Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2017, **27**, 464–465
Mendeleev Communications

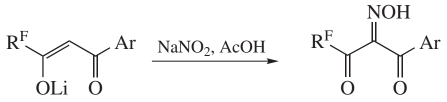
A simple and efficient synthesis of 3-(polyfluoroalkyl)-propane-1,2,3-trione 2-oximes

Vera I. Filyakova,*[a] Nadezhda S. Boltachova,[a] Marina G. Pervova,[a] Nadezhda V. Palysaeva,[b] Pavel A. Slepukhin,[a] Aleksei B. Sheremetev[b] and Valery N. Charushin[a]

[a] *I. Ya. Postovsky Institute of Organic Synthesis, Ural Branch of the Russian Academy of Sciences, 620990 Ekaterinburg, Russian Federation. E-mail: vif@ios.uran.ru*
[b] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: sab@ioc.ac.ru*

DOI: 10.1016/j.mencom.2017.09.011

A convenient direct synthesis of 1-aryl-3-(polyfluoroalkyl)-propane-1,2,3-trione 2-oximes from the corresponding lithium 3-(polyfluoroalkyl)-1,3-diketonates has been elaborated using sodium nitrite/acetic acid system under very mild conditions. The molecular structure of 4,4-difluoro-1-phenylbutane-1,2,3-trione 2-oxime has been determined by X-ray crystallography.



$R^F = HCF_2, CF_3, C_4F_9, H(CF_2)_4, C_6F_{13}$

Alkane-1,2,3-trione 2-oximes (2-hydroxyimino-1,3-diketones) are of interest as analytical reagents and metal extracting agents, but more commonly they are utilized as polyfunctional precursors in organic synthesis.[1] Meantime, 3-(polyfluoroalkyl)propane-1,2,3-trione 2-oximes are rare compounds whose low stability was noted in the literature. 5,5,5-Trifluoro-3-hydroxyimino-1-phenylpentane-2,4-dione obtained by nitrosation of the corresponding 1,3-diketone with sodium nitrite in acetic acid in 73% yield[1(b)] is believed to be the only stable member of such 1,2,3-triketone 2-oximes. Attempts to perform a similar reaction with trifluoroacetylacetone,[2,3] hexafluoroacetylacetone[3] and 4,4,5,5-tetrafluoro-1-phenylpentane-2,4-dione[1(b),2] resulted in considerable decomposition of these compounds.

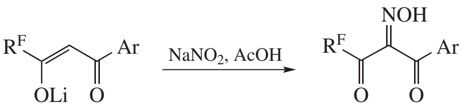
Note that nitrosation of methylene-active compounds is often accompanied by destruction of their carbon backbone. In particular, 4,4,5,5-tetrafluoro-1-phenylpentane-2,4-dione undergoes oxidative cleavage under nitrosation conditions to give benzoic acid in 80% yield.[1(b)] In a number of studies, 3-(polyfluoroalkyl)propane-1,2,3-trione 2-oximes were obtained *in situ* and used without isolation for next transformations. However, this approach often provides low yields of the target compounds. [1(b),2,4]

It was shown recently that nitrosation of CF_3-containing 1,3-diketones with sodium nitrite/acetic acid and sodium nitrite/citric acid systems did not afford the corresponding 4,4,4-trifluoro-1,2,3-propanetrione-2-oximes. These reactions led to a series of stable 4,4,4-trifluoro-3,3-dihydroxy-2-(hydroximino)butan-1-ones (4,4,4-trifluoro-1,2,3-propanetrione-2-oxime hydrates) in 50–55% yields (in acetic acid) or in 78–89% yields (in citric acid).[5] The formation of 4,4,4-trifluorobutane-1,2,3-trione 2-oxime hydrates was probably a result of nitrosation of the 1,3-diketone hydrate arising under the reaction conditions rather than the 1,3-diketone itself.[6]

In continuation of our studies on the chemistry of lithium 1,3-diketonates **1**[7] bearing fluoroalkyl groups, here we describe the nitrosation of these compounds. Note that 1,3-diketonates **1** are stable solids easy to synthesize and convenient for practical use. On the contrary, the corresponding 1,3-diketones are typically reactive liquids and only a few of them are commercially available (though expensive), while the synthesis and purification of some compounds of this group are quite laborious. In a set of processes, compounds **1** can be regarded as synthetic equivalents of the corresponding diketones. In some instances, diketonates **1** manifest specific reactivity even in acidic medium where the corresponding 1,3-diketones are generated *in situ*.[7]

We have shown that treatment of lithium 3-(polyfluoroalkyl)-1,3-diketonates **1a–f** with sodium nitrite in acetic acid is a convenient and efficient method for the synthesis of the required propane-1,2,3-trione 2-oximes **2a–f**. As a rule, the product yield is ~90% (Scheme 464).[†]

This difference in behaviors of lithium diketonates **1** and 1,3-diketones in nitrosation reactions is probably due to the higher nucleophilicity of the first. As a result, oximes **2a–f** are formed quickly. On the other hand, nitrosation of 1,3-diketones themselves occurs slowly, whereas their hydration and fragmentation are faster reactions (see, *e.g.*, ref. 6). Furthermore, the nitrosation efficiency of lithium 1,3-diketonates **1a–f** may be due to a specific solvation or a salt effect that is characteristic of the lithium cation.[8]



1a–f **2a–f**

a $R^F = HCF_2$, Ar = Ph
b $R^F = CF_3$, Ar = Ph
c $R^F = CF_3$, Ar = 4-MeC_6H_4
d $R^F = C_4F_9$, Ar = Ph
e $R^F = H(CF_2)_4$, Ar = Ph
f $R^F = C_6F_{13}$, Ar = Ph

Scheme 1

[†] *Compounds* **2a–f** *(general procedure)*. An aqueous solution of sodium nitrite was added dropwise to a solution of enolate **1** in acetic acid at 10 °C. The reaction mixture was stirred at room temperature for 1 h. The white precipitate of oxime **2** was filtered off and washed with water (100 ml). The mother solution was extracted with Et_2O (2 × 50 ml). The ethereal solution was filtered through silica gel. Diethyl ether was evaporated to give an additional crop of oxime **2**. The precipitates were combined and recrystallized from dichloromethane–hexane (1 : 3) to give compounds **2a–f** as white powders.

Oximes **2a–f** were isolated as white solids that are soluble in diethyl ether, dichloromethane, chloroform and ethanol. They were characterized by elemental analysis, gas chromatography/mass spectrometry, IR, ^{1}H and ^{19}F NMR spectroscopy. The mass spectra of all compounds **2a–f** revealed low intensive (0.7–3.0%) peaks of molecular ions [M]$^+$. In addition, the electron impact mass spectra show characteristic peaks due to loss of R^{F}CO$^+$ fragments (*i.e.*, [ArCOC=NOH]$^+$) with intensity from 0.9 to 1.4%. The base peak belongs to the [ArCO]$^+$ ion. The IR spectra of compounds **2a–f** include an intense broad NOH stretch at 3100–3500 cm^{-1}, sharp intense C=O stretches at 1720 and 1650 cm^{-1}, as well as medium intensity bands at 1615 and 1620 cm^{-1} (C=N).[9] The ^{1}H NMR spectra of oximes **2a–f** (in $CDCl_3$) contain broadened signals of the OH group in the region of δ 8.79–9.13 ppm (1H) and signals characteristic of aryl substituents in the region of δ 7.50–7.90 ppm. Furthermore, the spectrum of compound **2a** contains a triplet of the HCF_2 group with ^2J 53.2 Hz at δ_H 6.53 ppm, while the spectrum of compound **2e** contains a triplet of triplets of the $H(CF_2)_4$ group with ^2J 52 Hz and ^3J 5.3 Hz at δ_H 6.10 ppm. The ^{19}F NMR spectra are in agreement with the fluorinated groups present in the structures.

The structure of oxime **2a** was ultimately confirmed by X-ray single crystal analysis (Figure 1).[‡] Compound **2a** crystallizes in $P2_1/c$ centrosymmetric space group. The difluoromethylacetyl group is placed at the *trans*-position to the C=N bond of the oxime. The ketoxime moiety O(1)–C(2)–C(3)–N(2) is nearly planar and has an *s-trans* configuration. The bond length distribution in it is typical of a conjugated heterodiene system. In particular, the length of the C(2)–C(3) single bond is close to 1.48 Å, the length of the C(3)=N(2) bond is *ca.* 1.28 Å, and that of the C(2)=O(1) bond is about 1.20 Å.[10] Conversely, the planar aroyl moiety in the molecule is turned at a considerable angle (78°) relative to the plane of the ketoxime system, thus violating conjugation and increasing the length of the $C_{sp^2}(3)$–$C_{sp^2}(4)$ bond to 1.525(2) Å. The length of this bond approaches the measured length of the $C_{sp^2}(2)$–$C_{sp^3}(1)$ single bond in the difluoromethyl group (1.52 Å) and quite well matches the lengths of C–C bonds[10] in non-conjugated systems.

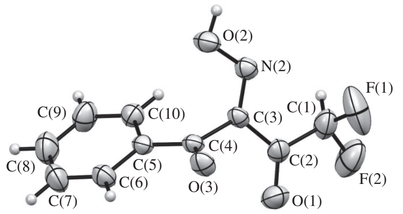


Figure 1 Compound **2a** in thermal vibration ellipsoids at 50% probability.

In conclusion, a simple and efficient method for synthesizing 3-(polyfluoroalkyl)propane-1,2,3-trione 2-oximes from lithium 3-(polyfluoroalkyl)-1,3-diketonates has been developed. The compounds obtained seem interesting for organic synthesis.

This study was supported by the Federal program for support of the leading scientific schools (grant no. NSh 8922.2016.3 for V.I.F., N.S.B., M.G.P., P.A.S. and V.N.C.).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2017.09.011.

References

1 (*a*) A. I. Mikhaleva, A. B. Zaitsev and B. A. Trofimov, *Russ. Chem. Rev.*, 2006, **75**, 797 (*Usp. Khim.*, 2006, **75**, 884); (*b*) V. I. Saloutin, Ya. V. Burgart, Z. E. Skryabina and O. G. Kuzueva, *Russ. J. Org. Chem.*, 1996, **32**, 792 (*Zh. Org. Khim.*, 1996, **32**, 828).

2 V. I. Saloutin, Y. V. Burgart, Z. E. Skryabina and O. G. Kuzueva, *J. Fluorine Chem.*, 1997, **84**, 107.

3 M. J. Crookes, P. Roy and D. L. H. Williams, *J. Chem. Soc., Perkin Trans. 2*, 1989, 1015.

4 (*a*) C. Scolastico, E. Conca, L. Prati, G. Guanti, L. Banfi, A. Berti, P. Farina and U. Valcavi, *Synthesis*, 1985, 850; (*b*) Ya. V. Burgart, O. G. Kuzueva, M. I. Kodess and V. I. Saloutin, *Russ. J. Org. Chem.*, 1998, **34**, 375 (*Zh. Org. Khim.*, 1998, **34**, 405); (*c*) O. G. Khudina, Ya. V. Burgart, V. I. Saloutin and M. A. Kravchenko, *Russ. Chem. Bull., Int. Ed.*, 2010, **59**, 1967 (*Izv. Akad. Nauk, Ser. Khim.*, 2010, 1917); (*d*) N. R. Emmadi, C. Bingi, S. S. Kotapalli, R. Ummanni, J. B. Nanubolu and K. Atmakur, *Bioorg. Med. Chem. Lett.*, 2015, 25, 2918.

5 D. N. Bazhin, Y. S. Kudyakova, N. A. Nemytova, Y. V. Burgart and V. I. Saloutin, *J. Fluorine Chem.*, 2016, **186**, 28.

6 K. I. Pashkevich, V. I. Saloutin and I. Ya. Postovskii, *Russ. Chem. Rev.*, 1981, **50**, 180 (*Usp. Khim.*, 1981, **50**, 325).

7 (*a*) V. I. Filyakova, N. S. Karpenko, O. A. Kuznetsova and K. I. Pashkevich, *Russ. J. Org. Chem.*, 1998, **34**, 381 (*Zh. Org. Khim.*, 1998, **34**, 411); (*b*) K. I. Pashkevich, V. I. Filyakova, V. G. Ratner and O. G. Khomutov, *Russ. Chem. Bull., Int. Ed.*, 1998, **47**, 1239 (*Izv. Akad. Nauk, Ser. Khim.*, 1998, 1279); (*c*) P. A. Slepukhin, G. L. Rusinov, V. N. Charushin, V. I. Filyakova, N. S. Karpenko, D. B. Krivolapov and I. A. Litvinov, *Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 1272 (*Izv. Akad. Nauk, Ser. Khim.*, 2004, 1221); (*d*) N. S. Boltachova, O. V. Fedorova, I. G. Ovchinnikova, O. N. Kazheva, A. N. Chekhlov, O. A. Dyachenko, G. L. Rusinov, V. I. Filyakova and V. N. Charushin, *J. Fluorine Chem.*, 2007, **128**, 762; (*e*) N. S. Boltacheva, V. I. Filyakova, E. F. Khmara, O. V. Koryakova and V. N. Charushin, *Russ. J. Gen. Chem.*, 2010, **80**, 179 [*Ross. Khim. Zh.*, 2010, **53** (1), 54].

8 A. Loupy and B. Tchoubar, *Effets de Sels en chimie organique et organométallique*, Ed. Dunod, Paris, 1988, p. 311.

9 D. Lin-Vien, N. B. Colthup, W. G. Faterley and J. G. Grasselli, *The Handbook of Infrared and Raman Charactiristic Frequencies of Organic Molecules*, Academic Press, New York, 1991.

10 F. H. Allen, D. G. Watson, L. Brammer, A. G. Orpen and R. Taylor, *International Tables for Crystallography*, 2006, vol. C, ch. 9.5, pp. 790–811.

11 G. M. Sheldrick, *Acta Crystallogr.*, 2008, **A64**, 112.

Received: 16th December 2016; Com. 16/5126

4,4-Difluoro-1-phenylbutane-1,2,3-trione 2-oxime **2a**. The reaction between lithium diketonate **1a** (0.77 g, 3.75 mmol) and sodium nitrite (0.3 g, 4.3 mmol) gave 0.75 g (88%) of compound **2a** as a white powder, mp 132.5–133.5 °C. IR (ν/cm^{-1}): 3237, 3207, 1728, 1646, 1619, 1593, 1420, 1323, 1299, 1228, 1141, 1077, 1046, 988, 906, 850, 772, 720, 682, 652, 553. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.53 (t, HCF_2 J 53.16 Hz), 7.50–7.55 (m, 2H, Ph), 7.65–7.70 (m, 1H, Ph), 7.80–7.86 (m, 2H, Ph), 8.79 (br. s, 1H, OH). ^{19}F NMR (470.5 MHz, $CDCl_3$) δ: 33.27 (d, CF_2, J 53.16 Hz). GC-MS (EI, in EtOH, TIC): t_R 19.93 min. MS, m/z (%): 227 [M]$^+$ (3.0), 183 [M$-CH_2NO$]$^+$ (0.3), 148 [M$-HCF_2CO$]$^+$ (0.9), 131 [PhCOCN]$^+$ (3.3), 105 [PhCO]$^+$ (100), 77 [Ph]$^+$ (52.4), 51 [HCF_2]$^+$ (24.8), 39 [HF_2]$^+$ (1.3), 27 [HCN]$^+$ (0.9). Found (%): C, 52.68; H, 3.08; N, 6.22; F, 16.71. Calc. for $C_{10}H_7F_2NO_3$ (%): C, 52.87; H, 3.11; N, 6.17, F, 16.73.

For characteristics of compounds **2b–f**, see Online Supplementary Materials.

[‡] *Crystal data for* **2a**. The XRD analysis was accomplished on an Xcalibur 3 automated four-circle diffractometer with a CCD-detector by a standard procedure [295(2) K, MoKα-irradiation, graphite monochromator, ω-scans with 1° steps]. No correction for absorption was applied. The structure was solved and refined with the SHELXTL program package.[11] All non-hydrogen atoms were refined in anisotropic approximation, the H-atoms were placed in the calculated positions and refined using a riding model with dependent isotropic displacement parameters.

The crystal of $C_{10}H_7F_2NO_3$ is monoclinic, space group $P2_1/c$, $a = 9.8467(9)$, $b = 11.6089(10)$ and $c = 8.7880(9)$ Å, $\beta = 91.141(10)°$, $V = 1004.34(16)$ Å^3, $Z = 4$, μ(MoKα) = 0.135 mm^{-1}, 4314 reflections were measured, of which 2597 unique reflections ($R_{int} = 0.0198$) were used in all calculations. The final parameters are $R_1 = 0.0841$, $wR_2 = 0.1250$ (all data) and $R_1 = 0.0495$, $wR_2 = 0.1087$ [$I > 2\sigma(I)$]. GOOF = 1.029. The largest diff. peak/hole is 0.20/–0.20 eÅ^{-3}.

CCDC 1529340 contains 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.