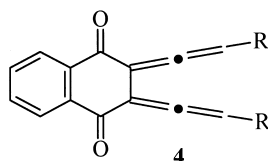


Figure 2.

In conclusion, heterocyclization of 2,3-diacetylenic derivatives of 1,4-naphthoquinone **1** under the action of NH_2NH_2 offers a way for synthesis of substituted 2*H*-2-aminobenzo[*f*]isindole-4,9-diones **2**, a new group of condensed heterocyclic compounds.

Acknowledgements

We thank the referee of this paper for helpful comments. Financial support from the Russian Foundation for Basic Research through Grant No. 98-03-32945a is acknowledged.

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- All compounds gave satisfactory analytical and spectroscopic data. **2a**: yield 80%; m.p. 189–191°C; ¹H NMR (CDCl₃, 250 MHz): δ 4.22 (s, 2H, NH₂), 4.57 (s, 4H, CH₂), 7.15–7.30 (m, 10H, Ph), 7.65–7.75 (m, 2H, H^{6,7}), 8.20–8.30 (m, 2H, H^{5,8}); ¹³C NMR (CDCl₃, 125 MHz): δ 30.1 (CH₂), 115.6, 135.8, 137.4, 138.3 (C arom.), 126.5, 126.6, 128.2, 128.7, 132.7 (CH arom.), 180.6 (C=O); IR (CHCl₃): cm⁻¹ 1660 (C=O), 3305, 3380 (NH₂). **2b**: yield 53%; m.p. 134–136°C; ¹H NMR: 1.27 (s, 12H, CH₃), 3.20 (s, 6H, OCH₃), 3.46 (s, 4H, CH₂), 4.50 (br. s, 2H, NH₂), 7.55–7.70 (m, 2H, H^{6,7}), 8.10–8.25 (m, 2H, H^{5,8}); IR: 1660 (C=O), 3280, 3365 (NH₂). **2c**: yield 75%; m.p. 237–239°C; ¹H NMR (benzene-*d*₆): 1.25–1.65 (m, 20H, cyclo-C₆H₁₀), 3.03 (br. s, 1H, OH), 3.28 (s, 4H, CH₂), 4.76 (s, 1H, OH),

7.05–7.30 (m, 2H, H^{6,7}), 8.35–8.50 (m, 2H, H^{5,8}); IR: 1660 (C=O), 3360, ~3400 (NH₂, OH, H-bond). **2d**: yield 72%; m.p. 207–209°C; ¹H NMR: 1.37 (s, 12H, CH₃), 2.55 (br. s, 4H, NH₂, OH), 3.40 (s, 4H, CH₂), 7.60–7.70 (m, 2H, H^{6,7}), 8.10–8.25 (m, 2H, H^{5,8}); ¹³C NMR (dioxane-*d*₈): 30.0 (CH₃), 38.1 (CH₂), 73.5 (C-OH), 117.2, 136.9, 137.5 (C arom.), 127.1, 133.2 (CH arom.), 180.9 (C=O). **3a**: m.p. 185–186°C; ¹H NMR: 4.42 (s, 4H, CH₂), 7.15–7.35 (m, 10H, Ph), 7.65–7.75 (m, 2H, H^{6,7}), 8.20–8.30 (m, 2H, H^{5,8}), 8.40 (br. s, 1H, NH); ¹³C NMR (CDCl₃): 32.7 (CH₂), 117.7, 136.0, 136.8, 137.0 (C arom.), 126.6, 127.0, 128.6, 128.8, 132.8 (CH arom.), 181.2 (C=O).

5. The X-ray analysis for compound **2a** was performed on a Bruker P4 diffractometer using Mo-K α radiation with a graphite monochromator. The crystals are monoclinic: $a = 5.6178(3)$, $b = 16.3014(9)$, $c = 10.9637(6)$ Å, $\beta = 101.832(4)^\circ$, $V = 982.8(1)$ Å³, space group $P2_1$, $Z = 2$, $C_{26}H_{20}N_2O_2$, $M = 392.44$, $F(000) = 412$, $\mu = 0.085$ mm⁻¹, $d_{\text{calc}} = 1.326$ g cm⁻³, crystal size 0.5×0.4×0.35 mm. The intensities of 1807 independent reflections with $2\theta < 50^\circ$ were measured using the $\theta/2\theta$ scanning technique. The structure was solved by a direct method using the SHELXS-97 program and refined by the least squares method in a full-matrix anisotropic–isotropic (for hydrogen atoms) approximation using the SHELXL-97 program to $wR_2 = 0.0852$, $S = 1.005$ for 1807 reflections ($R = 0.0321$ for 1603 reflections with $I > 2\sigma$). The positions of hydrogen atoms were obtained from difference Fourier synthesis.