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SHORT COMMUNICATIONS

Three-Component Heterocyclization of 2-Benzylidenemalononitrile with Aldehydes and Amino Acids

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The double C=C bond in benzylidenemalononitrile is highly reactive due to activation by two cyano groups; therefore, this compound is widely used in preparative organic synthesis. Increased interest in the chemistry of such compounds is related to the possibility of introducing into their molecules of pharmacophoric fragments [1–3] or preparing structures with practically important properties [4, 5]. In addition, combination of two reaction centers (cyano group and C=C bond) in such molecules makes them interesting models for studying 1,3-dipolar cycloaddition reactions with various 1,3-dipoles, in particular with azomethine ylides.

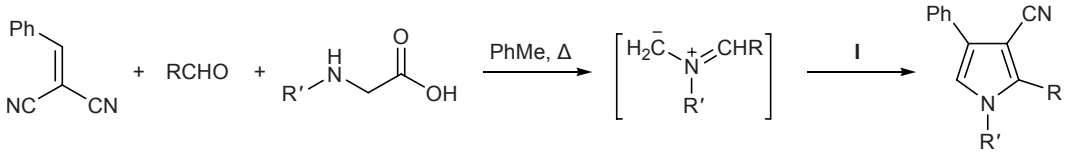
With a view to examine competing reactivity of the cyano groups and double C=C bond in the molecule of 2-benzylidenemalononitrile (**I**), the latter was brought into three-component heterocyclization with aldehydes **II** and **III** and N-substituted 2-aminoacetic acids **IV** and **V**. The reaction occurred on heating in boiling toluene and afforded substituted 1*H*-pyrrole-3-carbonitriles **VI**–**IX** in moderate yields.

In this transformation, the cyano group in molecule **I** does not act as dipolarophile. Presumably, thermolysis of 3,4-dimethoxybenzaldehyde (**II**) or paraformaldehyde (**III**) in the presence of *N*-methyl- or *N*-phenylglycine (**IV** or **V**) generates reactive azomethine ylide **A** [6], and 1,3-dipolar cycloaddition of the latter to dipolarophile **I** gives substituted pyrroles **VI**–**IX**.

The structure of pyrroles **VI**–**IX** was confirmed by the IR, ^{1}H NMR, UV, and mass spectra. The IR spectra of **VI**–**IX** lacked absorption band at 1630 cm^{-1}, which is typical of conjugated cyanoethenes [7]. The ^{1}H NMR spectra of **VI**–**IX** were consistent with the assumed structures and were similar to structurally related compounds of the pyrrole series [8]. The electronic absorption spectra indicate enhanced conjugation in molecules **VI**–**IX**. Compounds **VI**–**IX** displayed in the mass spectra $[M - 1]^+$ ion peaks and peaks of fragment ions resulting from retro-1,3-dipolar cycloaddition with cleavage of the N^1–C^2/C^3–C^4 or C^3–C^4/N^1–C^5 bonds in the heteroring. Ion peaks corresponding to benzyl type decomposition ($[C_7H_7]^+$) were also present in the mass spectra.

Thus the described three-component heterocyclization leads to the formation of pyrrole derivatives which may be promising from the viewpoint of their further functionalization.

4-Phenyl-1*H*-pyrrole-3-carbonitriles VI–IX (*general procedure*). 2-Benzylidenemalononitrile (**I**), 10 mmol, was dispersed in 100 ml of anhydrous toluene, 50 mmol of aldehyde **II** or **III** and 20 mmol of amino acid **IV** or **V** were added, and the mixture was heated for 7 h under reflux in a flask equipped with a Dean–Stark trap. The solvent was distilled off under reduced pressure, and the residue was subjected to column chromatography on silica gel (100–400 μm)



I **II**, **III** **IV**, **V** **A** **VI–IX**

II, **VI**, **VIII**, R = 3,4-$(MeO)_2C_6H_3$; **III**, **VII**, **IX**, R = H; **IV**, **VI**, **VII**, R′ = Me; **V**, **VIII**, **IX**, R′ = Ph.

using benzene (**VI**, **VIII**) or chloroform (**VII**, **IX**) as eluent.

2-(3,4-Dimethoxyphenyl)-1-methyl-4-phenyl-1*H*-pyrrole-3-carbonitrile (VI). Yield 41%, mp 95–97°C. IR spectrum ($CHCl_3$): ν 2230 cm^{-1} (C≡N). UV spectrum, λ_{max}, nm (logε): 245 (4.28), 373 (4.43). ^1H NMR spectrum, δ, ppm: 7.62–7.65 d (1H, H_{arom}), 7.48 m (5H, H_{arom}), 7.20–7.23 d (1H, H_{arom}), 7.10 s (1H, H_{arom}), 6.70 s (1H, CH), 3.85 s (3H, CH_3O), 3.80 s (3H, CH_3O), 3.77 s (3H, CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 317 (22) $[M - 1]^+$, 303 (16) $[M - CH_3]^+$, 292 (47) $[M - CN]^+$, 287 (10) $[M - CH_3O]^+$, 190 (100) $[M - CN - C_8H_6]^+$, 130 (7) $[M - CN - C_{10}H_{10}O_2]^+$, 91 (60) $[C_7H_7]^+$. Found, %: C 75.24; H 5.45; N 8.67. $C_{20}H_{18}N_2O_2$. Calculated, %: C 75.47; H 5.66; N 8.81. *M* 318.38.

1-Methyl-4-phenyl-1*H*-pyrrole-3-carbonitrile (VII). Yield 53%, mp 135–137°C. IR spectrum ($CHCl_3$): ν 2230 cm^{-1} (C≡N). UV spectrum, λ_{max}, nm (logε): 245 (4.29), 310 (4.41). ^1H NMR spectrum, δ, ppm: 7.46 m (5H, H_{arom}), 7.05 s (1H, CH), 6.72 s (1H, CH), 3.76 s (3H, CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 181 (25) $[M - 1]^+$, 168 (20) $[M - CH_3]^+$, 130 (100) $[M - CN - C_2H_2]^+$, 91 (55) $[C_7H_7]^+$. Found, %: C 78.94; H 5.32; N 15.21. $C_{12}H_{10}N_2$. Calculated, %: C 79.12; H 5.49; N 15.39. *M* 182.24.

2-(3,4-Dimethoxyphenyl)-1,4-diphenyl-1*H*-pyrrole-3-carbonitrile (VIII). Yield 51%, mp 162–163°C. IR spectrum ($CHCl_3$): ν 2230 cm^{-1} (C≡N). UV spectrum, λ_{max}, nm (logε): 245 (4.25), 380 (4.42). ^1H NMR spectrum, δ, ppm: 7.52 m (10H, H_{arom}), 7.63–7.66 d (1H, H_{arom}), 7.20–7.24 d (1H, H_{arom}), 7.12 s (1H, H_{arom}), 6.71 s (1H, CH), 3.85 s (3H, CH_3O), 3.80 s (3H, CH_3O). Mass spectrum, *m*/*z* (I_{rel}, %): 379 (20) $[M - 1]^+$, 354 (35) $[M - CN]^+$, 349 (10) $[M - CH_3O]^+$, 303 (6) $[M - C_6H_5]^+$, 252 (100) $[M - CN - C_8H_6]^+$, 192 (20) $[M - CN - C_{10}H_{10}O_2]^+$, 91 (62) $[C_7H_7]^+$. Found, %: C 78.74; H 5.06; N 7.18. $C_{25}H_{20}N_2O_2$. Calculated, %: C 78.95; H 5.26; N 7.37. *M* 380.45.

1,4-Diphenyl-1*H*-pyrrole-3-carbonitrile (IX). Yield 55%, mp 157–158°C. IR spectrum ($CHCl_3$): ν 2230 cm^{-1} (C≡N). UV spectrum, λ_{max}, nm (logε): 245 (4.26), 320 (4.40). ^1H NMR spectrum, δ, ppm: 7.51 m (10H, H_{arom}), 7.06 s (1H, CH), 6.74 s (1H, CH). Mass spectrum, *m*/*z* (I_{rel}, %): 243 (15) $[M - 1]^+$, 192 (100) $[M - CN - C_2H_2]^+$, 167 (5) $[M - C_6H_5]^+$, 91 (58) $[C_7H_7]^+$. Found, %: C 83.42; H 4.74; N 11.29. $C_{17}H_{12}N_2$. Calculated, %: C 83.61; H 4.92; N 11.48. *M* 244.31.

The IR spectra were recorded on an IKS-29 spectrometer from solutions in chloroform with a concentration of 40 mg/ml using 0.1-mm cells. The ^1H NMR spectra were measured on a Tesla BS-487C spectrometer (80 MHz) using acetone-d_6 as solvent and hexamethyldisiloxane as internal reference. The electronic absorption spectra were obtained on an SF-8 spectrophotometer from solutions in carbon tetrachloride. The mass spectra (electron impact, 70 eV) were recorded on a Finnigan SSQ-7000 instrument with direct sample admission into the ion source (vaporizer temperature 90–150°C). The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using acetone–hexane (2:3) as eluent; development with iodine vapor.

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