Available online at www.sciencedirect.com

ScienceDirect

Mendeleev Commun., 2022, **32**, 454–456

Mendeleev Communications

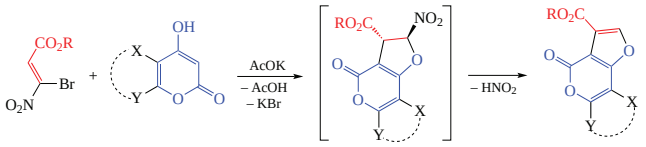
A convenient synthesis of furo[3,2-*c*]pyran-3-carboxylates from 3-bromo-3-nitroacrylates

Vasilii V. Pelipko,[a] Ruslan I. Baichurin,[a] Konstantin A. Lyssenko,[b] Victor V. Dotsenko*[c,d] and Sergey V. Makarenko*[a]

[a] *Herzen State Pedagogical University of Russia, 191186 St. Petersburg, Russian Federation. E-mail: makarenko.sv@gmail.com*
[b] *Department of Chemistry, M. V. Lomonosov Moscow State University, 119991 Moscow, Russian Federation*
[c] *Kuban State University, 350040 Krasnodar, Russian Federation. E-mail: victor_dotsenko_@mail.ru*
[d] *North-Caucasus Federal University, 355009 Stavropol, Russian Federation*

DOI: 10.1016/j.mencom.2022.07.009

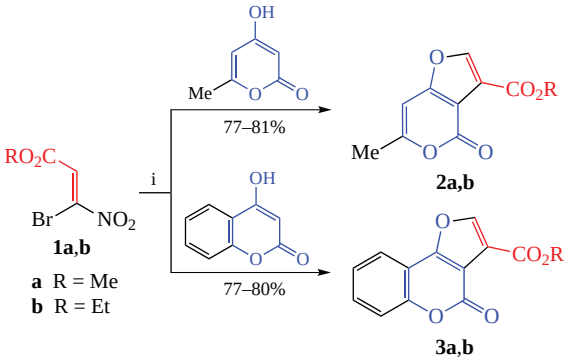
Novel 4-oxo-4*H*-furo[3,2-*c*]pyran-3-carboxylates and 4-oxo-4*H*-furo[3,2-*c*]chromene-3-carboxylates were prepared from available alkyl 3-bromo-3-nitroacrylates and 4-hydroxy-6-methyl-2*H*-pyran-2-one or 4-hydroxycoumarin, respectively. Their structures were confirmed by NMR and X-ray data.



Keywords: nitroacrylates, 1-halo-1-nitroethenes, heterocyclization, furo[3,2-*c*]pyrans, furo[3,2-*c*]chromenes.

Furocoumarins are plant-derived oxygen heterocycles which have long been the subject of interest because of their biological applications.[1–3] Compared to the biological properties and chemistry of psoralene and other related furocoumarins, the properties and synthesis of isomeric furo[3,2-*c*]coumarins have so far remained less studied.[4,5] Meanwhile, furo[3,2-*c*]-coumarins recently showed their potential as anticancer agents,[6] chemosensors[7] and fluorescent dyes,[8] antibacterials[9,10] or fungicides.[11] One of the most convenient approaches towards furo[3,2-*c*]coumarins and related 4*H*-furo[3,2-*c*]pyran-4-ones is based on the reaction of 4-hydroxycoumarin or 4-hydroxy-pyranone with substituted nitroethylenes.[12–15] In continuation of our studies on the reactions of 3-bromo-3-nitroacrylates,[16–19] we report herein the synthesis of new 4-oxo-4*H*-furo[3,2-*c*]-pyran-3-carboxylates and 4-oxo-4*H*-furo[3,2-*c*]chromene-3-carboxylates from alkyl 3-bromo-3-nitroacrylates[20] **1a**,**b** and 4-hydroxy-6-methyl-2*H*-pyran-2-one or 4-hydroxycoumarin (Scheme 1). Noteworthy, 3-alkoxycarbonyl-4-oxo-4*H*-furo[3,2-*c*]pyranes and -chromenes are hardly available and the data on their synthesis are scarce.[21–24] The transformation proceeded under mild conditions, the yields of products **2** and **3** approached 77–81%.†

The plausible mechanism includes the initial formation of the Michael adducts **A** and subsequent intramolecular O-alkylation of enol hydroxyl to form nitrofuran intermediates (Scheme 2). Further aromatization occurs by elimination of HNO_2. One of the intermediate products, ethyl 2-nitro-4-oxo-2,3-dihydro-4*H*-furo[3,2-*c*]chromene-3-carboxylate **4**, was isolated in 78% yield when ethyl 3-bromo-3-nitroacrylate **1b** was reacted with 4-hydroxycoumarin in anhydrous MeOH for 1 h in the presence of 1 equiv. AcOK.‡ This result provides evidence in support of the proposed mechanism. In addition, quantum-chemical studies[16] of the possible reaction pathways in the related reactions using 3-bromo-3-nitroacrylates are also in favour of the proposed mechanism. When compound **4** was treated with 1 equiv. AcOK in anhydrous MeOH for another 1 h, furochromene-3-carboxylate **3b** was formed in 90% yield.§ Compound **3b** was also prepared by heating of intermediate **4** in EtOH for 3 h in the absence of any base (see Scheme 2).

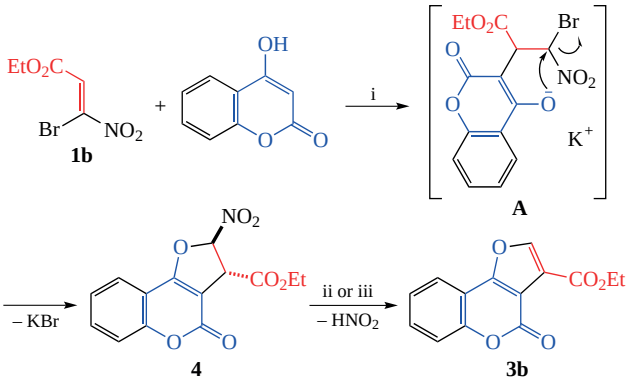


Scheme 1 *Reagents and conditions*: i, AcOK, MeOH, 18–20 °C, 3 h.

† *General procedure for the synthesis of 3-alkoxycarbonyl-4-oxo-4*H*-furo[3,2-c]pyranes and -chromenes* **2**, **3**. To a solution of 4-hydroxy-6-methyl-2*H*-pyran-2-one or 4-hydroxycoumarin (1.43 mmol) and freshly molten AcOK (210 mg, 2.14 mmol) in anhydrous MeOH (5 ml), a solution of the corresponding 3-bromo-3-nitroacrylate **1a**,**b** (1.43 mmol) in anhydrous MeOH (5 ml) was added dropwise. The resulted mixture was stirred at 18–20 °C for 3 h and then poured on crushed ice. The product was extracted with $CHCl_3$ (3 × 20 ml). The combined extracts were dried over $MgSO_4$, filtered and evaporated to dryness to give **2**, **3** as crystalline solids.

‡ *Ethyl 2-nitro-4-oxo-2,3-dihydro-4*H*-furo[3,2-c]chromene-3-carboxylate* **4**. To a solution of 4-hydroxycoumarin (362 mg, 2.23 mmol) and freshly molten AcOK (218 mg, 2.23 mmol) in anhydrous MeOH (16 ml), a solution of ethyl 3-bromo-3-nitroacrylate **1b** (500 mg, 2.23 mmol) in anhydrous MeOH (14 ml) was added dropwise. The mixture was stirred for 1 h and then poured on crushed ice. The formed solid was filtered off and recrystallized from EtOH to furnish compound **4** as light yellow crystals, yield 530 mg (78%), mp 141–144 °C (EtOH).

§ *Preparation of compound* **3b** *from intermediate* **4**. To a solution of compound **4** (70 mg, 0.23 mmol) in anhydrous MeOH (6 ml), a solution



Scheme 2 *Reagents and conditions*: i, AcOK (1 equiv.), MeOH, 18–20 °C, 1 h; ii, AcOK, MeOH, 18–20 °C, 1 h; iii, EtOH, reflux 3 h.

The structure of compounds **2**, **3** and intermediate **4** was confirmed by IR and NMR studies including 2D NMR ^{1}H–^{13}C correlation experiments (key correlations in the ^{1}H–^{13}C HMBC NMR spectrum of compound **2a** are given in Online Supplementary Materials). The observed in the ^{1}H NMR spectrum of **4** two doublets with coupling constant ^{3}J of 2.3 Hz as well as calculations using Haasnoot–DeLeeuw–Altona equation[25] suggested *trans*-geometry for C^{2}H–C^{3}H protons. The structures of products **3b** and **4** were ultimately established by X-ray diffraction analysis (Figure 1, see also Online Supplementary Materials).¶ The X-ray diffraction study of compound **4** showed that dihydrofuran ring had an envelope conformation with C(2) atom out of plane by 0.378 Å. Nitro and CO_2Et groups are located in axial positions. Noteworthy that NO_2 group is located antiperiplanar towards one of the lone pairs of atom O(1) with a *pseudo*-torsion angle Lp–O(1)–C(2)–N(11) equal to 25°. Since the length of C(2)–N(11) bond is somewhat shortened, we suggest that it is due to the crystal packing effect. In fact, very strong $NO_2\cdots NO_2$ intermolecular contacts with N(11)···O(12) distance equal to 2.799(4) Å were realized in the crystal (see Online Supplementary Materials).

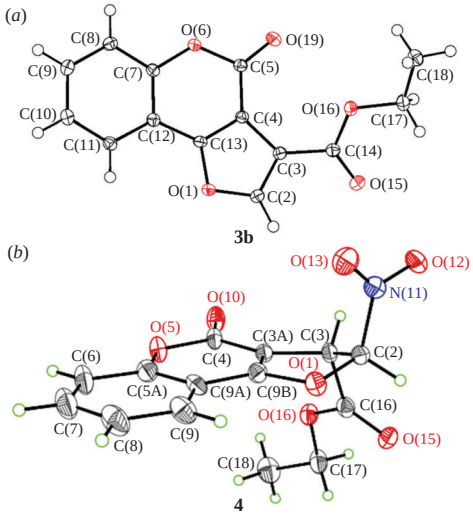


Figure 1 Perspective views of compounds (*a*) **3b** and (*b*) **4** (X-ray data).

In summary, we have proposed an effective synthesis of new 4-oxo-4*H*-furo[3,2-*c*]pyran-3-carboxylates and their chromene analogues. The approach is operationally simple and based on the reaction of accessible alkyl 3-bromo-3-nitroacrylates with 4-hydroxy-2*H*-pyran-2-ones. The reported reaction could broaden the scope of furo[3,2-*c*]pyran chemistry.

This study was performed as part of a state assignment with financial support from the Ministry of Education of the Russian Federation (project no. FSZN-2020-0026).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.07.009.

References

1 V. F. Traven, *Molecules*, 2004, **9**, 50.
2 M. M. Melough, E. Cho and O. K. Chun, *Food Chem. Toxicol.*, 2018, **113**, 99.
3 S. S. Thorat and R. Kontham, *Org. Chem. Front.*, 2021, **8**, 2110.
4 L. Santana, E. Uriarte, F. Roleira, N. Milhazes and F. Borges, *Curr. Med. Chem.*, 2004, **11**, 3239.
5 I. Cortés, L. J. Cala, A. B. Bracca and T. S. Kaufman, *RSC Adv.*, 2020, **10**, 33344.
6 S. Rani, N. Kamra, S. Thakral, D. Kumar, A. Singh, P. L. Sangwan and S. K. Singh, *Beilstein Arch.*, 2021, 202137.
7 N. M. Sarih, A. Ciupa, S. Moss, P. Myers, A. G. Slater, Z. Abdullah, H. A. Tajuddin and S. Maher, *Sci. Rep.*, 2020, **10**, 7421.
8 I. O. Akchurin, A. I. Yakhutina, A. Y. Bochkov, N. P. Solovjova and V. F. Traven, *Heterocycl. Commun.*, 2018, **24**, 85.
9 A. G. Al-Sehemi and S. R. El-Gogary, *Chin. J. Chem.*, 2012, **30**, 316.
10 S. Bondock, W. Khalifa and A. A. Fadda, *Eur. J. Med. Chem.*, 2011, **46**, 2555.
11 R. Zhang, Z. Xu, W. Yin, P. Liu and W. Zhang, *Synth. Commun.*, 2014, **44**, 3257.
12 M. Ghosh and A. Hajra, *Eur. J. Org. Chem.*, 2015, 7836.
13 S. Singh, A. Srivastava, S. M. Mobin and S. Samanta, *RSC Adv.*, 2015, **5**, 5010.
14 X. Dou, F. Zhong and Y. Lu, *Chem. – Eur. J.*, 2012, **18**, 13945.
15 D. L. Obydennov, A. I. El-Tantawy and V. Ya. Sosnovskikh, *Mendeleev Commun.*, 2019, **29**, 1.
16 V. V. Pelipko, R. I. Baichurin, E. V. Kondrashov and S. V. Makarenko, *Russ. J. Gen. Chem.*, 2021, **91**, 167 (*Zh. Obshch. Khim.*, 2021, **91**, 205).
17 S. V. Makarenko, V. V. Pelipko, M. M. Pavchenko and R. I. Baichurin, *Russ. J. Gen. Chem.*, 2019, **89**, 532 (*Zh. Obshch. Khim.*, 2019, **89**, 464).

of freshly molten AcOK (22.5 mg, 0.23 mmol) in anhydrous MeOH (4 ml) was added dropwise. The resulted mixture was stirred at 20 °C for 1 h and then poured on crushed ice. The solid was filtered off and recrystallized from EtOH to give 53 mg (90%) of product **3b** as light yellow crystals, mp 118–120 °C (EtOH).

¶ Crystals of compounds **3b** and **4** were grown from EtOH.

Crystal data for **3b**. $C_{14}H_{10}O_5$, M = 258.22, monoclinic, space group $P2_1/c$ (no. 14), 393(2) K, a = 7.5281(2), b = 20.3294(4) and c = 7.9529(2) Å, α = 90°, β = 111.7957(10)°, γ = 90°, Z = 4, V = 1130.12(5) Å^3, d_{calc} = 1.518 mg mm^{-3}, $F(000)$ = 536.0. A single crystal with dimensions 0.320 × 0.230 × 0.190 mm was selected and intensities of 50079 reflections were measured using a SMART APEX II CCD diffractometer [ω-scans, μ(MoKα) = 0.117 mm^{-1}, 2Θ range for data collection 4.008 to 59.998°]. After merging of equivalents and absorption correction, 3296 unique reflections (R_{int} = 0.0346) were used for the structure solution and refinement. Final R factors: R_1 = 0.0358 [$I > 2\sigma(I)$] and wR_2 = 0.1036 (all reflections), GOF = 1.043.

Crystal data for **4**. $C_{14}H_{11}NO_7$, M = 305.24, orthorhombic, space group $Pna2_1$ (no. 33), 393(2) K, a = 10.0342(12), b = 29.333(4) and c = 4.5913(6) Å, α = 90°, β = 90°, γ = 90°, Z = 4, V = 1351.4(3) Å^3, d_{calc} = 1.500 mg mm^{-3}, $F(000)$ = 632.0. A single crystal with dimensions 0.320 × 0.210 × 0.180 mm was selected and intensities of 6410 reflections measured, using a SMART APEX II CCD diffractometer [ω-scans, μ(MoKα) = 0.123 mm^{-1}, 2Θ range for data collection 4.29 to 54.996°]. After merging of equivalents and absorption correction, 2377 unique reflections (R_{int} = 0.1412) were used for the structure solution and refinement. Final R factors: R_1 = 0.0702 [$I > 2\sigma(I)$] and wR_2 = 0.1767 (all reflections), GOF = 0.968.

The structures were solved using Charge Flipping and refined using Gauss-Newton minimisation. All calculations were carried out with SHELXTL 5.10[26] software package.

CCDC 2108637 (for **3b**) and 2109286 (for **4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

18 R. I. Baichurin, K. A. Lyssenko, K. S. Kovalenko and S. V. Makarenko, *Russ. Chem. Bull.*, 2020, **69**, 2191.
19 V. V. Pelipko, K. A. Gomonov, I. A. Litvinov, R. I. Baichurin, S. V. Makarenko, *Russ. Chem. Bull*., 2022, **71**, 740.
20 M. A. Kuritsyna, V. V. Pelipko, O. N. Kataeva, R. I. Baichurin, K. D. Sadikov, A. S. Smirnov and S. V. Makarenko, *Russ. Chem. Bull*., 2021, **70**, 1605.
21 C.-J. Lee, Y.-J. Jang, Z.-Z. Wu and W. Lin, *Org. Lett*., 2012, **14**, 1906.
22 İ. Koca, İ. Yildirim and E. Şahin, *Helv. Chim. Acta*, 2010, **93**, 1336.
23 N. Yu. Lisovenko, A. V. Dryahlov and M. V. Dmitriev, *Russ. J. Org. Chem*., 2016, **52**, 1183 (*Zh. Org. Khim*., 2016, **52**, 1190).
24 O. Duval and L. Mavoungou Gomès, *J. Heterocycl. Chem*., 1991, **28**, 153.
25 C. A. G. Haasnoot, F. A. A. M. de Leeuw and C. Altona, *Tetrahedron*, 1980, **36**, 2783.
26 G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112.

Received: 2nd November 2021; Com. 21/6746