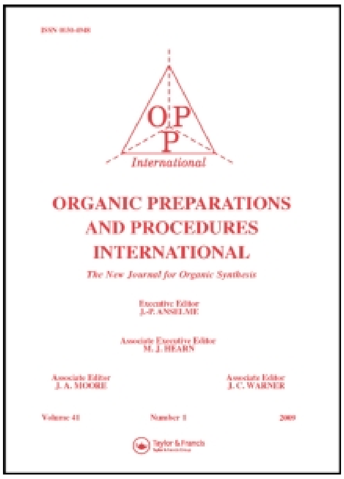

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A STUDY ON CYANOACETIC ACID HYDRAZIDE

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A STUDY ON CYANOACETIC ACID HYDRAZIDE

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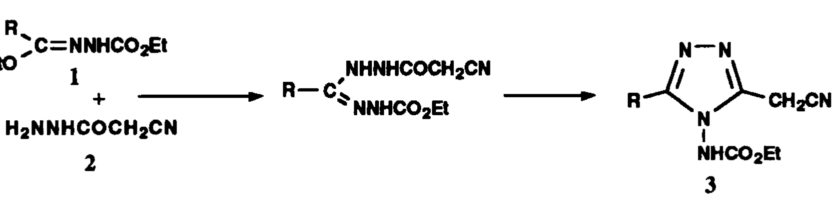
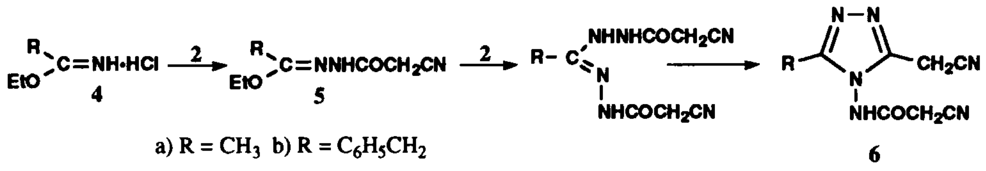
The reaction of various ester ethoxycarbonylhydrazones with amines and hydrazines has been reported.[1-5] The present study describes the treatment of some ester ethoxycarbonylhydrazones (**1**) with cyanoacetic acid hydrazide. Although the reaction of ester ethoxycarbonylhydrazone with amines or hydrazine generally led to the formation of 3,4-disubstituted-4,5-dihydro-1,2,4-triazol-5-ones, this type of compound was not obtained in this study. Instead, 3-alkyl-4-carbethoxyamino-5-cyanomethyl-4H-1,2,4-triazoles (**3**) were isolated.



a) R = CH_3 b) R = CH_3CH_2 c) R = n-C_3H_7 d) R = $C_6H_5CH_2$ e) 4-$ClC_6H_4CH_2$

The formation of ester hydrazone derivatives **5** or 2,5-disubstituted-1,3,4-oxadiazoles from the reaction of alkyl imidate hydrochlorides (**4**) with carboxylic acid hydrazides has also been



a) R = CH_3 b) R = $C_6H_5CH_2$

reported.[1,6] In contrast, the treatment of some alkyl imidate hydrochlorides with cyanoacetic acid hydrazide resulted in the formation of 3-alkyl-4-cyanoacetamido-5-cyanomethyl-4H-1,2,4-triazoles (**6**).

EXPERIMENTAL SECTION

Melting points were determined in a Büchi oil-heated melting point apparatus and are uncorrected. ^{1}H NMR spectra were obtained on a Varian 60A spectrometer. ^{13}C NMR spectra were recorded on a Brucker AC-200 FT instrument. IR spectra were run as potassium bromide pellets on a Perkin-Elmer 377 spectrophotometer. UV absorption spectra were measured between 210 and 350 nm with a Varian spectrophotometer using 10 mm quartz cells. Microanalyses were performed on a Carlo Erba 1106 elemental analyzer. The starting compounds **1** and **4** were synthesized by the methods previously reported. [1,2,4,7]

Preparation of 3-Alkyl-4-carbethoxyamino-5-cyanomethyl-4H-1,2,4-triazoles (3). General Procedure.- Ester ethoxycarbonylhydrazone **1** (0.01 mol) was heated with cyanoacetic acid hydrazide (0.99 g, 0.01 mol) for 2 hrs at 125-130° and then allowed to cool. The crude oil which formed solidified when allowed to stand in deep-freeze with 2-3 mL of ethyl acetate. Recrystallization of the product from an appropriate solvent gave pure **3**.

3-Methyl-4-carbethoxyamino-5-cyanomethyl-4H-1,2,4-triazole (3a): Yield 1.52 g (73%) of colorless crystals, mp. 124° (benzene), IR: 3120 (NH), 2240 (C≡N), 1760 (C=O), 1545, 1520 (C=N) cm^{-1} ; ^{1}H NMR (acetone-d$_6$): δ 1.22 (t, 3H, CH$_3$), 2.30 (s, 3H, CH$_3$), 4.15 (s, 2H, CH$_2$), 4.30 (q, 2H, CH$_2$), 10.20 (s, 1H, NH); ^{13}C NMR (acetone-d$_6$): δ 155.12 (C=O), 153.67 (triazole C$_5$), 147.00 (triazole C$_3$), 115.03 (C≡N), 63.51, 14.67, 14.54, 9.54 (aliphatic carbons); UV (ethanol 95%) λ_{max} (ε): 213 nm (800), 261 nm (490).

Anal. Calcd for $C_8H_{11}N_5O_2$: C, 45.93; H, 5.30; N, 33.48. Found: C, 45.63; H, 5.45; N, 33.60

3-Ethyl-4-carbethoxyamino-5-cyanomethyl-4H-1,2,4-triazole (3b).- Yield 1.54 g (69%) of colorless crystals, mp. 106° (AcOEt), IR: 3120 (NH), 2240 (C≡N), 1760 (C=O), 1545, 1525 (C=N) cm^{-1}, ^{1}H NMR (acetone-d$_6$): δ 1.25 (t, 3H, CH$_3$), 1.15 (t, 3H, CH$_3$), 2.67 (q, 2H, CH$_2$), 4.15 (s, 2H, CH$_2$), 4.25 (q, 2H, CH$_2$), 10.15 (s, 1H, NH); ^{13}C NMR (acetone-d$_6$): δ 157.73 (C=O), 155.15 (triazole C$_5$), 147.11 (triazole C$_3$), 114.98 (C≡N), 63.46, 17.92, 14.63, 14.52, 10.98 (aliphatic carbons); UV (ethanol 95%) λ_{max} (E): 214 nm (680), 261 nm (380).

Anal. Calcd for $C_9H_{13}N_5O_2$: C, 48.42; H, 5.87; N, 31.38. Found: C, 48.38; H, 6.07; N, 31.50

3-n-Propyl-4-carbethoxyamino-5-cyanomethyl-4H-1,2,4-triazole (3c).- Yield 1.56 g (66%) of colorless crystals, mp. 90° (AcOEt-petroleum ether, 1:1), IR: 3120 (NH), 2240 (C≡N), 1760 (C=O), 1540, 1525 (C=N) cm^{-1}; ^{1}H NMR (acetone-d$_6$): δ 0.95 (t, 3H, CH$_3$) 1.27 (t, 3H, CH$_3$), 1.77 (sext, 2H, CH$_2$), 2.65 (t, 2H, CH$_2$), 4.20 (s, 2H, CH$_2$), 4.30 (q, 2H, CH$_2$), 10.25 (s, 1H, NH); ^{13}C NMR (acetone-d$_6$): δ 156.48 (C=O), 155.09 (triazole C$_5$), 146.94 (triazole C$_3$), 115.02 (C≡N), 63.48, 26.18, 20.43, 14.55 (2C), 13.86 (aliphatic carbons); UV (ethanol, 95%) λ_{max} (ε): 214 nm (960), 261 nm (560).

Anal. Calcd for $C_{10}H_{10}N_5O_2$: C, 50.62; H, 6.37; N, 29.52. Found: C, 50.53; H, 6.53; N, 29.82

3-Benzyl-4-carbethoxyamino-5-cyanomethyl-4H-1,2,4-triazole (3d).- Yield 1.65 g (58%) of colorless crystals, mp. 150° (AcOEt), IR: 3120 (NH), 2240 (C≡N), 1760 (C=O), 1540, 1525 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d$_6$): δ 1.17 (t, 3H, CH$_3$), 4.00 (s, 2H, CH$_2$), 4.10 (s, 2H, CH$_2$), 4.22 (q, 2H, CH$_2$), 7.30 (m, 5H, arom. H), 10.20 (s, 1H, NH); ^{13}C NMR (DMSO-d$_6$): δ 155.00 (C=O), 154.27 (triazole C$_5$), 146.32 (triazole C$_3$), 135.12, 128.76 (2C), 128.45 (2C), 126.83 (aromatic carbons), 115.16 (C≡N), 62.28, 29.52, 13.86 (2C) (aliphatic carbons); UV (ethanol, 95%) λ_{max} (ε): 217 nm (1750), 258 nm (780).

Anal. Calcd for $C_{14}H_{15}N_5O_2$: C, 58.93; H, 5.30; N, 24.55. Found: C, 59.10; H, 5.48; N, 24.70

3-p-Chlorobenzyl-4-carbethoxyamino-5-cyanomethyl-4H-1,2,4-triazole (3e).- Yield 1.79 g (56%) of colorless crystals, mp. 166° (water), IR: 3120 (NH), 2240 (C≡N), 1760 (C=O), 1550, 1530 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d$_6$): δ 1.15 (t, 3H, CH$_3$), 3.95 (s, 2H, CH$_2$), 4.05 (s, 2H, CH$_2$), 4.20 (q, 2H, CH$_2$), 7.30 (m, 4H, arom. H), 10.18 (s, 1H, NH); ^{13}C NMR (DMSO-d$_6$): δ 154.95 (C=O), 153.91 (triazole C$_5$), 146.39 (triazole C$_3$), 134.11, 131.53, 130.64 (2C), 128.36 (2C) (aromatic carbons), 115.12 (C≡N), 62.28, 28.80, 14.06, 13.79, (aliphatic carbons); UV (ethanol, 95%) λ_{max} (ε): 216 nm (5640), 257 nm (520).

Anal. Calcd for $C_{14}H_{14}ClN_5O_2$: C, 52.59; H, 4.41; N, 21.90. Found: C, 52.89; H, 4.40; N, 21.98

3-Methyl-4-cyanoacetamido-5-cyanomethyl-4H-1,2,4-triazole (6a).- Ethyl imidoacetate hydrochloride (1.235 g, 0.01 mol) was dissolved in 25 mL of absolute ethanol with ice-bath cooling and cyanoacetic acid hydrazide (0.99 g, 0.01 mol) dissolved in 200 mL of 95% ethanol was added to the solution. After stirring for 5 hrs at 0-5°, the resulting solution was evaporated at 30-35° under reduced pressure. The solid residue was extracted with hot acetone and recrystallized from the same solvent to give pure compound **6a**. Yield 0.776 g (38%) of colorless crystals, mp. 221° (acetone), IR: 3125 (NH), 2242 (C≡N), 1715 (C=O), 1560, 1540 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d$_6$): δ 2.27 (s, 3H, CH$_3$), 4.05 (s, 2H, CH$_2$), 4.27 (s, 2H, CH$_2$), 10.10 (s, 1H, NH); ^{13}C NMR (DMSO-d$_6$): δ 162.60 (C=O), 151.75 (triazole C$_5$), 145.39 (triazole C$_3$), 115.26, 114.85 (C≡N), 24.38, 13.47, 9.02 (aliphatic carbons); UV (ethanol, 95%); λ_{max} (ε): 216 nm (360), 261 nm (200).

Anal. Calcd for $C_8H_8N_6O$: C, 47.05; H, 3.95; N, 41.16. Found: C, 47.05; H, 4.01, N, 41.15

Preparation of 3-Benzyl-4-cyanoacetamido-5-cyanomethyl-4H-1,2,4-triazole (6b).- Ethyl imidophenylacetate hydrochloride (1.995 g, 0.01 mol) was dissolved in 30 mL of absolute ethanol with ice-bath cooling and cyanoacetic acid hydrazide (0.99 g, 0.01 mol), dissolved in 200 mL of 95% ethanol, was added to the solution. After stirring for 6 hrs at 0-5°, the resulting solution was evaporated at 30-35° under reduced pressure. The solid residue was extracted with hot acetone and recrystallized from the same solvent to give pure compound **6b**. Yield 0.98 g (35%) of colorless crystals, mp. 205° (acetone), IR: 3125 (NH), 2242 (C≡N), 1710 (C=O), 1550, 1520 (C=N) cm^{-1}; ^{1}H NMR (DMSO-d$_6$): δ 4.00 (s, 4H, 2CH$_2$), 4.25 (s, 2H, CH$_2$), 7.35 (m, 5H, arom. H), 10.15 (s, 1H, NH); ^{13}C NMR (DMSO-d$_6$): δ 162.49 (C=O), 153.86 (triazole C$_5$), 145.72 (triazole C$_3$), 135.36, 128.74 (2C), 128.38 (2C), 126.72 (aromatic carbons), 115.22, 114.80 (C≡N), 29.09, 24.36, 13.46 (aliphatic carbons); UV (ethanol, 95%) λ_{max} (ε): 217 nm (1520), 258 nm (780).

Anal. Calcd for $C_{14}H_{12}N_6O$: C, 59.99; H, 4.32; N, 29.99. Found: C, 60.13; H, 4.31; N, 29.96

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