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CYANOACETYLENE AND ITS DERIVATIVES. 29*. NEW DATA ON SYNTHESIS AND PROPERTIES OF SUBSTITUTED 1,3-OXATHIOLAN-2-ONES

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We have determined the conditions for carrying out the reaction of 4-alkyl-4-hydroxy-2-alkynonitriles containing bulky or spirocyclic substituents with the KSCN–$KHSO_4$ system, leading to 5,5-dialkyl-4-cyanomethylene-1,3-oxathiolan-2-ones in quantitative yield (for this, we had to increase the reaction time and use a 10-fold excess of the hydrothiocyanating system compared with the known conditions). 5,5-Dimethyl-4-cyanomethyl-1,3-oxathiolan-2-one reacts with methanol in the presence of triethylamine (20±2°C), forming 2-cyanomethyl-4-cyanomethylene-2-[(1-methoxycarbonyloxyethyl-1-methyl)]-5,5-dimethyl-1,3-dithiolane (yield 90%).

Keywords: 4-alkyl-4-hydroxy-2-alkynonitriles, 5,5-dialkyl-4-cyanomethylene-1,3-oxathiolan-2-ones, 2-cyanomethyl-4-cyanomethylene-2-[(1-methoxycarbonyloxyethyl-1-methyl)]-5,5-dimethyl-1,3-dithiolane, intramolecular cyclization, hydrolysis, hydrothiocyanation, thiolysis.

The reaction of 4-alkyl-4-hydroxy-2-alkynonitriles **1a,b** with thiocyanic acid generated *in situ* from KSCN and $KHSO_4$ under mild conditions (mole ratio **1**:KSCN:$KHSO_4$ 1:1.1:2.2, 20±2°C, 1 h, dioxane) leads to formation of 5,5-dialkyl-4-cyanomethylene-1,3-oxathiolan-2-ones **2a,b** in quantitative yield.

In this work, with the aim to synthesize of 5,5-dialkyl-4-cyanomethylene-1,3-oxathiolan-2-ones **2** with bulky substituents and spirocyclic moieties, supposedly by capable of eliminating more stable cyanomethylene thiiranes upon pyrolysis, we tested the applicability of this reaction to 4,4-dialkyl-4-hydroxy-2-alkynonitriles containing isobutyl, *tert*-butyl, and pentamethylene substituents. Furthermore, it might be expected that the bulky environment of the hydroxyl group in primary adducts **3** hinders cyclization and lets the reaction stop in the step of addition of thiocyanic acid.

As expected, the hydrothiocyanation reaction conditions depend on the structure of the starting alkynonitriles **1**. Thus on going from alkynonitriles **1a,b** with methyl and ethyl substituents, used in this reaction in [2], to alkynonitriles with bulky substituents **1c,d** or spirocyclic fragments **1e**, the reaction time sharply increases (from 1 h to 15 h). Furthermore, 5,5-dialkyl-4-cyanomethylene-1,3-oxathiolan-2-ones **2c-e** can be obtained in quantitative yield only with a 10-fold or more molar excess of the hydrothiocyanating system (**1c-e:**KSCN:$KHSO_4$ 1:10:20).

* For Communication 28, see [1].

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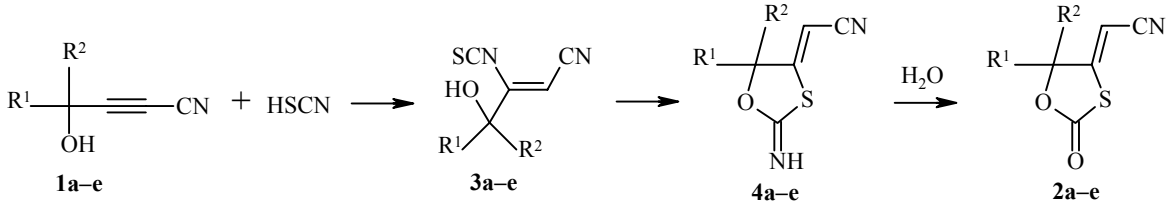


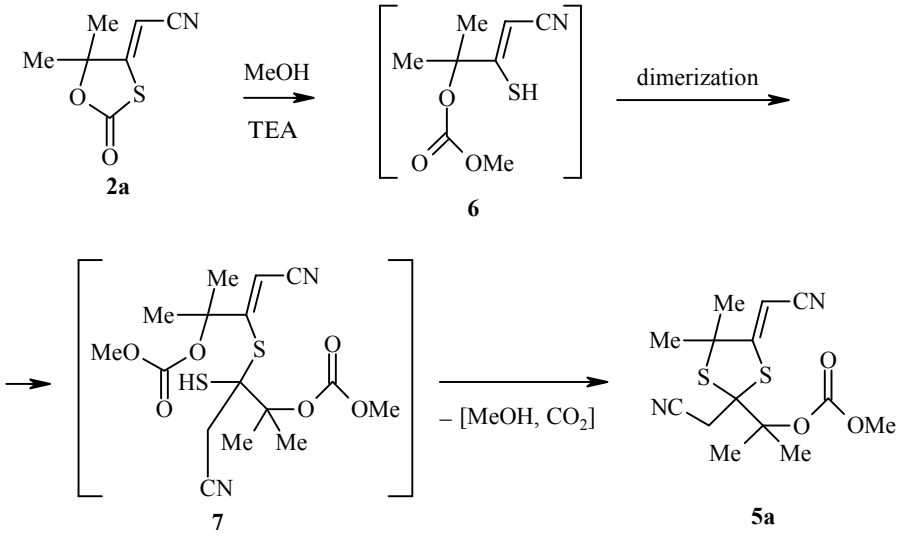
a $R^1 = R^2 = Me$; **b** $R^1 = Me$; $R^2 = Et$; **c** $R^1 = Me$, $R^2 = i\text{-Bu}$;
d $R^1 = Me$, $R^2 = t\text{-Bu}$; **e** $R^1 = R^2 = (CH_2)_5$

Surprisingly, introducing bulky (**c,d**) or spirocyclic (**e**) substituents into nitriles **1** does not stop the reaction in the step of formation of the intermediate hydroxythiocyanates **3** or 2-imino-1,3-oxathiolanes **4**. Even in this case, despite the obvious steric hindrances, intramolecular cyclization and subsequent hydrolysis of intermediates **3** and **4** occur nevertheless, although they proceed at a much slower rate and for a fundamentally different ratio of reagents.

The synthesized 1,3-oxathiolan-2-ones **2c-e** are crystalline materials that are soluble in most organic solvents. In their IR spectra, we see absorption bands at 3051-3050 (C=CH), 2220-2218 (C=CH–CN), 1764-1752 (C=O), and 1608-1602 cm^{-1} (C=C).

The ^1H NMR spectra of 1,3-oxathiolan-2-ones **2c-e**, show a singlet for the olefin proton in the 5.35-5.38 ppm region and signals for alkyl protons, which chemical shifts are given in the experimental section.

Earlier we showed [6, 7] that 4-cyanomethylene-5,5-dimethyl-1,3-oxathiolan-2-one (**2a**) when reacted with amines (primary, secondary, ammonia) in methanol (20±2°C, 2-5 h) forms [1-(carbamoyloxy)-1-methylethyl]-2-cyanomethyl-4-cyanomethylene-5,5-dimethyl-1,3-dithiolanes. We found that the same 1,3-oxathiolan-2-one **2a** in the presence of triethylamine (TEA) reacts with methanol (20±2°C, 5 h) to form 2-cyanomethyl-4-cyanomethylene-2-[(1-methoxycarbonyloxy-1-methyl)ethyl]-5,5-dimethyl-1,3-dithiolane (**5a**) (90% yield). Probably in the first step, treatment with TEA results in nucleophilic opening of the 1,3-oxathiolane ring in compound **2a** and addition of methanol to form the intermediate **6**, which subsequent dimerization by addition of the mercapto group of one molecule to the double bond of a second molecule leads to intermediate **7**. Then intramolecular thiolysis of the carbonate group occurs, with closure of the 1,3-dithiolane ring **5a**.



1,3-Dithiolane **5a** is a crystalline material that is soluble in most organic solvents. Its IR spectrum contains characteristic absorption bands at 3050 (C=CH), 2240 (CH_2–CN), 2205 (C=CH–CN), 1740 (C=O), and 1580 cm^{-1} (C=C). The ^1H NMR spectrum (DMSO-d_6), shows one signal for the olefin proton in the 5.98 ppm region. The chemical shifts of the signals for alkyl protons are presented in the experimental section.

EXPERIMENTAL

The IR spectrum of the compounds were taken on a Specord IR-75 spectrometer in KBr pellets. The ^1H NMR spectra were obtained on a Jeol FX-90Q (90 MHz) and a Bruker DPX-250 (250 MHz) in $CDCl_3$, internal standard HMDS.

4-Alkyl-4-hydroxy-2-alkynonitriles (1c-e) were obtained by the method described in [8,9]. The method for obtaining 1,3-oxathiolan-2-ones **2a,b** is described in [2]. The course of the reaction was monitored by thin-layer chromatography on Al_2O_3 (eluent, 20:4:1 chloroform–benzene–alcohol).

5-*iso*-Butyl-4-cyanomethylene-5-methyl-1,3-oxathiolan-2-one (2c). A solution of 4-hydroxy-4,6-dimethyl-2-heptynonitrile **1c** (0.38 g, 2.5 mmol) in dioxane (10 ml) was added over a 30 min period at 20±2°C to a solution of KSCN (2.42 g, 25 mmol) and $KHSO_4$ (6.80 g, 50 mmol) in water (50 ml). The mixture was stirred for 15 h. The precipitate was filtered off and washed with acetone. Most of the solvent was removed from the filtrate, ether was added, the ether solution was washed with water and dried with $MgSO_4$. After removal of the ether, 0.44 g (83%) of compound **2c** was isolated; mp 30-32°C (ether). IR spectrum, ν, cm^{-1}: 3051, 2961, 2935, 2874, 2218, 1755, 1608, 1468, 1453, 1383, 1368, 1278, 1208, 1179, 1113, 1053, 969, 943, 877, 795, 671, 645, 627, 587. ^1H NMR spectrum ($CDCl_3$), δ, ppm, *J*(Hz): 5.35 (1H, s, =CH); 1.84 (1H, m, CH); 1.73-1.90 (2H, dd, J_{AB} = 14, $^3J_{CH–CH2}$ = 5.6, ^3J = 5.8, CH_2); 1.64 (3H, s, CH_3); 0.99 (3H, d, CH_3); 0.97 (3H, d, CH_3). Found, %: C 56.40; H 6.51; N 6.79; S 15.38. $C_{10}H_{13}NO_2S$. Calculated, %: C 56.87; H 6.16; N 6.63; S 15.16.

5-*tert*-Butyl-4-cyanomethylene-5-methyl-1,3-oxathiolan-2-one (2d). Compound **2d** (0.38 g, 72%) was obtained from KSCN (2.42 g, 25 mmol), $KHSO_4$ (6.80 g, 50 mmol) in water (50 ml) and 4-hydroxy-4-*tert*-butyl-2-pentynonitrile (**1d**) (0.38 g, 2.5 mmol); mp 28-30°C (ether). IR spectrum, ν, cm^{-1}: 3050, 2970, 2931, 2876, 2220, 1764, 1599, 1481, 1468, 1399, 1373, 1227, 1115, 1085, 983, 935, 917, 852, 771, 725, 625, 576, 559, 500. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 5.37 (1H, s, =CH); 1.47 (3H, s, CH_3); 1.03 (9H, s, $3CH_3$). Found, %: C 57.05; H 5.95; N 7.00; S 14.87. $C_{10}H_{13}NO_2S$. Calculated, %: C 56.87; H 6.16; N 6.63; S 15.16.

2-(2-Oxo-1-oxa-3-thiaspiro[4,5-dec-4-ylidene)acetonitrile (2e). Compound **2e** (0.64 g, 92%) was obtained from KSCN (2.42 g, 25 mmol), $KHSO_4$ (6.80 g, 50 mmol) in water (50 ml) and 3-(1-hydroxy-1-cyclohexyl)-2-propynonitrile **1e** (0.50 g, 3.6 mmol); mp 88-90°C (ether). IR spectrum, ν, cm^{-1}: 3051, 2940, 2865, 2218, 1752, 1602, 1444, 1365, 1348, 1282, 1179, 1154, 1112, 1029, 974, 957, 909, 881, 861, 800, 776, 734, 674, 638, 622, 582, 568, 508. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 5.38 (1H, s, =CH); 1.58-2.10 (10H, m, $5CH_2$). Found, %: C 57.47; H 5.26; N 6.59; S 14.45. $C_{10}H_{11}NO_2S$. Calculated, %: C 57.42; H 5.22; N 6.70; S 15.31.

2-Cyanomethyl-4-cyanomethylene-5,5-dimethyl-2[(1-methoxycarbonyloxy-1-methyl)ethyl]-1,3-dithiolane (5a). A solution of 1,3-oxathiolan-2-one **2a** (0.17 g, 1 mmol) and TEA (0.5 g) in methanol (2 ml) was stirred at 20±2°C for 6 h and allowed to stand overnight. The solvent was removed under vacuum and 0.15 g (90%) of compound **5a** was obtained; mp 140-142°C (ether). IR spectrum, ν, cm^{-1}: 3050, 2990, 2980, 2880, 2240, 2205, 1740, 1580, 1430, 1395, 1380, 1280, 1115, 940, 880, 800, 660, 590, 540. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 5.98 (1H, s, =CH); 3.73 (3H, s, OCH_3); 3.61 (2H, d, CH_2); 1.82 (3H, s, CH_3); 1.78 (3H, s, CH_3); 1.73 (3H, s, CH_3); 1.69 (3H, s, CH_3). Found, %: C 50.97; H 5.26; N 8.65; S 19.45. $C_{14}H_{18}N_2O_3S_2$. Calculated, %: C 51.51; H 5.56; N 8.58; S 19.67.

REFERENCES

1. V. V. Nosyreva, L. V. Andriyankova, A. G. Mal'kina, A. V. Afonin, and B. A. Trofimov, *Zh. Org. Khim.*, in press.
2. A. G. Mal'kina, Yu. M. Skvortsov, E. I. Moshchevitina, and B. A. Trofimov, *Zh. Org. Khim.*, **24**, 2454 (1988).
3. B. A. Trofimov, Yu. M. Skvortsov, E. I. Moshchevitina, A. G. Mal'kina, and V. K. Bel'skii, *Zh. Org. Khim.*, **27**, 1188 (1991).
4. B. A. Trofimov, A. G. Mal'kina, and Yu. M. Skvortsov, *Zh. Org. Khim.*, **29**, 1268 (1993).
5. B. A. Trofimov and A. G. Mal'kina, *Heterocycles*, **51**, 2485 (1999).
6. A. G. Mal'kina, Yu. M. Skvortsov, E. I. Moshchevitina, V. K. Bel'skii, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 855 (1989).
7. A. G. Mal'kina, Yu. M. Skvortsov, E. I. Moshchevitina, V. K. Bel'skii, and B. A. Trofimov, *Khim. Geterotsikl. Soedin.*, 335 (1992).
8. S. R. Landor, B. Demetriou, R. Grzeskowiak, and D. Pavey, *J. Organometal. Chem.*, **93**, 129 (1975).
9. Yu. M. Skvortsov, A. G. Mal'kina, A. N. Volkov, B. A. Trofimov, E. B. Oleinikova, I. V. Kazin, and V. V. Gedymin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 872 (1978).