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> SHORT COMMUNICATIONS

Solvent-Free Synthesis of 4-Oxoalkane-1,1,2,2-tetracarbonitriles

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Problems related to directed synthesis of complex functionalized heterocyclic compounds constitute an important field of modern organic chemistry. Target structures may be constructed in several steps via successive introduction of particular substituents. However, this approach is often associated with low conversion of initial reactants, high expenditures of time, energy, and labor, the necessity of isolation and purification of intermediate products in every step, and other difficulties. These difficulties can be avoided by using special substrates capable of reacting in a domino (cascade) mode which implies that several consecutive chemical transformations can be accomplished as a single synthetic operation. Examples of such compounds are 4-oxoalkane-1,1,2,2-tetracarbonitriles 1 which were successfully used as starting compounds in the synthesis of difficultly accessible heterocyclic systems [1-6]. Up to now, more than 20 types of heterocycles have been obtained on the basis of 4-oxoalkane-1,1,2,2-tetracarbonitriles 1, and some compounds have been found to possess practically useful properties (e.g., fluorescence), which determines the importance of studies in this line [1].

Several known procedures for the synthesis of 4-oxoalkane-1,1,2,2-tetracarbonitriles are not free from a number of disadvantages. The historically first procedure based on the use of "molecular" silver requires expensive catalyst [7]. Methods for the preparation of 4-oxoalkane-1,1,2,2-tetracarbonitriles **1** from tetra-

cyanoethylene and carbonyl compounds in the presence of a catalytic amount of water, propan-1-ol, or ethanol [8], sulfur dioxide [9], and acetic or trichloroacetic acid [10] have been reported. However, these procedures are not general, and their results were demonstrated only with a few particular aliphatic ketones. The most widely used method is the reaction of tetracyanoethylene with ketones in 1,4-dioxane containing a catalytic amount of HCl [6, 11–13]. It is the most general among the above listed ones, and it provides the possibility of obtaining 4-oxoalkane-1,1,2,2-tetracarbonitriles 1 with two aromatic substituents R^1 and R^2 . A drawback of this method is long reaction time (up to several days for some ketones).

We have developed a new experimentally convenient procedure for the synthesis of 4-oxoalkane-1,1,2,2-tetracarbonitriles 1 in 84–98% yield under solvent-free conditions; this procedure conforms to the green chemistry principles since it requires no toxic solvents and ensures high conversion of the initial compounds.

Tetracyanoethylene and the corresponding ketone were mixed at a molar ratio of 1:1, and addition of *p*-toluenesulfonic acid as catalyst considerably shortened the reaction time. For example, the synthesis of 4-oxo-4-phenylbutane-1,1,2,2-tetracarbonitrile (1a) in the presence of a catalytic amount of hydrochloric acid required 2–3 days, whereas the solvent-free reaction was complete in 5 min.



 $R^{1} = Ph, R^{2} = H (a), Me (b); R^{1} = 3,4-(MeO)_{2}C_{6}H_{3}, R^{2} = H (c); R^{1} = 4-MeC_{6}H_{4}, R^{2} = Me (d); R^{1} = 3-O_{2}NC_{6}H_{4}, R^{2} = H (e); R^{1} = 4-ClC_{6}H_{4}, R^{2} = Me (f); R^{1} = 2,5-dimethylthiophen-3-yl, R^{2} = Ph (g).$

Compound 1a was reported previously [7], while compounds 1b-1g were synthesized for the first time. Their structure was confirmed by IR, ¹H NMR, and mass spectra and elemental analyses. The IR spectra of 1a-1g contained absorption bands 1672-1699 and 2250–2256 cm⁻¹ due to stretching vibrations of carbonyl group and unconjugated cyano groups, respectively. In the ¹H NMR spectra of these compounds the acidic CH(CN)₂ proton resonated at δ 5.74–6.15 ppm, and signals from protons in the α -position with respect to the carbonyl group were observed in the region δ 4.56–4.84 ppm (**1a–1f**) or at δ 5.57 ppm (**1g**). Their downfield position is determined by strong deshielding by the electron-withdrawing CO and CN groups. Signals from protons in the corresponding alkyl and aryl groups were also present.

4-Oxo-4-phenylbutane-1,1,2,2-tetracarbonitrile (1a). A mixture of 1.28 g (0.01 mol) of tetracyanoethylene, 0.011 mol of acetophenone, and 2–3 crystals of *p*-toluenesulfonic acid was thoroughly stirred and heated to 50–60°C with stirring until a homogeneous solution was formed. When the reaction was complete (the absence of tetracyanoethylene was checked by a hydroquinone test), the mixture was cooled and treated with 100 mL of water. The precipitate was filtered off and washed with water and propan-2-ol. Yield 2.31 g (93%).

Compounds **1b–1g** were synthesized in a similar way.

3-Methyl-4-oxo-4-phenylbutane-1,1,2,2-tetracarbonitrile (1b). Yield 2.54 g (97%), mp 130–131°C (decomp.). IR spectrum, v, cm⁻¹: 2256 (C=N), 1672 (C=O). ¹H NMR spectrum (acetone- d_6), δ , ppm: 1.81 d (3H, CHCH₃, J = 7.2 Hz), 4.84 q (1H, CH₃CH, J = 7.2 Hz), 5.99 (1H, CHCN), 7.65 t (2H, Ph, J = 7.7 Hz), 7.65 t (1H, Ph, J = 7.7 Hz), 8.19 d (2H, Ph, J = 7.7 Hz). Mass spectrum: m/z 262 (I_{rel} 2%) [M]⁺. Found, %: C 68.78; H 3.82; N 21.40. C₁₅H₁₀N₄O. Calculated, %: C 68.69; H 3.84; N 21.36. M 262.08.

4-(3,4-Dimethoxyphenyl)-4-oxobutane-1,1,2,2tetracarbonitrile (1c). Yield 2.71 g (88%), mp 156– 157°C (decomp.). IR spectrum, v, cm⁻¹: 2250 (C=N), 1694 (C=O). ¹H NMR spectrum, δ , ppm: in acetone-*d*₆: 3.91 s (3H, CH₃O), 3.94 s (3H, CH₃O), 4.56 s (2H, CH₂CO), 6.14 s (1H, CHCN), 7.13 d (1H, H_{arom}, *J* = 8.5 Hz), 7.64 d (1H, H_{arom}, *J* = 2.1 Hz), 7.55 d.d (1H, H_{arom}, *J* = 2.1, 8.5 Hz); in CDCl₃: 3.96 s (3H, CH₃O), 4.01 s (3H, CH₃O), 4.03 s (2H, CH₂CO), 5.50 s (1H, CHCN), 6.96 d (1H, H_{arom}, J = 8.4 Hz), 7.49 d (1H, H_{arom}, J = 2.1 Hz), 7.55 d.d (1H, H_{arom}, J = 2.1, 8.4 Hz). Mass spectrum: m/z 308 (I_{rel} , 3%) [M]⁺. Found, %: C 62.27; H 3.90; N 18.19. C₁₆H₁₂N₄O₃. Calculated, %: 62.33; H 3.92; N 18.17. M 308.09.

3-Methyl-4-(methylphenyl)-4-oxobutane-1,1,2,2tetracarbonitrile (1d). Yield 2.48 g (90%), mp 166– 167°C (decomp.). IR spectrum, v, cm⁻¹: 2250 (C=N), 1699 (C=O). ¹H NMR spectrum (acetone- d_6), δ , ppm: 1.52 d (3H, CH₃CH, J = 7.3 Hz), 2.39 s (3H, CH₃), 4.71 q (1H, CH₃CH), 5.83 s (1H, CHCN), 7.16 d (2H, H_{arom}, J = 8.8 Hz), 8.15 d (2H, H_{arom}, J = 8.8 Hz). Mass spectrum: m/z 276 (I_{rel} 5%) [M]⁺. Found, %: C 69.46; H 4.41; N 20.35. C₁₆H₁₂N₄O. Calculated, %: 69.55; H 4.38; N 20.28. M 276.10.

4-(3-Nitrophenyl)-4-oxobutane-1,1,2,2-tetracarbonitrile (1e). Yield 2.87 g (98%), mp 137–138°C (decomp.). IR spectrum, v, cm⁻¹: 2255 (C=N), 1693 (C=O). ¹H NMR spectrum (acetone- d_6), δ , ppm: 4.82 s (2H, CH₂CO), 6.15 s (1H, CHCN), 7.95 t (1H, H_{arom}, J = 8.0 Hz), 8.59 m (2H, H_{arom}) 8.93 t (1H, H_{arom}, J = 1.8 Hz). Mass spectrum: m/z 293 (I_{rel} 6%) [M]⁺. Found, %: C 57.27; H 2.40; N 23.94. C₁₄H₇N₅O₃. Calculated, %: 57.34; H 2.41; N 23.88. M 293.05.

4-(4-Chlorophenyl)-3-methyl-4-oxobutane-1,1,2,2-tetracarbonitrile (1f). Yield 2.49 g (84%), mp 160–161°C (decomp.). IR spectrum, v, cm⁻¹: 2255 (C=N), 1693 (C=O). ¹H NMR spectrum (acetone- d_6), δ , ppm: 1.84 d (3H, CH₃, J = 7.3 Hz), 4.79 m (1H, CH₃CH), 5.98 s (1H, CHCN), 7.12 d (2H, H_{arom}, J = 8.7 Hz), 8.14 d (2H, H_{arom}, J = 8.7 Hz). Mass spectrum: m/z 296 (I_{rel} 2%) [M]⁺. Found, %: C 60.61; H 3.04; N 18.92. C₁₅H₉ClN₄O. Calculated, %: 60.72; H 3.06; N 18.88. M 296.04.

4-(2,5-Dimethylthiophen-3-yl)-4-oxo-3-phenylbutane-1,1,2,2-tetracarbonitrile (1g). Yield 3.29 g (92%), mp 125–126°C (decomp.). IR spectrum, v, cm⁻¹: 2254 (C=N), 1678 (C=O). ¹H NMR spectrum (acetone- d_6), δ , ppm: 2.27 s (3H, CH₃), 2.73 s (3H, CH₃), 5.57 s (1H, CHCO), 5.74 s (1H, CHCN), 7.11 d (1H, 4'-H), 7.54–7.58 m (3H, Ph), 7.66–7.69 m (2H, Ph). Mass spectrum: m/z 358 (I_{rel} 1%) [M]⁺. Found, %: C 66.93; H 3.92; N 15.66. C₂₀H₁₄N₄OS. Calculated, %: 67.02; H 3.94; N 15.63. *M* 358.09.

The purity of the isolated compounds was checked by TLC on Sorbfil PTSKh-AF-A-UF plates; spots were visualized under UV light, by treatment with iodine vapor, or by calcination. The decomposition points were determined on an Optimelt MPA100 melting point apparatus. The IR spectra were recorded on an FSM-1202 spectrometer with Fourier transform from samples dispersed in mineral oil. The ¹H NMR spectra were recorded on a Bruker DRX-500 spectrometer at 500.13 MHz relative to tetramethylsilane as internal standard. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT INCOS-50 instrument. The elemental compositions were determined using a Vario Micro cube CHN analyzer.

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