

Reaction of Tetracyanoethylene with 2-Substituted Cyclohexanones

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Abstract—Reactions of 2-methylcyclohexanone and menthone with tetracyanoethylene gave 2-(1,1,2,2-tetracyanoethyl)cyclohexanones which underwent quantitative transformation in the solid phase into 3,4-cyano-substituted 2-aminopyrans in 2–3 days at room temperature. 2-Methyl-2-(1,1,2,2-tetracyanoethyl)cyclohexanone reacted with hydroiodic acid to afford 8a-hydroxy-2-iodo-4a-methyl-1,4,4a,5,6,7,8,8a-octahydroquinoline-3,4,4-tricarbonitrile. The reaction of 2,2'-methylene-di(cyclohexanone) with tetracyanoethylene resulted in formation of 7-imino-4,5-tetramethylene-2'-oxo-6-oxabicyclo[3.2.1]octane-2-spiro-1'-cyclohexane-1,8,8-tricarbonitrile.

As follows from the data summarized in [1], cyclic carbonyl compounds were involved mainly in reactions with α,β -unsaturated nitriles. This is explained by higher reactivity of cyclic ketones as compared to open-chain analogs. Cyclic ketones are used as initial compounds for the synthesis of fused pyran derivatives [2–4]. Substituted tetrahydrobenzo[*b*]pyrans are formed in 10 min by reaction of cyclohexanone with α,β -unsaturated nitriles in boiling ethanol in the presence of triethylamine [3]. Derivatives of dihydrofuran [5] and pyridine [6–9] were obtained in two steps from cyclohexanone and tetracyanoethylene.

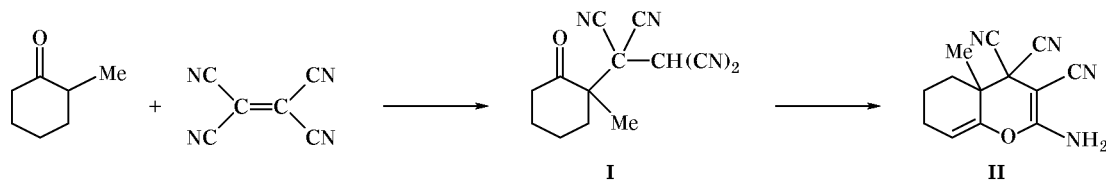
Reactions of linear ketones, such as acetone, methyl ethyl ketone, and diethyl ketone, with tetracyanoethylene take 6–24 h. Cyclohexanone reacts with tetracyanoethylene much more vigorously (in 1–2 min) [10, 11]. Wide application of tetracyanoethylene in reactions with carbonyl compounds with the goal of obtaining carbo- and heterocycles [1–10] stimulates our further studies in this field and emphasizes prospects in the use of these reactions

for modification of organic compounds possessing a $\text{CR}_3\text{C}(\text{O})\text{CHR}_2$ fragment.

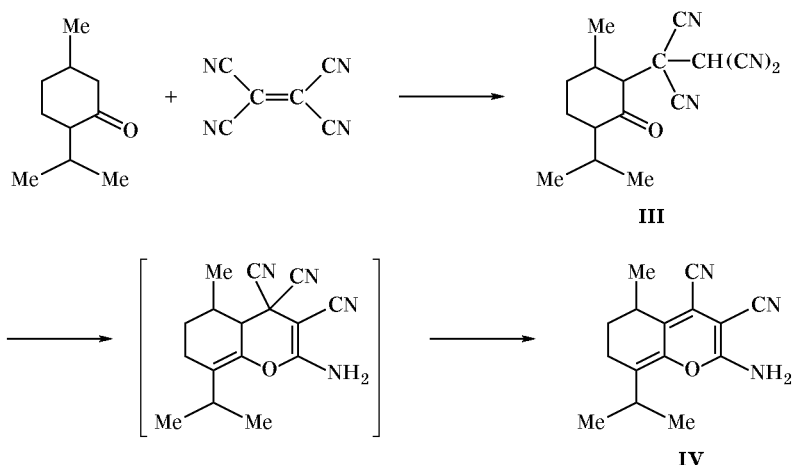
We have found that, unlike unsubstituted cyclohexanone, reactions of 2-substituted cyclohexanones with tetracyanoethylene either occur under different conditions or yield unexpected products. The reaction of tetracyanoethylene with 2-substituted cyclohexanones, including 2-chlorocyclohexanone, was reported for the first time in [11]. Instead of the expected 2-chloro-2-(1,1,2,2-tetracyanoethyl)cyclohexanone, 6,6,7,7-tetracyanospiro[2.4]heptan-1-one was isolated. Cyclohexanone reacts with tetracyanoethylene to give 2-(1,1,2,2-tetracyanoethyl)cyclohexanone; the latter undergoes complete decomposition in 5–7 days at room temperature [10, 11].

The present work continues our studies on tetracyanoethylation of 2-substituted cyclohexanones. As substrates we used 2-methylcyclohexanone, menthone (2-isopropyl-5-methylcyclohexanone), and 2,2'-methylene-di(cyclohexanone). The reactions were carried out in dioxane in the presence of hydrochloric

Scheme 1.



Scheme 2.



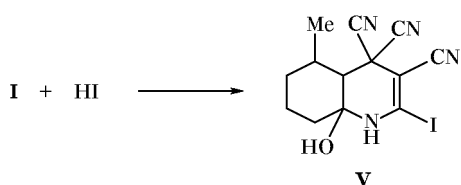
acid. From 2-methylcyclohexanone in 3 h we obtained 90% of 2-methyl-2-(1,1,2,2-tetracyanoethyl)cyclohexanone (**I**) (Scheme 1), i.e., tetracyanoethylation of 2-methylcyclohexanone occurs at position 2.

An unusual transformation was revealed when cyclohexanone **I** was stored for 1–2 days at room temperature. As a result, 2-amino-4a-methyl-4a,5,6,7-tetrahydro-4*H*-chromene-3,4,4-tricarbonitrile (**II**) was formed in quantitative yield (Scheme 1).

Analogous transformations were observed in the tetracyanoethylation of menthone. The latter reacted with tetracyanoethylene to afford 69% of 6-isopropyl-2-(1,1,2,2-tetracyanoethyl)-3-methylcyclohexanone (**III**) which was quantitatively converted into 2-amino-8-isopropyl-5-methyl-6,7-dihydro-5*H*-chromene-3,4-dicarbonitrile (**IV**) on storage in the solid state (Scheme 2).

The reaction with HI indicates high reactivity of ketone **I**. Stirring of 2-methyl-2-(1,1,2,2-tetracyanoethyl)cyclohexanone (**I**) in concentrated hydroiodic acid for 1–2 h gave 83% of 8a-hydroxy-2-iodo-5-methyl-1,4,4a,5,6,7,8,8a-octahydroquinoline-3,4,4-tricarbonitrile (**V**) (Scheme 3).

Scheme 3.

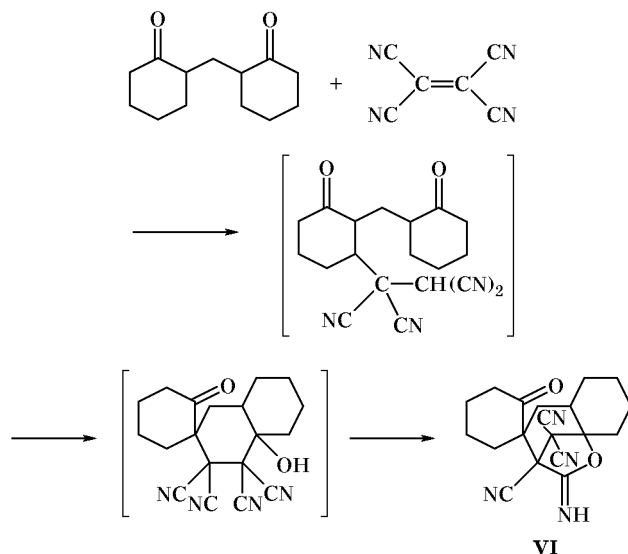


This reactions provides a support for the scheme of formation of 2-iodocyanopyridines by reaction of $\beta,\beta,\gamma,\gamma$ -tetracyanoalkanes with HI, which was

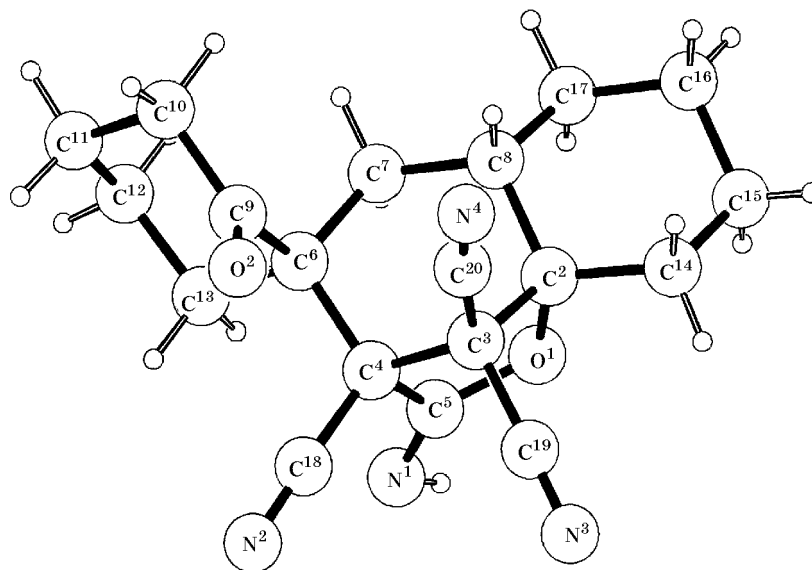
proposed by us in [8]: an analogous structure was assumed to be the last intermediate.

The reaction of 2,2'-methylene-di(cyclohexanone) with tetracyanoethylene occurs under mild conditions and at a high rate. The product is oxabicyclo[3.2.1]-octane-7,8,8-tricarbonitrile **VI** which is formed in high yield. The main difference of this reaction from those described above is intramolecular interaction between the acid dicyanomethyl fragment CH(CN)₂ and the carbonyl group, leading to closure of two rings (Scheme 4).

Scheme 4.



The structure of compounds **I–VI** was confirmed by the data of IR and ¹H NMR spectroscopy and mass spectrometry. The structure of product **VI** was proved by X-ray analysis.



Structure of the molecule of 7-imino-4,5-tetramethylene-2'-oxo-6-oxabicyclo[3.2.1]octane-2-spiro-1'-cyclohexane-1,8,8-tricarbonitrile (VI) according to the X-ray diffraction data.

EXPERIMENTAL

The IR spectra were recorded on a UR-20 spectrometer in mineral oil. The ^1H NMR spectra were obtained on a Bruker AM-300 instrument (300 MHz) in $\text{DMSO-}d_6$. The molecular weights were determined from the mass spectra which were run on a Finnigan Mat Incos 50 instrument (70 eV). The unit cell parameters and reflection intensities for a single crystal of VI were measured on a Siemens P3/PC four-circle diffractometer (λMoK_α irradiation, graphite monochromator, $\theta/2\theta$ scanning). The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates.

2-Methyl-2-(1,1,2,2-tetracyanoethyl)cyclohexanone (I) and 6-isopropyl-3-methyl-2-(1,1,2,2-tetracyanoethyl)cyclohexanone (III) (*general procedure*). 2-Methylcyclohexanone or menthone, 0.02 mol, and 3–4 drops of concentrated hydrochloric acid were added to 0.01 mol of tetracyanoethylene in 20 ml of dioxane. After 24 h, 100 ml of water was added, and the precipitate was filtered off and washed with 2-propanol and ether.

Compound I. Yield 90%, mp 168–167°C. ^1H NMR spectrum, δ , ppm: 6.35 s (1H, CH), 2.6 m (2H, CH_2CO), 1.74–1.29 m [8H, $(\text{CH}_2)_4$], 0.94 s (3H, Me). IR spectrum, ν , cm^{-1} : 1710, 2270.

Compound III. Yield 69%, mp 145–146°C. ^1H NMR spectrum, δ , ppm: 7.01 s [1H, $\text{CH}(\text{CN})_2$], 3.81 d (1H, CHCO , $J = 7.9$), 2.52 m (1H, CH_2CHCO), 2.27–

1.58 m (6H, CH_2CH_2 , $\text{CH}(\text{CH}_3)_2$, CHCH_3), 1.44 d (3H, CH_3 , $J = 6.4$), 0.93 d (3H, CH_3 , $J = 6.0$), 0.85 d (3H, CH_3 , $J = 6.0$). IR spectrum, ν , cm^{-1} : 1705, 2270.

2-Amino-4a-methyl-4a,5,6,7-tetrahydro-4H-chromene-3,4,4-tricarbonitrile (II) and 2-amino-8-isopropyl-5-methyl-6,7-dihydro-5H-chromene-3,4-dicarbonitrile (IV) (*general procedure*). Compound I or III, 0.01 mol, was kept for 2–3 days at room temperature.

Compound II. Yield 98%, mp 197–198°C. ^1H NMR spectrum, δ , ppm: 6.12 s (2H, NH_2), 2.71 m (1H, CHCH_2), 2.7–1.8 m [6H, $(\text{CH}_2)_3$], 0.98 s (3H, CH_3). IR spectrum, ν , cm^{-1} : 2215, 2270, 3225, 3310. Mass spectrum: m/z 240 $[M]^+$.

Compound IV. Yield 99%, mp 211–212°C. ^1H NMR spectrum, δ , ppm: 7.68 s (2H, NH_2), 3.04 m (1H, CHCH_3), 2.68–2.42 m [4H, $(\text{CH}_2)_2$], 1.53 m [1H, $\text{CH}(\text{CH}_3)_2$], 1.15 d (3H, CH_3 , $J = 6.2$), 0.92 d (6H, CH_3 , $J = 6.5$). IR spectrum, ν , cm^{-1} : 2210, 3215, 3295. Mass spectrum: m/z 255 $[M]^+$.

8a-Hydroxy-2-iodo-4a-methyl-1,4,4a,5,6,7,8,8a-octahydroquinoline-3,4,4-tricarbonitrile (V). A mixture of 3.68 g (0.01 mol) of 2-methyl-2-(1,1,2,2-tetracyanoethyl)cyclohexanone (I) and 10–15 ml of concentrated hydroiodic acid was stirred for 2 h at 20°C. The mixture was diluted with 40 ml of water, and the precipitate was filtered off and washed with water and 2-propanol. Yield 83%, mp 178–179°C. ^1H NMR spectrum, δ , ppm: 9.24 s (1H, NH), 8.97 s (1H, OH), 1.86–1.24 m [8H, $(\text{CH}_2)_4$], 0.98 s (3H, CH_3). IR

spectrum, ν , cm^{-1} : 2220, 2270, 3200, 3410. Mass spectrum: m/z 368 $[M]^+$.

7-Imino-4,5-tetramethylene-2'-oxo-6-oxabicyclo-[3.2.1]octane-2-spiro-1'-cyclohexane-1,8,8-tricarbonitrile (VI). 2,2'-Methylenedi(cyclohexanone), 2.08 g (0.01 mol), and 3–4 drops of concentrated hydrochloric acid were added to 1.28 g (0.01 mol) of tetracyanoethylene in 20 ml of dioxane. After 12 h, the mixture was diluted with 50 ml of water, and the precipitate was filtered off and washed with 2-propanol and ether. Yield 85%, mp 218–219°C. IR spectrum, ν , cm^{-1} : 1700, 2260, 3280. Mass spectrum: m/z 336 $[M]^+$. Crystallographic data: space group $P2_1/c$; unit cell parameters (-90°C): $a = 8.932(2)$, $b = 10.008(5)$, $c = 19.404(3)$ Å; $\alpha = 90^\circ$, $\beta = 93.56(10)^\circ$, $\gamma = 90^\circ$; $V = 1731.2(10)\text{Å}^3$; $z = 4$; $R = 0.0436$.

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