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Synthesis of 1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-quinazolines and 1,5-dihydro-1,3-dimethyl-5-nitromethyl-2*H*-pyrano[4,3-*d*]pyrimidine-2,4(3*H*)-diones

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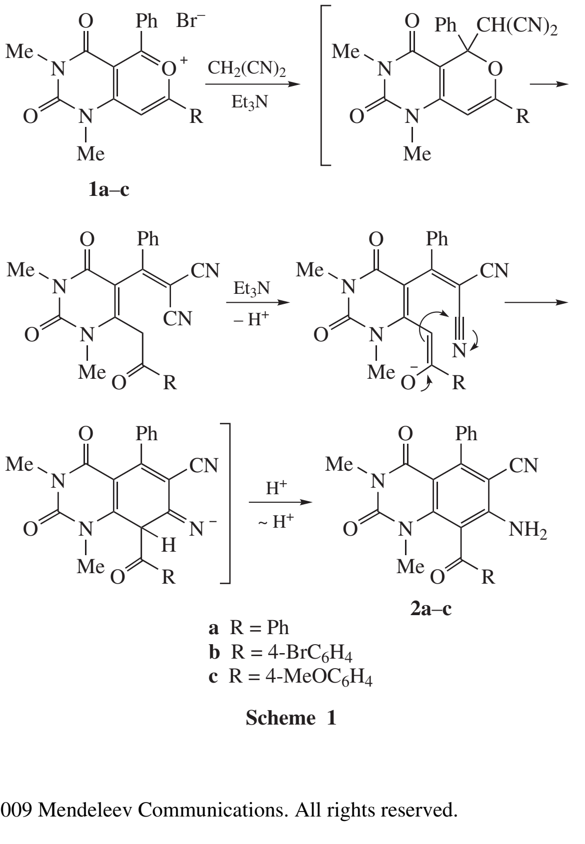
5,7-Diaryl-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium bromides react with malonodinitrile to form 1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-quinazolines, whereas their reaction with nitromethane gives dihydro-1,3-dimethyl-5-nitromethyl-2*H*-pyrano[4,3-*d*]pyrimidine-2,4(3*H*)-diones, the structure of one of them was established by X-ray analysis.

Recently, we reported the preparation of pyrimidopyrylium salts and their reactions with N-nucleophiles.[1,2] Pyrylium and benzo[*c*]pyrylium salts are capable of reacting with not only N- but also C-nucleophiles.[3,4] Pyrylium salts undergo recyclization involving the cyano group of malonodinitrile, which yields *o*-aminocyanobenzenes and 2-amino-3-cyanonaphthalenes. Monocyclic pyrylium salts turn into nitrobenzenes upon treatment with nitromethane,[3] while benzo[*c*]pyrylium salts give adducts – 1-nitromethylbenzo[*c*]pyrans.[5]

Here, we report the reaction of 5,7-diaryl-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium salts[2] with malonodinitrile and nitromethane.

The reaction of bromides **1a**–**c** with twice the amounts of malonodinitrile and triethylamine results in their recyclization into 7-amino-8-aroyl-6-cyano-1,3-dimethyl-2,4-dioxo-5-phenyl-1*H*,2*H*,3*H*,4*H*-quinazolines **2a**–**c**[†] (Scheme 1).



Scheme 1

The structure of compounds **2a**–**c** was established by ^1H NMR and IR spectra. The ^1H NMR spectra contain deuterium-exchangeable double proton singlets, which we believe to be the signals of NH_2 group. In the IR spectra, an absorption maximum is observed at 2217–2219 cm^{-1}, which is typical of a CN group, and two absorption maxima are also found in the regions 3303–3356 and 3422–3466 cm^{-1}, which were assigned to NH_2 group.

The reaction of bromides **1a**–**c** with nitromethane in the presence of triethylamine afforded 7-aryl-1,5-dihydro-1,3-dimethyl-5-nitromethyl-5-phenyl-2*H*-pyrano[4,3-*d*]pyrimidine-2,4(3*H*)-diones **3a**–**c**;[‡] the structures of the products were suggested on the basis of spectral data. The X-ray analysis of crystalline **3a**[§] proved that the reaction occurs at the 5-position (Scheme 2).

In line with the molecular geometry examination for **3a** (Figure 1), its bond lengths and angles fall into the range typical

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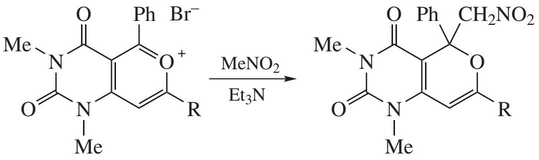
[†] The IR spectra of compounds were recorded on a Varian Excalibur 3100 FT-IR spectrometer. The ^1H NMR spectra were recorded on a Bruker Avance DPX-250 spectrometer in $CDCl_3$; HMDS was used as the internal standard. Salts **1a**–**c** were obtained according to published procedures.[2]

General procedure for the synthesis of compounds **2a**–**c**. Triethylamine (0.14 ml, 101 mg, 1 mmol) was added to a suspension of salts **1** (0.5 mmol) and malonodinitrile (66 mg) in DMF (2 ml) and was kept for 4 h at room temperature. H_2O (4 ml) was added to the reaction mixture. The precipitate formed was filtered off, dissolved in $CHCl_3$ and passed through an aluminium oxide column (eluent: $CHCl_3$). A pale yellow fraction was collected and evaporated to give the desired compound in a pure form.

2a: yield 52%, mp 237–239 °C. ^1H NMR, δ: 3.17 (s, 3H, N^{3}Me), 3.23 (s, 3H, N^{1}Me), 5.97 (s, 2H, NH_2), 7.26–7.36 (m, 2H, Ph), 7.41–7.56 (m, 5H, Ph), 7.58–7.76 (m, 3H, Ph). IR (ν/cm^{-1}): 1606, 1666, 1712 (C=O), 2217 (CN), 3326, 3427 (NH_2). Found (%): C, 70.41; H, 4.35. Calc. for $C_{24}H_{18}N_4O_3$ (%): C, 70.23; H, 4.42.

2b: yield 65%, mp 275–278 °C. ^1H NMR, δ: 3.17 (s, 3H, N^{3}Me), 3.24 (s, 3H, N^{1}Me), 6.03 (s, 2H, NH_2), 7.25–7.33 (m, 2H, Ph), 7.46–7.52 (m, 3H, Ph), 7.55 (d, 2H, Ar, *J* 8.76 Hz), 7.62 (d, 2H, Ar, *J* 8.83 Hz). IR (ν/cm^{-1}): 1604, 1652, 1708 (C=O), 2219 (CN), 3303, 3422 (NH_2). Found (%): C, 59.13; H, 3.41; Br, 16.54. Calc. for $C_{24}H_{17}BrN_4O_3$ (%): C, 58.91; H, 3.50; Br, 16.33.

2c: yield 56%, mp 231–233 °C. ^1H NMR, δ: 3.20 (s, 3H, N^{3}Me), 3.24 (s, 3H, N^{1}Me), 3.88 (s, 3H, OMe), 5.82 (s, 2H, NH_2), 6.93 (d, 2H, Ar, *J* 9.09 Hz), 7.25–7.34 (m, 2H, Ph), 7.43–7.55 (m, 3H, Ph), 7.63–7.76 (m, 2H, Ar). IR (ν/cm^{-1}): 1624, 1668, 1713 (C=O), 2219 (CN), 3356, 3466 (NH_2). Found (%): C, 68.32; H, 4.69. Calc. for $C_{25}H_{20}N_4O_4$ (%): C, 68.17; H, 4.58.



1a–c

3a–c

a R = Ph
b R = 4-BrC_6H_4
c R = 4-$MeOC_6H_4$

Scheme 2

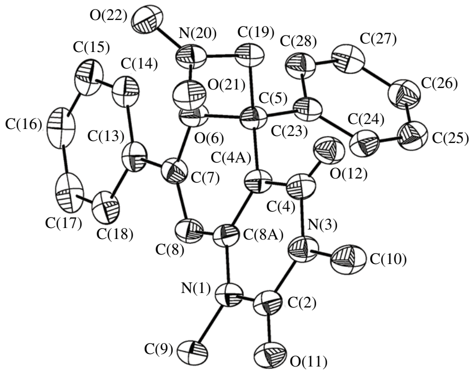


Figure 1 General view of compound **3a** in representation of atoms *via* thermal ellipsoids (p = 50%). Selected bond lengths (Å): N(1)–C(2) 1.388(2), C(2)–N(3) 1.382(2), N(3)–C(4) 1.403(2), C(4)–C(4A) 1.442(3), C(4A)–C(8A) 1.366(2), N(1)–C(8A) 1.384(2), C(4A)–C(5) 1.516(2), C(5)–O(6) 1.453(2), O(6)–C(7) 1.368(2), C(7)–C(8) 1.343(2), C(8A)–C(8) 1.445(3); selected bond angles (°): N(3)–C(4)–C(4A) 114.86(16), C(8A)–N(1)–C(2) 121.83(15), O(6)–C(5)–C(4A) 110.63(14), C(7)–C(8)–C(8A) 119.52(16).

of such a type of compounds. The introduction of CH_2NO_2 group into the central cycle breaks the delocalization of electron density over this fragment causing its conformation to vary from planar one to a twist with the deviation of C(5) and O(6) atoms from the C(7)–C(8)–C(8A)–C(4A) plane by 0.28 and 0.26 Å, respectively. Nevertheless, the mutual disposition of phenyl and pyrimidine rings is close to planarity; the corresponding dihedral angle is only 12.3(3)°. This is apparently due to conjugation in the O(12)=C(4)–C(4A)=C(8A)–C(8)=C(7)–Ph fragment, which appears from the shortening of formally single C–C bonds down to 1.442(2) Å. Although adduct **3a** contains several atoms with high H-bonding abilities, the absence of convenient proton-donor defines that the molecules of **3a** are held together only by weak contacts. Thus, the aggregation of molecular species is mainly governed by C–H···O interactions (C···O 3.265–3.566 Å), where the strongest one is the NO_2CH_2 to C=O binding. Oxygen atoms of NO_2CH_2 fragment are also involved in the bifurcated C–H···O bond with the intermediate values of C···O separation (3.450 and 3.448 Å). In addition, the aromatic nature of R substituent (Scheme 2) resulted in the formation of the C–H···π interactions (C···C 3.457–3.671 Å), completing the 3D framework in the crystal of **3a**.

Thus, 5,7-diaryl-1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-pyrano[4,3-*d*]pyrimidinium bromides react with C-nucleophiles yielding derivatives of 1,3-dimethyl-2,4-dioxo-1*H*,2*H*,3*H*,4*H*-quinazolines **2a–c** and 1,5-dihydro-1,3-dimethyl-5-nitromethyl-2*H*-pyrano[4,3-*d*]pyrimidine-2,4(3*H*)-diones **3a–c**.

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[‡] *General procedure for the synthesis of compounds* **3a–c**: Triethylamine (0.14 ml, 101 mg, 1 mmol) was added to a suspension of salts **1** (0.5 mmol) in $MeNO_2$ (2 ml) and was heated to complete dissolution of initial salt. After the reaction mixture was cooled, the precipitate formed was filtered off and washed with $MeNO_2$.

3a: yield 75%, mp 249–251 °C. ^{1}H NMR, δ: 3.46 (s, 3H, N^{3}Me), 3.54 (s, 3H, N^{1}Me), 5.15 (d, 1H, CH_2, J 13.33 Hz), 6.18 (s, 1H, C^{8}H), 6.37 (d, 1H, CH_2, J 13.33 Hz), 7.30–7.39 (m, 3H, Ph), 7.41–7.58 (m, 5H, Ph), 7.75–7.88 (m, 2H, Ph). IR (ν/cm^{-1}): 1544 (C–NO_2), 1649, 1693 (C=O). Found (%): C, 65.05; H, 4.70. Calc. for $C_{22}H_{19}N_3O_5$ (%): C, 65.18; H, 4.72.

3b: yield 68%, mp 239–240 °C. ^{1}H NMR, δ: 3.42 (s, 3H, N^{3}Me), 3.50 (s, 3H, N^{1}Me), 5.09 (d, 1H, CH_2, J 13.25 Hz), 6.13 (s, 1H, C^{8}H), 6.32 (d, 1H, CH_2, J 13.32 Hz), 7.26–7.42 (m, 5H, Ph), 7.54–7.68 (d + d, 4H, Ar, J 8.76 Hz, J 8.75 Hz). IR (ν/cm^{-1}): 1553 (C–NO_2), 1651, 1692 (C=O). Found (%): C, 54.37; H, 3.81; Br, 16.73. Calc. for $C_{22}H_{18}BrN_3O_5$ (%): C, 54.56; H, 3.75; Br, 16.50.

3c: yield 60%, mp 236–239 °C. ^{1}H NMR, δ: 3.42 (s, 3H, N^{3}Me), 3.49 (s, 3H, N^{1}Me), 3.86 (s, 3H, OMe), 5.11 (d, 1H, CH_2, J 13.23 Hz), 6.03 (s, 1H, C^{8}H), 6.31 (d, 1H, CH_2, J 13.23 Hz), 6.96 (d, 2H, Ar, J 9.01 Hz), 7.26–7.35 (m, 3H, Ph), 7.36–7.47 (m, 2H, Ph), 7.74 (d, 2H, Ar, J 9.01 Hz). IR (ν/cm^{-1}): 1548 (C–NO_2), 1643, 1694 (C=O). Found (%): C, 63.68; H, 4.76. Calc. for $C_{23}H_{21}N_3O_6$ (%): C, 63.44; H, 4.86.

[§] *Crystallographic data.* Crystals of **3a** ($C_{22}H_{19}N_3O_5$, M = 405.40) are monoclinic, space group $P2_1/n$, at 120 K: a = 8.2649(5), b = 13.7977(8) and c = 16.4066(9) Å, β = 93.636(5)°, V = 1867.19(19) Å^3, Z = 4 (Z' = 1), d_{calc} = 1.442 g cm^{-3}, μ(MoKα) = 1.04 cm^{-1}, F(000) = 848. Intensities of 19853 reflections were measured with a Bruker SMART 1000 CCD diffractometer [λ(MoKα) = 0.71072 Å, ω-scans, $2\theta < 58°$] and 4953 independent reflections [R_{int} = 0.0283] were used in further refinement. Structure was solved by a direct method and refined by the full-matrix least-squares against F^2 in anisotropic approximation for non-hydrogen atoms. The H(C) atom positions were calculated and they were refined in an isotropic approximation in riding model with the U_{iso}(H) parameters equal to $1.2U_{\mathrm{eq}}(C_i)$, for methyl groups equal to $1.5U_{\mathrm{eq}}(C_{ii})$, where $U(C_i)$ and $U(C_{ii})$ are respectively the equivalent thermal parameters of the carbon atoms to which corresponding H atoms are bonded. For **3a**, the refinement converged to wR_2 = 0.1488 and GOF = 1.004 for all independent reflections [R_1 = 0.0568 was calculated against F for 3590 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS 5.0.[6]

CCDC 735640 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.