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SHORT COMMUNICATIONS

First Synthesis and Structure of Ethyl 3,3,5,5-Tetracyano-2-hydroxy-2-methyl-4,6-diphenylcyclohexane-1-carboxylate

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Abstract—Ethyl 3,3,5,5-tetracyano-2-hydroxy-2-methyl-4,6-diphenylcyclohexane-1-carboxylate was synthesized for the first time by three-component condensation of benzaldehyde with ethyl acetoacetate and malononitrile in the presence of trichloroacetic acid. The product structure was proved by X-ray analysis.

Keywords: ethyl 3,3,5,5-tetracyano-2-hydroxy-2-methyl-4,6-diphenylcyclohexane-1-carboxylate, ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4*H*-pyrane-3-carboxylate, three-component condensation, X-ray analysis.

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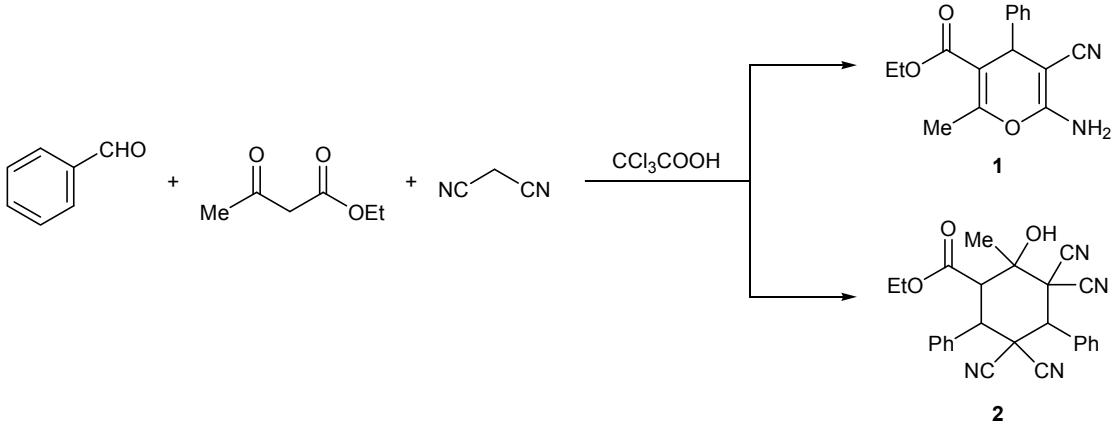
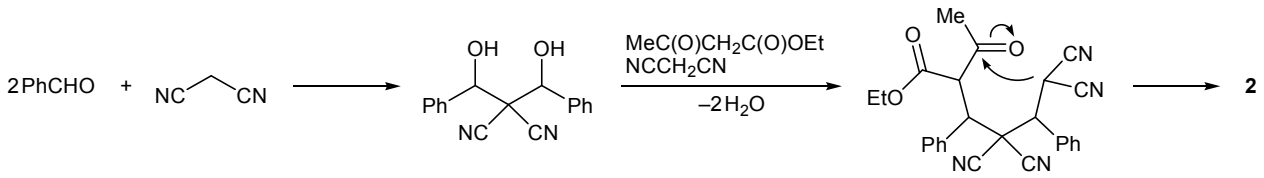
An important aspect of modern organic chemistry is the development of methods and approaches allowing the synthesis of compounds with practically valuable properties to be accomplished with minimum consumption of reagents, solvents, energy, and time. This should make organic synthesis more efficient from the ecological and economic viewpoints. One of such approaches is based on multicomponent reactions which have now been firmly established in the arsenal of methods of synthetic organic chemistry. Cascade (domino) reactions provide access to heterocyclic systems that are difficult or impossible to obtain by conventional methods. Pyran derivatives occupy an important position in the series of heterocyclic compounds of both natural and synthetic origins. Among them, functionalized 2-amino-4*H*-pyrans containing electron-withdrawing groups in the 3-position constitute one of the most extensively studied subclasses. The presence of such functional groups as amino, cyano, or carbonyl in molecules of known 2-amino-4*H*-pyrans makes them promising intermediate products for the synthesis of fused heterocycles. Many fused 2-amino-4*H*-pyrans were found to exhibit biological activity [1–4].

Taking into account the above stated, we previously studied three-component condensations of malono-

Scheme 1.



Scheme 2.



nitrile with various aldehydes and carbonyl compounds containing an active methylene group [5]. In continuation of these studies, herein we report the three-component condensation of benzaldehyde with ethyl acetoacetate and malononitrile in the presence of trichloroacetic acid. It was found that, depending on the conditions, the condensation product was the expected product, ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (**1**), or previously unknown ethyl 3,3,5,5-tetracyano-2-hydroxy-2-methyl-4,6-diphenylcyclohexane-1-carboxylate (**2**) (Scheme 1). Compound **1** was formed as the major product when the reactants were heated in boiling ethanol for 1–2 h. New compound **2** was obtained when the reaction mixture was stirred for 7–9 h at room temperature. The progress of the reaction was monitored by TLC, and the product structure was confirmed by elemental analyses and ^{1}H NMR and X-ray diffraction data (Fig. 1). A probable mechanism for the formation of **2** is shown in Scheme 2.

Compounds 1 and 2 (*general procedure*). A round-bottom flask equipped with a reflux condenser and a mechanical stirrer was charged with 0.102 mL (1 mmol) of benzaldehyde, 0.07 g (1 mmol) of malononitrile, 0.127 mL (1 mmol) of ethyl acetoacetate, 25 mg of trichloroacetic acid, and 10 mL of ethanol. The mixture was stirred under reflux or at room temperature and cooled (if necessary), and the precipitate was filtered off, washed with ethanol, dried, and recrystallized from aqueous ethanol.

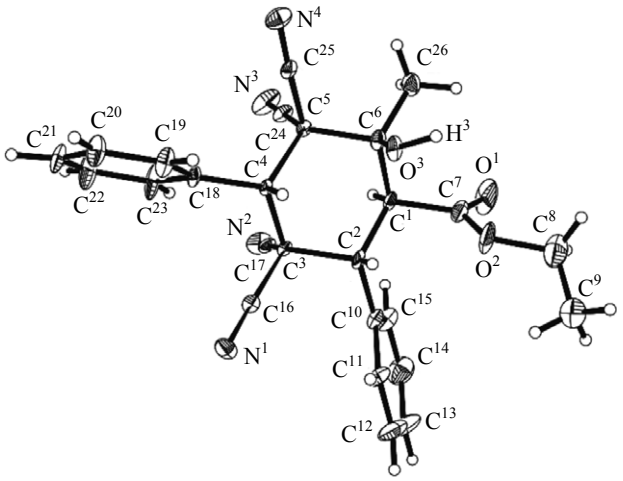


Fig. 1. Structure of the molecule of ethyl 3,3,5,5-tetracyano-2-hydroxy-2-methyl-4,6-diphenylcyclohexane-1-carboxylate (**2**) according to the X-ray diffraction data.

Ethyl 6-amino-5-cyano-2-methyl-4-phenyl-4*H*-pyran-3-carboxylate (1). Yield 72%, mp 112–114°C [6]. ^{1}H NMR spectrum, δ, ppm: 7.30 t (1H, H_{arom}), 7.25 m (1H, H_{arom}), 7.17 d (1H, H_{arom}), 6.89 s (2H, NH_2), 4.33 s (1H), 3.93 m (2H, CH_2), 2.27 s (3H, CH_3), 1.06 t (3H, CH_3). Found, %: C 67.63; H 5.59; N 9.89. $C_{16}H_{16}N_2O_3$. Calculated, %: C 67.60; H 5.63; N 9.85.

Ethyl 3,3,5,5-tetracyano-2-hydroxy-2-methyl-4,6-diphenylcyclohexane-1-carboxylate (2). Yield 63%, mp 120–124°C. Found %: C 71.29; H 5.09; N 12.72. $C_{26}H_{22}N_4O_3$. Calculated, %: C 71.23; H 5.02; N 12.78.

The ^{1}H NMR spectrum of **1** was recorded in DMSO-d_6 on a Bruker 300 spectrometer (300 MHz) at 25°C. The purity of the isolated compounds was checked by TLC on *Sorbfil* plates using ethyl acetate–benzene (1:3) as eluent; spots were visualized by treatment with iodine vapor.

A single crystal of **2** suitable for X-ray analysis was obtained by double recrystallization from ethanol. The X-ray diffraction data were obtained on a Bruker APEX II CCD diffractometer at 100 K (Mo K_α radiation, graphite monochromator, φ- and ω-scanning, $2\theta_{max}$ = 56°). The structure was solved by the direct method and was refined by the least-squares method in anisotropic approximation for non-hydrogen atoms. The OH hydrogen atom was localized objectively by difference Fourier syntheses, and its position was refined in isotropic approximation with fixed positional and thermal parameters. The other hydrogens were placed in geometrically calculated positions which were refined in a similar way. All calculations were performed using SHELXTL PLUS and SADABS [7, 8]. The complete set of X-ray diffraction data for compound **2** was deposited to the Cambridge Crystallographic Data Centre (CCDC entry no. 1839026) and is available at *www.ccdc.cam.ac.uk*.

CONFLICT OF INTERESTS

The authors declare the absence of conflict of interests.

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