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Condensation of α-Cyanothioacetamide with Aldehydes Catalysed by Alumina

Didier Villemin [a] & Benoît Martin [a]

[a] Ecole Nationale Supérieure d'Ingénieurs de Caen I. S. M. R.A., U. R. A. 480 CNRS, 14050, Caen Cedex, France

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CONDENSATION OF α-CYANOTHIOACETAMIDE WITH ALDEHYDES CATALYSED BY ALUMINA

Didier Villemin* and Benoît Martin

Ecole Nationale Supérieure d'Ingénieurs de Caen
I. S. M. R.A., U. R. A. 480 CNRS, 14050 Caen Cedex, France.

Abstract:

α-Cyanothioacetamide was condensated with aldehydes at room temperature with alumina as catalyst.

Chromatographic alumina possesses basic centres able to deprotonate acid methylene of pKa less than 13 units, as Meldrum's acid [1], dimedone [2], barbituric acid [2], malonodinitrile [3] and acetylthiohydantoin [4]. α-cyano-thioacetamide possesses an acid methylene and this compound is very useful in syntheses of heterocycles under low basic conditions [5]. Condensation with aldehydes is poorly described in literature [6-7].

In order to study biological properties of cyanothioacrylamides (**3**) very close to cyanoacrylonitriles, we have investigated the condensation of α-cyanothio-acetamide (**2**) with aldehyde (**1**) catalysed by alumina. At room temperature in methanol, the olefins (**3**) were obtained in quasi quantitative yield (95-98 %). The reaction took place also without methanol (dry conditions).

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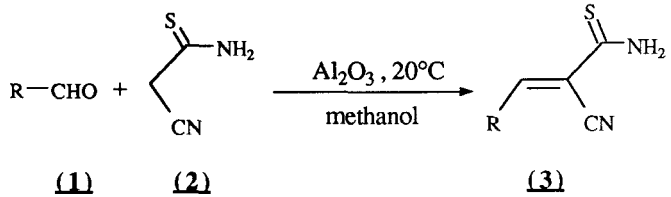
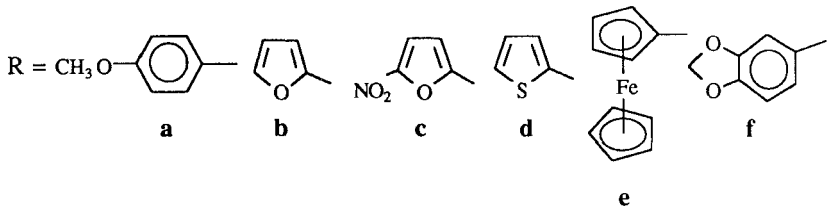
* To whom correspondence should be addressed

Scheme 1: Reaction of α-cyanothioacetamide with aldehyde :



(1) (2) (3)



a b c d e f

This result is not a surprise because malononitrile gave a condensation with aldehyde in the presence of alumina [3] and also because thiocarbonyl group is a powerful electron-withdrawing group [8]. Thiononesters are known to condensate with aldehydes in the presence of alumina [9].The cyanothioacrylamides (**3**) are interesting dienes or dienophiles for Diels-Alder reactions [7].We attempt the Diels-Alder reactions of **(3d)** with maleic anhydride in methylene chlorid (20°C, 48 h) or without solvent by melting without success. The reaction of cyanothioacrylamides (**3**) with dienes and the biological properties of (**3**) are under investigation.

We thank Chemische Betriebe Pluto for the generous gift of ferrocene carboxaldehyde.

Experimental

Infrared spectra were recorded on Perkin Elmer 684 IR spectrophotometer in KBr with absorptions in cm^{-1}. Proton NMR spectra (PMR) and ^{13}C NMR spectra (CMR) in ppm downfield from internal Me_4Si were recorded on a Brucker AC

250 instrument from a solution in d^6 -DMSO of the product. Mass spectra were recorded on Nermag R10.10H spectrometer.

α-Cyanothioacetamine was prepared from malononitrile and hydrogen sulfide using the method by Howard and al [10].

General procedure:

Aldehyde (5 mmol) and α-cyanothioacetamine (5 mmol) were stirred in methanol (30 ml) with chromatographic neutral alumina(Woelm-N, 2087) (3 g) for 24 h at room temperature. The solution, after filtration on Celite, was evaporated in vacuum and the residue was washed with ether (100 ml).The solid was crystallized in methanol.

3-(Paramethoxyphenyl)-2-cyanothioacrylamide (3a)

Orange solid; Mp=184°(lit. Mp = 188°); $C_{11}H_{10}N_2SO$; PMR (δ): 3.85(s, 3 H, CH_3O) 7.18(d, 2H, H arom, J=8.4 Hz) 7.98(d, 2H, H arom, J=8.4 Hz) 8.08(s, 1 H, CH=) 9.5 and 10(br, 2H, NH_2); CMR (δ): 55.6($\underline{C}H_3$ O) 109($\underline{C}$=CH) 114.9($\underline{C}$arom) 116.8($\underline{C}\equiv$N) 124.2($\underline{C}$-CH) 132.7($\underline{C}$arom) 147($\underline{C}$H=C) 162.6(CH_3O-$\underline{C}$) 192.6($\underline{C}$=S); MS m/z (%): 218($M^{+\cdot}$,96) 217(100) 187(29).

3-(Furan-2-yl)-2-cyanothioacrylamide (3b)

Brown solid; Mp=160°(lit. Mp =158°); $C_8H_6N_2SO$; PMR (δ): 6.85(dd, 1H, H arom, J_1=1.6 Hz, J_2 =3.5 Hz) 7.45(d, 1H, H arom, J_2 =3.5Hz) 8.03(s, 1H,CH=) 8.16(d, 1H, Harom, J_1=1.6 Hz) 9.44 and 10.02(br, 2H, NH_2); CMR (δ): 106.8(CH=$\underline{C}$) 114($\underline{C}$H=CH-O) 115.9($\underline{C}\equiv$N) 121.6($\underline{C}$H=C-CH) 133.5 ($\underline{C}$H=C) 148($\underline{C}$-CH=) 148.8($\underline{C}$H-O) 191.4($\underline{C}$=S); MS m/z (%): 179(29.8) 178($M^{+\cdot}$,100) 177(16 3) 150(27.6).

3-(5-Nitrofuran-2-yl)-2-cyanothioacrylamide (3c)

Brown solid; Mp=218°C; $C_8H_5N_3S0_3$; PMR (δ): 7.6(d, 1H, Harom, J=4 Hz) 7.84(d, 1H, H arom, J=4 Hz) 8.0(s, 1H, CH=C) 9.7 and 10.26(br, 2H, NH_2); CMR(δ): 112.8(CH=$\underline{C}$) 114.5(NO_2-C=CH-$\underline{C}$H=) 114.8($\underline{C}\equiv$N) 121.1(NO_2-

C=CH) 130.8(CH=C) 149.2(C-CH=) 151.1(NO_2-C) 190.3(C=S); MS m/z (%): 223($M^{+\cdot}$,35) 193(57) 141(100).

3-(Thien-2-yl)-2-cyanothioacrylamide (3d)

Brown solid; Mp=170°C (lit.Mp=168°); $C_8H_6N_2S_2$; PMR (δ): 7.32(dd, 1H, H arom, J_1=5 Hz, J_2=3.8 Hz) 7.89(dd, 1H, H arom, J_2=3.8 Hz, J_3=0.6 Hz) 8.13(d, 1H, Harom, J=5Hz) 8.41(s, 1H, CH=) 9.45 and 10(br, 2H, NH_2); CMR (δ): 107.8(CH=C) 116.4(C≡N) 128.6(CH=CH-S) 135.3(CH-S) 135.6(CH=C) 138(CH=C-CH=) 140.7(C-CH=) 191.5(C=S); MS m/z (%): 195(90) 194($M^{+\cdot}$,100) 162(26.7) 161(23.2).

3-(Ferrocenyl)-2-cyanothioacrylamide (3e)

Red solid; Mp=202°C; $C_{14}H_{12}N_2SFe$; PMR (δ): 4.33(s, 5H, H arom) 4.81(s, 2H, H arom) 5.0(s, 2H, H arom) 8.15(s, 1H, CH=C) 9.2 and 9.81(br, 2H, NH_2); CMR (δ): 69.3 to 74.6(C arom) 106.5(C=) 118.75(C≡N) 151.9(CH=) 192(C=S); MS m/z (%): 296($M^{+\cdot}$,100) 262(34) 231(36) 197(41).

3-[3,4-(methylenedioxyphenyl)]-2-cyanothioacrylamide (3f)

Orange solid; Mp=214°C; $C_{11}H_8O_2N_2S$; PMR (δ): 6.15(s, 2H, CH_2) 7.08(d, 1H, H arom, J=8.4 Hz) 7.42 to 7.51(br, 2H, H arom) 8.52(s, 1H, CH=C) 9.6 and 10.05(br, 2H, NH_2); CMR (δ): 101.9(CH_2) 105.9(C arom) 108.5(C arom) 108.7(CH=C) 115.3(C≡N) 126.7(C arom) 130.1(C arom) 148.0(C arom) 151.0(C arom) 155(CH=C) 191.8(C=S); MS m/z (%): 232($M^{+\cdot}$,40) 231(42) 207(32) 198(28) 197(32) 135(88).

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