Pergamon

Tetrahedron, Vol. 53, No. 12, pp. 4437-4440, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00115-4

Electrochemical Trifluoromethylation of Acrylonitrile and Crotonitrile. Preparation of 2,3-Bis(2,2,2-trifluoroethyl)succinonitrile and 3,4-Dicyano-2,5-bis(trifluoromethyl)-n-hexane

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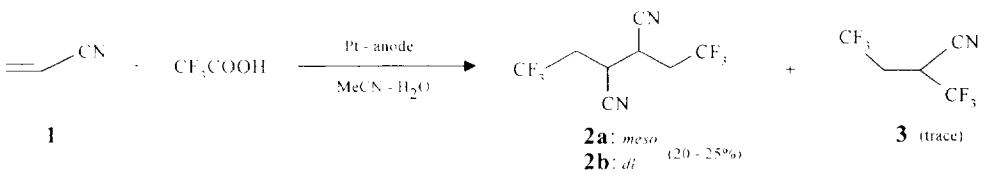
Abstract: *Electrooxidation of trifluoroacetic acid in the presence of acrylonitrile in an acetonitrile-water solution, followed by simple steam distillation of the reaction mixture, provided almost pure 2,3-bis(2,2,2-trifluoroethyl)succinonitrile in a 20 - 25% yield and in a 1 : 1 diastereoisomers ratio. The meso isomer has been isolated and its structure confirmed by X-ray analysis. Similarly, the reaction in the presence of crotonitrile gave a diastereoisomeric mixture of 3,4-dicyano-2,5-bis(trifluoromethyl)-n-hexanes albeit in lower yield.* © 1997 Elsevier Science Ltd.

INTRODUCTION

It has been well established that electrooxidation of trifluoroacetic acid and its perfluorinated homologues produces the respective perfluoroalkyl radicals almost quantitatively. These radicals can be efficiently trapped with electron-deficient olefins such as esters, amides and nitriles of maleic and acrylic acids providing perfluoroalkylated products.[1,2] The electrolysis of trifluoroacetic acid (TFA) is a simple and economically feasible method of generating $CF_3^{\cdot}$ radicals. Trapping these radicals by an olefin leads to the trifluoromethylated carbon radicals of whose further fate depends on the substrate structure and the experimental conditions. In general the olefinic substrate can undergo a number of competing reactions: dimerization of initial trifluoromethylated radicals, bistrifluoromethylation, trifluoromethylacetamidation (in a CH_3CN solution), trifluoromethylhydrogenation and monotrifluoromethylation with substitution.[2] Usually, the synthetic utility of electrochemical trifluoromethylation is limited by the complexity of the mixture of products, nevertheless, in certain cases trifluoromethylated compounds were obtained as single products. Thus, a 1 : 1 mixture of *meso* and *dl* dimethyl 2,3-bis(2,2,2-trifluoroethyl)succinate (50%)[3] and 4,4,4-trifluoro-2-(trifluoromethyl)butyramide (35%)[4] were prepared from methyl acrylate and acrylamide, respectively, and readily isolated by simple workup of the electrolysis mixture. Those compounds were transformed into a number of useful trifluoromethylated building blocks.[3,4]

RESULTS AND DISCUSSION

Electrochemical trifluoromethylation of acrylonitrile (**1**) in an acetonitrile-water-trifluoroacetic acid solution , partially neutralized with K_2CO_3, gives a dimeric product, 2,3-bis(2,2,2-trifluoroethyl)succinonitrile (**2**), as *ca.* 1 : 1 mixture of *meso* (**2a**) and *dl* (**2b**) isomers. Dinitrile **2** was practically the only isolable product formed in reproducible 20 - 25% yields. The product is easily isolable from the reaction mixture by distilling off the acetonitrile followed by steam distillation of the residue. Compounds **2** were obtained in the distillate as white or slightly yellowish crystals. At the beginning of the steam distillation a drop of liquid collected which was found by GC-MS analysis to consist mostly of monomeric product, 4,4,4-trifluoro-2-(trifluoromethyl)butyronitrile (**3**).



1 **2a**: *meso* **2b**: *dl* (20 - 25%) **3** (trace)

The longer GLC retention time isomer **2a** was separated by multiple crystallisation from isopropanol and its *meso* configuration was unambiguously assigned from the X-ray crystallographic data (Fig.). Preparative GLC permitted the isolation of pure *dl* (**2b**) from the enriched fraction obtained after crystallisation of **2a**. Both **2a** and **2b** showed identical mass spectra and almost identical NMR spectra, thus confirming their isomeric structures.

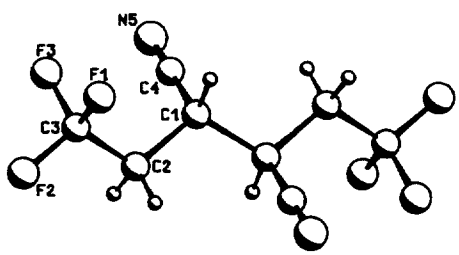
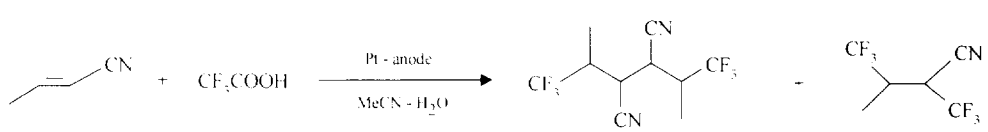


Figure. X-ray crystal structure of **2a**.

Trifluoromethylation of crotonitrile (**4**) under conditions identical to those applied for **1** followed by similar work up gave a white crystalline dimeric product, 3,4-dicyano-2,5-bis(trifluoromethyl)-n-hexane (**5**) together with trace amounts of liquid 2,3-bis(trifluoromethyl)butyronitrile (**6**).



4 **5** (10 - 12%) **6** (trace)

Steam distillation gave compound **5** in a *ca* 10 - 12% yield which was found by the GC-MS investigations to be a multicomponent mixture of stereoisomers. Attemped separation of isomers by crystallisation failed: no noticeable changes in composition of particular fractions were observed. The ^{19}F NMR analysis allowed to detect seven isomers of **5** in ratios as 10 : 9 : 9 : 5 : 3 : 2 : 1, each of them showing one signal for both CF_3 groups as a doublet with $^3J_{HF}$ = 8.2 - 8.6 Hz. Compound **6** was characterised by GC-MS, only. The low yield of **5** is probably the results of stereochemical complexity of the reaction with crotonitrile.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. Elemental analyses for C, H, and N, were done with a Perkin-Elmer 240 Elemental Analyzer. The fluorine was determined by a Rowley and Churchill method[5] after combustion of samples in an atmosphere of oxygen in a Schöniger flask[6]. The ^1H and ^{19}F NMR spectra were recorded in acetone-d_6 with a Varian Gemini 200 spectrometer at 200 and 188 MHz, respectively; chemical shifts are in p.p.m. from internal TMS for protons and from internal $CFCl_3$ for fluorine nuclei (positive upfield). GC-MS analyses were carried out with a Hewlett-Packard 5890 apparatus (70eV) using a 30 m capillary coated with a HP-5 oil. The preparative GLC separation was performed with a GCHF-18.3 apparatus (Germany) equipped with a 4 m x 10 mm column packed with 3% Silicon Oil SE-52 on Chromosorb WAW.

Crystal structure analysis of 2a

The X-ray structure analysis of compound **2a** was obtained with a MACH-3 (Enraf-Nonius) automated diffractometer using CuK_α radiation, and an $\omega/2\theta$ scanning mode. A total 1163 reflections were collected of which 884 were found to be $I > 2\sigma_I$.

Crystal data: $C_8H_6N_2F_6$, M = 244.13, monoclinic; space group $P2_1/c$; unit cell parameters: a = 8.223(1), b = 6.057(3), c = 10.145(1) Å, β = 104.67(1)°; V = 488.8(3) Å^3; Z = 2; F(000) = 244; $\mu(CuK_\alpha)$ = 16.6 cm^{-1}; D_x =1.66 g cm^{-1}.

The data were corrected for Lorentz, polarisation and absorption effects. The structure was solved by direct method with SHELXS-86 (Sheldrick, 1986) and refined by full-matrix least squares procedure using program SHELX-93 (Sheldrick, 1993). The positions of hydrogen atoms were generated from assumed geometries.

The molecule of **2a** was found centered at [½, 0, ½]. A conventional R-factor for anisotropic refinement is 0.0518.

Electrochemical trifluoromethylation of 1 and 4

General procedure

A solution of TFA (46 g, 0.4 mol), $Na_2CO_3 \cdot 10H_2O$ (17.2 g, an equivalent of 0.12 mol CF_3CO_2Na) and **1** (10.6 g, 0.2 mol) or **4** (20 g, 0.3 mol) in CH_3CN (80 - 100 ml) and H_2O (10 - 30 ml) was electrolyzed in an undivided cell at 12 -16°C using a platinum anode (44 cm^2) and stainless steel cathode. A constant current (500

or 1000 mA) was applied until ca. 11 Ah (1F/mol to TFA) of electricity passed. The reaction mixture was diluted with H_2O to ca. 300 ml and CH_3CN was removed by distillation under atmospheric pressure, then the remaining water-oil suspension was steam distilled (no external steam was required). At the beginning, a drop of oil distilled off which was collected and analysed by GC-MS. Further distillation gave a white (or yellowish) crystalline products **2** or **5** which were filtered off and dried over P_5O_{10}.

***meso* and *dl* 2,3-Bis(2,2,2-trifluoroethyl)succinonitrile (2a) and (2b)**

A 1 : 1 mixture of diastereoisomers. Yield: 20 -25%. Found: C, 39.2; H, 2.4; F, 46.7; N, 11.4. $C_8H_6F_6N_2$ requires: C, 39.36; H, 2.48; F, 46.69; N, 11.47. GC-MS m/z: (this same for both isomers) 244 (<1%) M^+; 225 (10) $(M-F)^+$; 198 (20) $(M-FCN)^+$; 175 (75) $(M-CF_3)^+$; 123 (35) $(M-CF_3-2CN)^+$; 122 (30) $C_4H_3F_3N^+$; $C_4H_2F_2N^+$; 69 (65) CF_3^+; 54 (100) $C_3H_4N^+$.

meso-2,3-Bis(2,2,2-trifluoroethyl)succinonitrile (**2a**) was isolated by triple crystallization from isopropanol; GLC purity: 99% (longer RT isomer): m.p. 132 - 134°C; δ 2.96 and 3.08 (AB, J_{AB} = 29.3 Hz, J_{HF} = 10 Hz, CH_2), 3.93 (m, CH); 64.24 (t, J = 10 Hz, CF_3).

dl-2,3-Bis(2,2,2-trifluoroethyl)succinonitrile (**2b**) was isolated by preparative GLC from enriched fraction remaining after removal of **2a**; GLC purity: 99.9% (shorter RT isomer); m.p. 98 - 100°C; δ 3.01 and 3.08 (AB, J_{AB} = 23 Hz, J_{HF} = 10.1 Hz, CH_2), 3.86 (m, CH); 64.38 (t, J = 10.2 Hz, CF_3).

4,4,4-Trifluoro-2-(trifluoromethyl)butyronitrile (3): Yield: trace; Liquid; GC-MS m/z: 172 (5%) $(M-F)^+$; 152 (10) $(M-HF_2)^+$; 122 (40) $(M-CF_3)^+$; 102 (8) $(M-CF_3-HF)^+$; 69 (100) CF_3^+.

3,4-Dicyano-2,5-bis(trifluoromethyl)-n-hexane (5): Yield: 10 - 12%. Found: C, 44.0; H, 3.6; F, 41.9; N,10.2. $C_{10}H_{10}F_6N_2$ requires: C, 44.13; H, 3.70; F, 41.88; N, 10.29. Mixture of seven isomers; δ 1.42 - 1.54 (complex, 6H, CH_3); 2.95 - 3.30 (broad, 2H, $CHCF_3$); 3.65 - 3.98 (complex, 2H, CHCN); 67.0, 67.5, 68.8, 68.9, 71.5, 71.7, 71.8 (doublets, J = 8.2 - 8.6 Hz, relative intensities: 1.7 : 10 : 1 : 9.2 : 5.2 : 3 : 9.4, CF_3). GC-MS m/z: (this same for all isomers) 253 (5%) $M-F)^+$; 226 (10) $(M-HF-CN)^+$; 203 (25) $(M-CF_3)^+$; 175 (45) $(M-C_3H_4F_3)^+$; 136 (50) $C_5H_5F_3N^+$; 116 (25) $C_5H_4F_2N^+$; 79 (100) $C_3H_5F_2^+$; 69 (45) CF_3^+; 68 (90) $C_4H_6N^+$.

2,3-Bis(trifluoromethyl)butyronitrile (6): Yield: trace; Liquid; GC-MS m/z: 204 (2%) $(M-H)^+$; 186 (5) $(M-F)^+$; 136 (20) $(M-CF_3)^+$; 109 (90) $(M-CF_3-HCN)^+$; 97 (10) $C_3H_4F_3^+$; 90 (50) $C_4H_4F_2^+$; 77 (70) $C_3H_3F_2^+$; 69 (100) CF_3^+.

REFERENCES

1. Uneyama K.; Watanabe S.; Tokunaga Y.; Kitagawa K.; Sato Y. *Bull.Chem.Soc.Jpn.*, **1992**, *65*, 1976, and references therein.
2. Uneyama K. *Tetrahedron* **1991**, *47*, 555.
3. Uneyama K.; Makio S.; Nanbu, H. *J.Org.Chem.* **1989**, *54*, 872.
4. Uneyama K.; Morimoto O.; Nanbu H. *Tetrahedron Lett.* **1989**, *30*, 109.
5. Rowley R.J.; Churchill H.V. *Ind.Eng.Chem.Anal.Ed.* **1937**, *9*, 551.
6. Schöniger W. *Microchim.Acta* **1955**, 123; Małysz D. *Acta Pol.Pharm.* **1968**, *3*, 275.

(*Received in UK* 5 *December* 1996; *revised* 24 *January* 1997; *accepted* 30 *January* 1997)