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SHORT COMMUNICATIONS

Synthesis of 3-Arylcyclopropane-1,1,2,2-tetracarbonitriles under Micellar Catalysis

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Abstract—An environmentally benign procedure has been developed for the synthesis of 3-arylcyclopropane-1,1,2,2-tetracarbonitriles in an aqueous surfactant solution.

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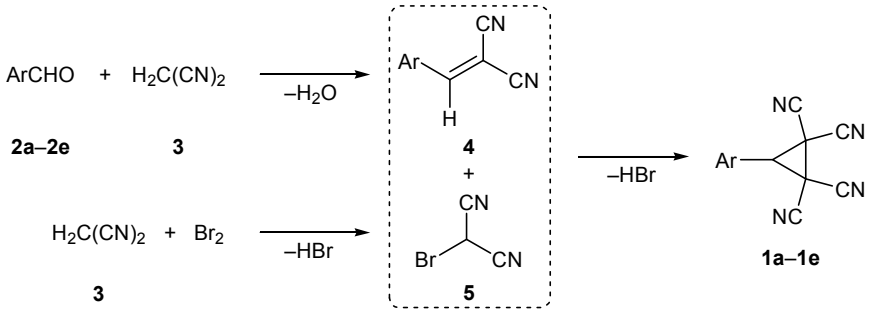
Cyclopropane ring is an important structural unit of many synthetic and natural biologically active compounds possessing anticancer [1, 2], anticonvulsant [3], and antimicrobial activity [4, 5] and used in the treatment of HIV [6] and varicella infections [7].

Most known methods of synthesis of 1,1,2,2-tetracyanocyclopropanes are based on the Wideqvist reaction [8], Michael addition of bromomalononitrile to ylidene derivatives of malononitrile [9], and reactions of diazo alkanes with tetracyanoethylene [10]. Later on, some modifications of these methods have been proposed, in particular one-pot syntheses [11, 12] and reactions with electrochemically generated reagents [13]. All these methods utilize organic solvents.

Herein, we describe the synthesis of 1,1,2,2-tetracyanocyclopropanes **1a**–**1e** by multicomponent reaction of aromatic aldehydes **2a**–**2e** with malononitrile (**3**) and bromine in aqueous medium in the presence of a surfactant [13]. We used a nonionic surfactant, cocamidopropyl dimethylamine oxide (*OKSIPAV AP*), which successfully catalyzed Knoevenagel condensation [14]. Well known Triton X-100 also provided satisfactory results, but the yields were somewhat lower, 75–86%. When the reaction was carried out in the presence of an anionic surfactant, sodium lauryl sulfate, the yield did not exceed 30%.

We believe that the process begins with the Knoevenagel condensation of aldehyde **2a**–**2e** with malononitrile (**3**), which leads to the formation of 2-benzylidenemalononitriles **4**. Simultaneously, the bromination of **3** gives 2-bromomalononitrile (**5**). The subsequent Michael addition of bromomalononitrile **5** to benzylidenemalononitrile **4**, followed by cyclization, yields cyclopropanes **1a**–**1e**.

Thus, we have developed a simple and environmentally safe procedure for the synthesis of 3-aryl-



Ar = Ph (**a**), 2-ClC_6H_4 (**b**), 4-MeC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**), 3-$O_2NC_6H_4$ (**e**).

cyclopropane-1,1,2,2-tetracarbonitriles in 85–94% yield. The reaction requires no base catalyst, and the products crystallize directly from the reaction mixture.

3-Phenylcyclopropane-1,1,2,2-tetracarbonitrile (1a). A solution of 0.160 g of bromine in 2 mL of 5% aqueous potassium bromide was added dropwise to a suspension of 0.106 g (1 mmol) of benzaldehyde **2a**–**2e**, 0.132 g (2 mmol) of malononitrile (**3**), and 0.046 g (0.15 mmol) of cocamidopropyl dimethylamine oxide in 5 mL of water. The mixture was stirred for 4 h at room temperature (TLC) and diluted with 5 mL of water, and the precipitate was filtered off and washed with 10 mL of water and 5 mL of ethanol. Yield 92%, mp 229–230°C; published data [9]: mp 227–230°C. IR spectrum, ν, cm^{-1}: 3035 (C–H), 2242 (C≡N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.27 s (1H, CH), 7.44–7.52 m (3H, H_{arom}), 7.74–7.82 m (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 218 (10) $[M]^+$, 154 (100) $[M - 64]^+$. Found, %: C 71.63; H 2.81; N 25.52. $C_{13}H_6N_4$. Calculated, %: C 71.55; H 2.77; N 25.68. *M* 218.22.

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

3-(2-Chlorophenyl)cyclopropane-1,1,2,2-tetracarbonitrile (1b). Yield 94%, mp 246–247°C; published data [9]: mp 246–248°C. IR spectrum, ν, cm^{-1}: 3030 (C–H), 2240 (C≡N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.48 s (1H, CH), 7.48–7.62 m (2H, H_{arom}), 7.68–7.74 m (1H, H_{arom}), 8.03–8.09 m (1H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 254/252 (3/8) $[M]^+$, 190/188 (33/100) $[M - 64]^+$. Found, %: C 61.89; H 2.03; N 22.01. $C_{13}H_5ClN_4$. Calculated, %: C 61.80; H 1.99; N 22.18. *M* 252.66.

3-(4-Methylphenyl)cyclopropane-1,1,2,2-tetracarbonitrile (1c). Yield 89%, mp 216–217°C; published data [9]: mp 227–230°C. IR spectrum, ν, cm^{-1}: 3035 (C–H), 2245 (C≡N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.33 s (3H, CH_3), 5.23 s (1H, CH), 7.30 d (2H, C_6H_4, *J* = 7.9 Hz), 7.68 d (2H, C_6H_4, *J* = 7.8 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 232 (13) $[M]^+$, 168 (100) $[M - 64]^+$. Found, %: C 72.51; H 3.55; N 23.92. $C_{14}H_8N_4$. Calculated, %: C 72.40; H 3.47; N 24.12. *M* 232.25.

3-(4-Methoxyphenyl)cyclopropane-1,1,2,2-tetracarbonitrile (1d). Yield 85%, mp 209–210°C [9]. IR spectrum, ν, cm^{-1}: 3038 (C–H), 2240 (C≡N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.79 s (3H, OCH_3), 5.15 s (1H, CH), 7.04 d (2H, C_6H_4, *J* = 8.4 Hz), 7.73 d (2H, C_6H_4, *J* = 8.4 Hz). Mass spectrum: *m*/*z* 248 (I_{rel} 10%) $[M]^+$. Found, %: C 67.80; H 3.35; N 22.41. $C_{14}H_8N_4O$. Calculated, %: C 67.74; H 3.25; N 22.57. *M* 248.25.

3-(3-Nitrophenyl)cyclopropane-1,1,2,2-tetracarbonitrile (1e). Yield 88%, mp 250–251°C; published data [9]: mp 246–248°C. IR spectrum, ν, cm^{-1}: 3033 (C–H), 2242 (C≡N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.46 s (1H, CH), 7.82 t (1H, H_{arom}, *J* = 8.0 Hz), 8.28–8.41 m (2H, H_{arom}), 9.01 s (1H, H_{arom}). Mass spectrum: *m*/*z* 263 (I_{rel} 5%) $[M]^+$. Found, %: C 59.43; H 1.98; N 26.47. $C_{13}H_5N_5O_2$. Calculated, %: C 59.32; H 1.91; N 26.61. *M* 263.22.

The IR spectra were recorded on an FSM-1202 spectrometer with Fourier transform from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Bruker DRX-500 spectrometer from solutions in DMSO-d_6 using tetramethylsilane as internal standard. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT INCOS-50 instrument. The elemental analyses were obtained on a Vario Micro cube CHN analyzer. The melting points were determined on an OptiMelt MPA100 automated melting point apparatus. The progress of reactions was monitored, and the purity of the isolated compounds was checked, by TLC on Sorbfil PTSKh-AF-A-UF plates using ethyl acetate as eluent; spots were visualized under UV light, by treatment with iodine vapor, or by thermal decomposition.

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