Provided for non-commercial research and educational use only.
Not for reproduction or distribution or commercial use.

This article was originally published in a journal published by Elsevier in cooperation with Mendeleev Communications, and the attached copy is provided for the author's benefit and for the benefit of the author's institution, for non-commercial research and educational use including without limitation use in instruction at your institution, sending it to specific colleagues that you know, and providing a copy to your institution's administrator.

All other uses, reproduction and distribution, including without limitation commercial reprints, selling or licensing copies or access, or posting on open internet sites, your personal or institution's website or repository, are prohibited. For exceptions, permission may be sought for such use through Elsevier's permissions site at:

http://www.elsevier.com/locate/permissionusematerial

Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2016, **26**, 174–176

Mendeleev Communications

Synthesis of 2-octyloxy-7*H*-benzo[*e*]perimidin-7-one and 3-substituted 3*H*-benzo[*e*]perimidine-2,7-diones

Denis S. Baranov*[a,b] and Dmitry S. Fadeev[c]

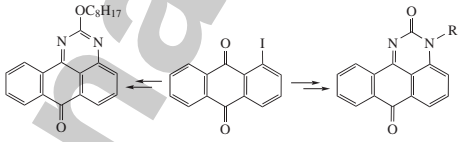
[a] *V. V. Voevodsky Institute of Chemical Kinetics and Combustion, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation. Fax: +7 383 330 7350; e-mail: baranov@kinetics.nsc.ru*

[b] *Novosibirsk State University, 630090 Novosibirsk, Russian Federation*

[c] *N. N. Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 630090 Novosibirsk, Russian Federation*

DOI: 10.1016/j.mencom.2016.03.032

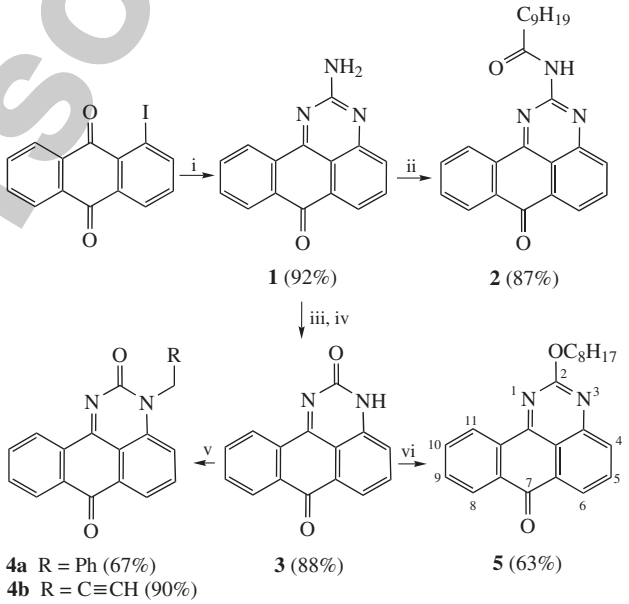
New 2-octyloxy-7*H*-benzo[*e*]perimidin-7-one and 3-benzyl- or 3-propargyl-3*H*-benzo[*e*]perimidine-2,7-diones were synthesized from 1-iodoanthraquinone. The propargyl derivative was subjected to Mannich and cycloaddition reactions.



Benzoperimidines are promising materials for medicinal chemistry.[1] Their structure is close to that of oxoisoaporphines which exhibit various biological activity.[2] A few methods available for constructing a benzoperimidine skeleton are reported.[3] The diversity within this chemotype is renewed mainly by introducing various substitutes into the polycondensed nucleus.[1,4] Note that the methods for N-substituted benzoperimidinedione synthesis are rather scarce.[5] Here we report a novel approach to 2-R-7*H*-benzo[*e*]perimidin-7-ones and 3-R-1*H*,7*H*-benzo[*e*]perimidine-2,7-diones.

As a starting compound, we used 2-amino-7*H*-benzo[*e*]perimidin-7-one **1** prepared by condensation of guanidine with 1-iodoanthraquinone in pyridine under Ullman conditions (Scheme 1).†

Aminoperimidine **1** is readily acylated with decanoyl chloride in boiling pyridine in 87% yield.‡ However, amide **2** is not stable.



4a R = Ph (67%)
4b R = C≡CH (90%)

Scheme 1 *Reagents and conditions*: i, $(NH_2)_2CNH·HCl$, CuI, K_2CO_3, Py, reflux, 4 h; ii, $C_9H_{19}C(O)Cl$, Py, reflux, 20 min; iii, H_2SO_4, $NaNO_2$, AcOH, 1 h; iv, H_2O; v, $ClCH_2R$, K_2CO_3, dibenzo-18-crown-6, DMF, heating, 40 min; vi, $C_8H_{17}Br$, K_2CO_3, dibenzo-18-crown-6, DMF, 120 °C, 40 min.

† Combustion analysis was performed with a Carlo Erba 1106 CHN-analyzer. The NMR spectra were recorded at 25 °C on Bruker AV 400 and AV 600 spectrometers (400.13 and 600.31 MHz, respectively), and were referenced using residual solvent resonances (^{1}H, δ 7.26 ppm; ^{13}C, δ 77.16 ppm for $CDCl_3$). Chemical shifts of ^{15}N are given with a reference to an external standard of 90% formamide in DMSO-d_6 (112.7 ppm) and recalculated to liquid ammonia. Adjustments for bulk magnetic susceptibility were not done. Simulations of ^{1}H NMR spectra were performed with gNMR 5.0 software.[11] Melting points were determined with a Kofler apparatus. Mass spectra were obtained on a Thermo Electron Corporation DFS mass spectrometer (70 eV), using direct injection, the temperature of the ionization chamber was 220–270 °C. The IR spectra were recorded on a Shimadzu IRTracer-100 instrument with GS10802-X Quest ATR ZnSe Accessory (Specac). Column chromatography was performed on alumina (50–150 μm, TU 6-09-3916-75) and the Kieselgel 60 plates (Merck) were used for TLC analysis.

*2-Amino-7*H*-benzo[*e*]perimidin-7-one* **1**. A mixture of 1-iodoanthraquinone (1 g, 3.0 mmol), guanidine hydrochloride (1.5 g, 16.0 mmol), K_2CO_3 (2.9 g, 21.0 mmol) and CuI (120 mg, 0.6 mmol) in pyridine (23 ml) was refluxed for 4 h. The mixture was cooled, the precipitate formed was filtered, washed with ethanol and hot water and dried. Yield 680 mg (92%), mp 290–292 °C (lit.,[3(a)] 290–295 °C).

‡ *N-(7-Oxo-7*H*-benzo[*e*]perimidin-2-yl)decanamide* **2**. A mixture of amine **1** (100 mg, 0.4 mmol) and decanoyl chloride (180 mg, 0.9 mmol) in pyridine (1 ml) was refluxed for 20 min. Then ethyl acetate (20 ml) was added, the organic layers were washed with water (3×20 ml), dried over $MgSO_4$ and evaporated to dryness under reduced pressure. The crude product was purified by flash chromatography on Al_2O_3 (elution with toluene–ethyl acetate, 2:1). Yield 140 mg (87%), mp 150–152 °C (ethanol–toluene). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.88 (t, 3H, Me, *J* 6.9 Hz), 1.33 (m, 10H, 5CH_2), 1.48 (m, 2H, CH_2), 1.84 (m, 2H, CH_2), 2.99 [br. t, 2H, $CH_2C(O)$, *J* 7.4 Hz], 7.78 (td, 1H, H_{Ar}, *J* 1.5 and 7.5 Hz), 7.83 (td, 1H, H_{Ar}, *J* 1.5 and 7.5 Hz), 8.01 (m, 1H, H_{Ar}), 8.17 (dd, 1H, H_{Ar}, *J* 0.9 and 8.5 Hz), 8.26 (br. s, 1H, NH), 8.43 (m, 2H, H_{Ar}), 8.77 (dd, 1H, H_{Ar}, *J* 1.3 and 7.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 22.8, 25.1, 29.4, 29.5, 29.6, 29.7, 32.0, 37.9 (C_9H_{19}), 117.3 (C), 125.9 (CH), 127.5 (CH), 128.3 (CH), 129.1 (C), 133.1 (CH), 133.9 (C), 134.0 (CH), 134.3 (C), 134.4 (CH), 134.8 (CH), 150.9 (C), 155.9 (C), 158.9 (C), 173.8 (NHC=O), 182.2 (C=O). IR (ν/cm^{-1}): 1670, 1695 (2C=O), 2853, 2922, 2955 (Alk), 3251 (NH). Found (%): C, 75.32; H, 6.52; N, 10.34. Calc. for $C_{25}H_{27}N_3O_2$ (%): C, 74.79; H, 6.78; N, 10.47.

© 2016 Mendeleev Communications. Published by ELSEVIER B.V. on behalf of the N. D. Zelinsky Institute of Organic Chemistry of the Russian Academy of Sciences.

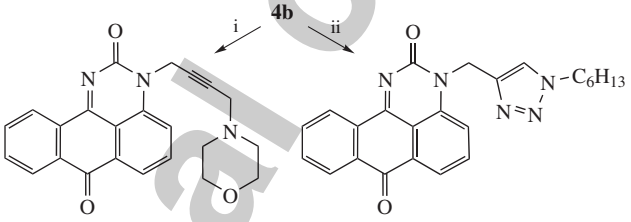
Author's personal copy

Upon isolation and purification it is gradually hydrolyzed, particularly, during chromatography.

The diazotation of aminoperimidine **1** with nitrosylsulfuric acid in acetic acid with subsequent water treatment readily results in benzoperimidone **3** in 88% yield (see Scheme 1).[§] The previously applied method for synthesizing compound **3** is based on the condensation of urea with 1-aminoanthraquinone in phenol at 180–185 °C.[6]

Benzoperimidone **3** appears to be a convenient intermediate for derivatization. Its alkylation with benzyl or propargyl chlorides in DMF in the presence of K_2CO_3 and dibenzo-18-crown-6 under heating leads to N-alkylated products **4a**,**b** (see Scheme 1).[¶] The similar reaction of compound **3** with less active 1-bromooctane affords O-alkylated derivative **5**. This is in agreement with the data on alkylation of pyridones and pyrimidones,[7,8] although due to low yields and selectivity they are rarely used for preparative purposes. Alkylation of benzoperimidone **3** looks to be of wider synthetic possibilities.

A synthetic potential of an intermediate is greater when its substituent can be readily modified. Terminal acetylene moiety of compound **4b** opens good possibilities for further modification.[9] In fact, treatment of alkyne **4b** with bis(morpholino)methane in 1,4-dioxane in the presence of CuCl at room temperature gives a Mannich base **4c** in 95% yield (Scheme 2).[††] Obviously, such a chemistry can be extended to a series of other bis(amino)methanes.



Scheme 2 *Reagents and conditions*: i, bis(morpholino)methane, CuCl, 1,4-dioxane, room temperature, 1 h; ii, $C_6H_{13}N_3$, CuI, CH_2Cl_2, room temperature, 6 h.

Compound **4b** is also a promising alkyne substrate for click-reactions widely applied in medicinal chemistry.[10] Indeed, its 1,3-dipolar cycloaddition to 1-azidohexane in dichloromethane in the presence of CuI afforded triazole **4d** in 87% yield (see Scheme 2).[‡‡]

[§] *3H-Benzo[e]perimidine-2,7-dione* **3**. Nitrosylsulfuric acid [$NaNO_2$ (375 mg, 5.6 mmol), H_2SO_4 (3.5 ml)] was added in portions over 5 min to a stirred mixture of amine **1** (680 mg, 2.8 mmol) and concentrated H_2SO_4 (2 ml) in AcOH (17 ml) at room temperature. After the mixture had been stirred for 1 h, water (15 ml) was added. The precipitate formed was filtered, washed with water and dried. Yield 610 mg (88%), mp > 360 °C (lit.,[5] > 360 °C).

[¶] *Alkylation of 3H-benzo[e]perimidine-2,7-dione (general procedure)*. A mixture of benzoperimidone **3** (180 mg, 0.7 mmol), $HalCH_2R$ (2.5 mmol), K_2CO_3 (345 mg, 2.5 mmol) and dibenzo-18-crown-6 (15 mg, 0.04 mmol) in DMF (4 ml) was stirred at 120 °C for 40 min. Then toluene (100 ml) and water (100 ml) were added, the organic layer was separated, dried over $MgSO_4$ and evaporated to dryness under reduced pressure. The residue was purified by flash chromatography on Al_2O_3 (elution with toluene–ethyl acetate, 1:1). Subsequent recrystallization gave pure compounds **4a**,**b** and **5**.

3-Benzyl-3H-benzo[e]perimidine-2,7-dione **4a**. Benzyl chloride was used as alkylating agent. Yield 160 mg (67%), mp 272–273 °C (toluene). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.62 (s, 2H, CH_2), 7.27 (m, 1H, *p*-H), 7.31–7.33 (m, 4H, *o*-H, *m*-H), 7.54 (dd, 1H, H^4, *J* 0.9, 8.6 Hz), 7.79 (dd, 1H, H^5, *J* 7.5, 8.6 Hz), 7.80 (ddd, 1H, H^9, *J* 1.3, 7.4, 7.8 Hz), 7.84 (ddd, 1H, H^{10}, *J* 1.3, 7.4, 7.9 Hz), 8.17 (dd, 1H, H^6, *J* 0.9, 7.5 Hz), 8.36 (ddd, 1H, H^8, *J* 0.2, 1.3, 7.8 Hz), 8.89 (ddd, 1H, H^{11}, *J* 0.2, 1.3, 7.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 48.0 (CH_2), 113.5 (C^{11c}), 120.0 (C^4), 122.6 (C^6), 126.9 (*o*-C), 127.1 (C^{11}), 127.9 (C^8), 128.0 (*p*-C), 129.2 (*m*-C), 130.1 (C^{6a}), 133.3 (C^{7a}), 133.6 (C^{11a}), 133.8 (C^9), 134.6 (C^{10}), 135.5 (C^5), 135.6 (*i*-C), 142.5 (C^{3a}), 156.3 (C^2), 162.7 (C^{11b}), 182.2 (C^7). IR (ν/cm^{-1}): 1657 (C=O). Found (%): C, 77.94; H, 4.14; N, 8.14. Calc. for $C_{22}H_{14}N_2O_2$ (%): C, 78.09; H, 4.17; N, 8.28.

3-(Prop-2-ynyl)-3H-benzo[e]perimidine-2,7-dione **4b**. Propargyl chloride was used as alkylating agent at 57 °C. Yield 180 mg (90%), mp 292–293 °C (ethyl acetate). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 2.36 (t, 1H, ≡CH, *J* 2.5 Hz), 5.19 (d, 2H, CH_2, *J* 2.5 Hz), 7.80 (dd, 1H, H^4, *J* 0.9, 8.5 Hz), 7.81 (ddd, 1H, H^9, *J* 1.3, 7.3, 7.8 Hz), 7.84 (ddd, 1H, H^{10}, *J* 1.4, 7.3, 7.9 Hz), 7.99 (dd, 1H, H^5, *J* 7.5, 8.5 Hz), 8.21 (dd, 1H, H^6, *J* 0.9, 7.5 Hz), 8.38 (ddd, 1H, H^8, *J* 0.4, 1.4, 7.8 Hz), 8.86 (ddd, 1H, H^{11}, *J* 0.4, 1.3, 7.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 33.9 (CH_2), 74.2 (≡CH), 77.0 (–C≡), 113.7 (C^{11c}), 119.7 (C^4), 122.9 (C^6), 127.2 (C^{11}), 128.0 (C^8), 130.2 (C^{6a}), 133.3 (C^{7a}), 133.5 (C^{11a}), 134.0 (C^9), 134.6 (C^{10}), 135.8 (C^5), 141.6 (C^{3a}), 155.1 (C^2), 163.0 (C^{11b}), 182.1 (C^7). IR (ν/cm^{-1}): 1667, 1672 (C=O), 2120 (C≡C), 2887 (CH_2), 3231 (≡C–H). Found (%): C, 74.94; H, 3.79; N, 9.66. Calc. for $C_{18}H_{10}N_2O_2$ (%): C, 75.52; H, 3.52; N, 9.79. HRMS, *m/z*: 286.0738 (calc. for $C_{18}H_{10}N_2O_2$, *m/z*: 286.0737 [M]$^+$).

2-Octyloxy-7H-benzo[e]perimidin-7-one **5**. 1-Bromooctane was used as alkylating agent. Yield 160 mg (63%), mp 105–106 °C (light petroleum). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.87 (t, 3H, Me, *J* 7.0 Hz), 1.18–1.43 [m, 8H, $(CH_2)_4$], 1.54 (m, 2H, $OCH_2CH_2CH_2$), 1.92 (m, 2H, OCH_2CH_2), 4.52 (t, 2H, OCH_2, *J* 6.6 Hz), 7.67 (ddd, 1H, H^9, *J* 1.3, 7.3, 7.7 Hz), 7.72 (ddd, 1H, H^{10}, *J* 1.4, 7.3, 7.8 Hz), 7.87 (dd, 1H, H^5, *J* 7.2, 8.4 Hz), 7.98 (dd, 1H, H^4, *J* 1.1, 8.4 Hz), 8.24 (dd, 1H, H^6, *J* 1.1, 7.2 Hz), 8.28 (ddd, 1H, H^8, *J* 0.4, 1.4, 7.7 Hz), 8.74 (ddd, 1H, H^{11}, *J* 0.4, 1.3, 7.8 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.2 (Me), 22.8, 29.4, 29.5, 31.9 (4CH_2), 29.1 (OCH_2CH_2), 26.2 ($OCH_2CH_2CH_2$), 68.3 (OCH_2), 116.8 (C^{11c}), 125.8 (C^{11}), 126.2 (C^6), 127.9 (C^8), 129.0 (C^{6a}), 132.7 (C^9), 133.2 (C^4), 133.6 (C^{7a}), 134.0 (C^{10}), 134.2 (C^{11a}), 134.3 (C^5), 151.7 (C^{3a}), 159.8 (C^2), 163.4 (C^{11b}), 182.1 (C^7). ^{15}N NMR (61 MHz, $CDCl_3$) δ: 229.0 (N^3), 260.1 (N^1). IR (ν/cm^{-1}): 1667 (C=O), 2851, 2930, 2951 (OC_8H_{17}). Found (%): C, 76.76; H, 6.65; N, 7.71. Calc. for $C_{23}H_{24}N_2O_2$ (%): C, 76.64; H, 6.71; N, 7.77.

[††] *3-(4-Morpholinobut-2-yn-1-yl)-3H-benzo[e]perimidine-2,7-dione* **4c**. The solution of bis(morpholino)methane (100 mg, 0.54 mmol) in 1,4-dioxane (3 ml) was added under argon to a suspension of alkyne **4b** (150 mg, 0.52 mmol) and CuCl (10 mg) in 1,4-dioxane (12 ml) and the mixture was stirred for 1 h at room temperature. Then ethyl acetate (100 ml) was added, the organic layers were washed with 5% aqueous NH_3 (50 ml) and water (100 ml), dried over $MgSO_4$ and flash-chromatographed on Al_2O_3 (elution with ethyl acetate). Yield 190 mg (95%), mp 240–241 °C (ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.49 (br. t, 4H, 2CH_2, *J* 4.6 Hz), 3.26 (br. t, 2H, CH_2N, *J* 1.9 Hz), 3.69 (br. t, 4H, 2CH_2, *J* 4.6 Hz), 5.21 (s, 2H, CH_2C≡), 7.82 (m, 3H, H_{Ar}), 7.97 (m, 1H, H_{Ar}), 8.20 (m, 1H, H_{Ar}), 8.39 (m, 1H, H_{Ar}), 8.86 (m, 1H, H_{Ar}). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 34.3 (OCH_2), 47.6 (CH_2N), 52.5 (2CH_2), 66.9 (2CH_2), 78.8, 80.7 (C≡C), 113.7 (C), 119.8 (CH), 122.9 (CH), 127.2 (CH), 128.0 (CH), 130.2 (C), 133.3 (C), 133.5 (C), 134.0 (CH), 134.6 (CH), 135.7 (CH), 141.7 (C), 155.1 (C), 162.9 (C), 182.2 (C=O). IR (ν/cm^{-1}): 1667 (C=O), 2224 (C≡C), 2824, 2868, 2970 [$N(CH_2CH_2)_2O$]. Found (%): C, 71.02; H, 4.80; N, 10.84. Calc. for $C_{23}H_{19}N_3O_3$ (%): C, 71.67; H, 4.97; N, 10.90. HRMS, *m/z*: 385.1419 (calc. for $C_{23}H_{19}N_3O_3$, *m/z*: 385.1421 [M]$^+$).

[‡‡] *3-[(1-Hexyl-1H-1,2,3-triazol-4-yl)methyl]-3H-benzo[e]perimidine-2,7-dione* **4d**. A mixture of alkyne **4b** (200 mg, 0.70 mmol), 1-azidohexane (95 mg, 0.75 mmol) and CuI (10 mg) in CH_2Cl_2 (7 ml) was stirred for 6 h at room temperature. Then ethyl acetate (100 ml) was added, the organic layers were washed with 5% aqueous NH_3 (50 ml) and water (100 ml), dried over $MgSO_4$ and evaporated under reduced pressure. The crude product was purified by column chromatography on Al_2O_3 (elution with toluene–ethyl acetate, 5:1). Yield 250 mg (87%), mp 248–249 °C (toluene). ^{1}H NMR (600 MHz, $CDCl_3$) δ: 0.77 (t, 3H, Me, *J* 7.0 Hz), 1.15–1.29 [m, 6H, $NC_2H_4(CH_2)_3Me$], 1.82 (m, 2H, NCH_2CH_2), 4.27 (t, 2H, $NCH_2C_5H_{11}$, *J* 7.2 Hz), 5.53 (br. s, 2H, NCH_2Tr), 7.67 (ddd, 1H, H^9, *J* 1.2, 7.4, 8.2 Hz), 7.68 (ddd, 1H, H^{10}, *J* 1.1, 7.4, 8.0 Hz), 7.80 (dd, 1H, H^5, *J* 7.6, 8.4 Hz), 7.87 (s, 1H, H_{Tr}), 7.95 (dd, 1H, H^6, *J* 0.4, 7.6 Hz), 8.18 (ddd, 1H, H^8, *J* 0.2, 1.1, 8.2 Hz), 8.19 (dd, 1H, H^4, *J* 0.4, 8.4 Hz), 8.58 (ddd, 1H, H^{11}, *J* 0.2, 1.2, 8.0 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 13.9 (Me), 22.3, 26.1, 31.1 [$NC_2H_4(CH_2)Me$], 30.1 (NCH_2CH_2), 39.9 (NCH_2Tr), 50.6 ($NCH_2C_5H_{11}$), 113.1 (C^{11c}), 120.4 (C^4), 122.6 (C^6), 124.0 (CH_{Tr}),

Personal copy

Structures of compounds **4a**,**b**,**d** and **5** were determined using ^{1}H, ^{13}C 1D NMR experiments as well as ^{1}H–^{1}H and ^{1}H–^{13}C correlations (COSY, NOESY, HSQC, HMBC).[§§] N-Alkylated **4a**,**b**,**d** exhibit intensive cross-peaks corresponding to interactions of CH_2-protons of R-substitute with H^4 in NOESY spectra and cross-peaks corresponding to interaction of CH_2-protons with C^2 and C^{3a} in HMBC spectra. O-Alkylated compound **5** reveals no cross-peaks for CH_2-protons with aromatic system in NOESY experiment and one interaction with C^2 due to HMBC. We also investigated compounds **4d** and **5** by ^{15}N NMR spectroscopy and found that N^3 in compound **5** is highly shielded relative to that in **4d**.

In conclusion, a new series of 2-R-7*H*-benzo[*e*]perimidin-7-ones and 3-R-3*H*-benzo[*e*]perimidine-2,7-diones can readily be accessed from 1-iodoanthraquinone. Selectivity of alkylation of benzoperimidone **3** depends on the nature of the alkylating reagent. Benzoperimidones equipped with alkyne functional group seem to be the most promising substrates for further modification.

This work was supported by the Russian Foundation for Basic Research (grant no. 16-03-00082A) and the Ministry of Education and Science of the Russian Federation. Authors acknowledge the Multi-Access Chemical Service Center of the SB RAS for spectral and analytical measurements.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2016.03.032.

References

1 (*a*) W. R. Jones, J. K. Landquist and N. Senior, *Brit. J. Pharmacol.*, 1952, **7**, 486; (*b*) B. Stefańska, M. Dzieduszycka, S. Martelli, J. Tarasiuk, M. Bontemps-Gracz and E. Borowski, *J. Med. Chem*., 1993, **36**, 38; (*c*) D. R. Bhumralkar, R. A. Bychowski, D. S. Dhanoa, D. R. Luthin and A. K. Rabinovich, *US Patent WO 1998008821 A1*, 1998; (*d*) B. Stefańska, M. Dzieduszycka, M. M. Bontemps-Gracz, E. Borowski, S. Martelli, R. Supino, G. Pratesi, M. De Cesare, F. Zunino, H. Kusnierczyk and C. Radzikowski, *J. Med. Chem*., 1999, **42**, 3494; (*e*) X. Bu, L.W. Deady, G. J. Finlay, B. C. Baguley and W. A. Denny, *J. Med. Chem.*, 2001, **44**, 2004; (*f*) M. Dzieduszycka, S. Martelli, M. Arciemiuk, M. M. Bontemps-Gracz, A. Kupiec and E. Borowski, *Bioorg. Med. Chem*., 2002, **10**, 1025; (*g*) X. Bu, J. Chen, L. W. Deady, C. L. Smith, B. C. Baguley, D. Greenhalgh, S. Yang and W. A. Denny, *Bioorg. Med. Chem*., 2005, **13**, 3657.

2 (*a*) B.-W. Yu, L.-H. Meng, J.-Y. Chen, T.-X. Zhou, K.-F. Cheng, J. Ding and G.-W. Qin, *J. Nat. Prod.*, 2001, **64**, 968; (*b*) Y. D. Min, S. U. Choi and K. R. Lee, *Arch. Pharm. Res*., 2006, **29**, 627; (*c*) H. Tang, F.-X. Ning, Y.-B. Wei, S.-L. Huang, Z.-S. Huang, A. S.-C. Chan and L.-Q. Gu, *Bioorg. Med. Chem. Lett*., 2007, **17**, 3765; (*d*) H. Tang, X.-D. Wang, Y.-B. Wei, S.-L. Huang, Z.-S. Huang, J.-H. Tan, L.-K. An, J.-Y. Wu, A. S.-C. Chan and L.-Q. Gu, *Eur. J. Med. Chem*., 2008, **43**, 973; (*e*) V. Castro-Castillo, M. Rebolledo-Fuentes, C. Theoduloz and B. K. Cassels, *J. Nat. Prod*., 2010, **73**, 1951; (*f*) Y.-P. Li, F.-X. Ning, M.-B. Yang, Y.-C. Li, M.-H. Nie, T.-M. Ou, J.-H. Tan, S.-L. Huang, D. Li, L.-Q. Gu and Z.-S. Huang, *Eur. J. Med. Chem*., 2011, **46**, 1572; (*g*) V. Castro-Castillo, C. Suárez-Rozas, A. Pabón, E. G. Pérez, B. K. Cassels and S. Blair, *Bioorg. Med. Chem. Lett.*, 2013, **23**, 327.

3 (*a*) M. Battegay, *French Patent 736174*, 1931; (*b*) I. G. Farbenind, *UK Patent 385295*, 1931; (*c*) M. Battegay and H. Silbermann, *Compt. Rend*., 1932, **194**, 380; (*d*) I. G. Farbenind, *UK Patent 401731*, 1933; (*e*) H. Weidinger, H. Eilingsfeld and G. Haese, *German Patent 1159456*, 1963; (*f*) W. Hohmann, *German Patent 1232296*, 1967; (*g*) J.-M. Adam, T. Winkler and G. Rihs, *Helv. Chim. Acta*, 1982, **65**, 2318; (*h*) Z. Golubski and R. Kowal, *Polish Patent 192093*, 2006; (*i*) Z. D. Wang, J. Eilander, M. Yoshida and T. Wang, *Eur. J. Org. Chem.*, 2014, 7664.

4 J. F. Ryley and G. J. Stacey, *UK Patent 876719*, 1959.

5 S. I. Popov, I. B. Krasnova and N. S. Dokunichin, *SU Patent 388557*, 1974.

6 K. Nishio, T. Kasai and S. Tsuruoka, *Kogyo Kagaku Zasshi*, 1968, **71**, 2026.

7 (*a*) D. J. Brown, E. Hoerger and S. F. Mason, *J. Chem. Soc*., 1955, 211; (*b*) D. J. Brown and R. V. Foster, *J. Chem. Soc.*, 1965, 4911.

8 E. L. Lanni, M. A. Bosscher, B. D. Ooms, C. A. Shandro, B. A. Ellsworth and C. E. Anderson, *J. Org. Chem*., 2008, **73**, 6425.

9 (*a*) *Acetylene Chemistry: Chemistry, Biology and Material Science*, eds. F. Diederich, P. J. Stang and R. R. Tykwinski, Wiley-VCH, Weinheim, 2005; (*b*) R. Chinchilla and C. Nájera, *Chem. Rev*., 2014, **114**, 1783.

10 (*a*) G. C. Tron, T. Pirali, R. A. Billington, P. L. Canonico, G. Sorba and A. A. Genazzani, *Med. Res. Rev*., 2008, **28**, 278; (*b*) P. Thirumurugan, D. Matosiuk and K. Jozwiak, *Chem. Rev*., 2013, **113**, 4905.

11 *gNMR 5.0 software*, http://home.cc.umanitoba.ca/~budzelaa/gNMR/gNMR.html.

126.6 (C^{11}), 127.7 (C^{8}), 129.6 (C^{6a}), 133.0 (C^{7a}), 133.2 (C^{11a}), 133.6 (C^{9}), 134.2 (C^{10}), 135.7 (C^{5}), 142.0 (C^{3a}), 142.3 (C_{Tr}), 155.6 (C^{2}), 162.4 (C^{11b}), 181.7 (C^{7}). ^{15}N NMR (61 MHz, $CDCl_3$) δ: 141.6 (N^3), 250.9 (NC_6H_{13}), 285.0 (N^1), 349.4 ($\mathit{N}NNC_6H_{13}$), 361.0 ($N\mathit{N}NC_6H_{13}$). IR (ν/cm^{-1}): 1667 (C=O), 2859, 2916, 2955 (C_6H_{13}). Found (%): C, 69.96; H, 5.47; N, 17.31. Calc. for $C_{24}H_{23}N_5O_2$ (%): C, 69.72; H, 5.61; N, 16.94.

[§§] For experimental details, see Online Supplementary Materials.

Received: 13th August 2015; Com. 15/4706

Author's personal copy