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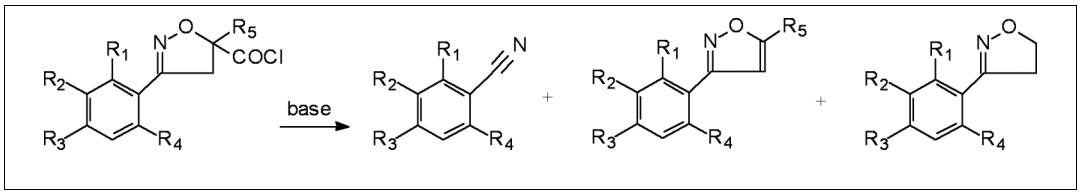
Received July 22, 2005



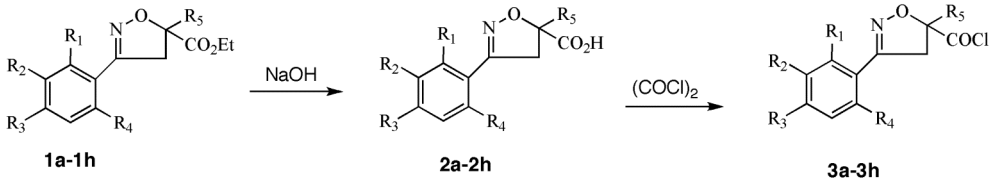
A novel base promoted degradation of 3-aryl-2-isoxazoline-5-carboxylic acid chlorides to aryl nitriles has been discovered.

J. Heterocyclic Chem., **43**, 509 (2006).

Amides of heterocyclic acids frequently show biological activity [1-3]. Whilst attempting to prepare anilides of 3-aryl-2-isoxazoline-5-carboxylic acids we found, that reaction of the corresponding 5-acyl chlorides with weakly nucleophilic anilines in the presence of triethylamine (TEA) resulted in formation of a mixture of compounds of which the expected amides were only minor components. Composition of the reaction products depended on the nature of the aromatic substituents. In case of an electron donating alkyl substituents on the aryl ring a major product was the 4-alkylbenzonitrile accompanied by up to 6% of 3-aryl-2-isoxazoline and several oligomeric compounds formed due to competitive formation of ketenes and their reactions [4]. When an aromatic electron withdrawing substituent (CF_3) was present most of the product was oligomeric material containing a small amount of 3-(4-trifluoromethylphenyl)-isoxazole (ca 0.5%). The level of the isoxazole was increased to 6% when sodium hydride was added to the reaction mixture. These results prompted us to investigate the action of TEA and other bases on 3-aryl-2-isoxazoline-5-carboxylic acid chlorides, which were easily prepared from esters produced in 1,3-dipolar cycloaddition of nitrile oxides and acrylates (Scheme 1).

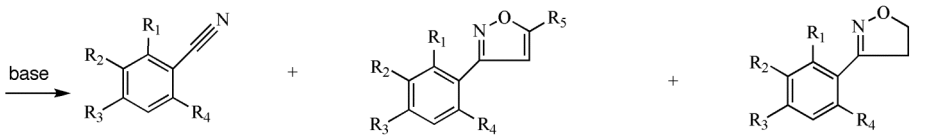
To examine the influence of aniline on the course of the reaction it was carried out by heating acyl chloride with TEA without any derivative of aniline. Once again, aromatic nitriles were the major products as expected, though composition of the oligomeric products was changed. 3-Aryl-2-isoxazolines were isolated only in reactions involving alkylphenyl substituted acid chlorides. The formation of 3-arylisoxazoles did not depend on the character of the aromatic substituents. Formation of arylnitriles from 3-arylisoxazoline-5-carboxylic acid

Scheme 1



1a-1h **2a-2h** **3a-3h**

a R_{1-5} = H; **b** R_3 = Et, $R_{1,2,4,5}$ = H; **c** R_3 = iPr, $R_{1,2,4,5}$ = H; **d** R_3 = CF_3, $R_{1,2,4,5}$ = H; **e** R_4 = OMe, $R_{1,2,3,5}$ = H, **f** $R_{1,2,4}$ = Cl, R_3 = R_5 = H; **g** R_3 = CF_3, R_5 = Me, $R_{1,2,4}$ = H; **h** R_3 = Et, R_5 = Me, $R_{1,2,4}$ = H



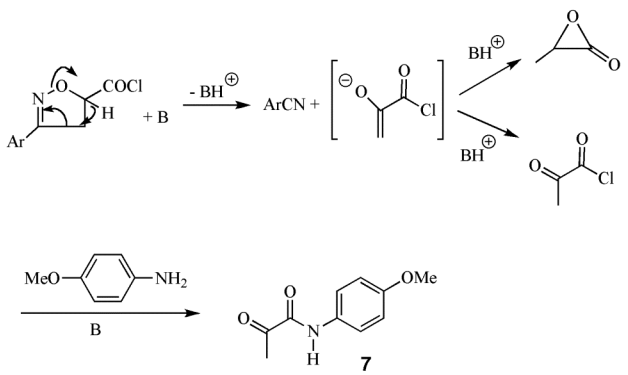
4a R_{1-4} = H
4b R_3 = Et, $R_{1,2,4}$ = H
4c R_3 = iPr, $R_{1,2,4}$ = H
4d R_3 = CF_3, $R_{1,2,4}$ = H
4e $R_{1,2,4}$ = Cl, R_3 = H

5a R_3 = CF_3, $R_{1,2,4,5}$ = H
5b R_4 = OMe, $R_{1,2,3,5}$ = H
5c R_3 = CF_3, R_5 = Me, $R_{1,2,4}$ = H
5d R_3 = Et, R_5 = Me, $R_{1,2,4}$ = H

6a R_3 = Et, $R_{1,2,4}$ = H
6b R_3 = iPr, $R_{1,2,4}$ = H

chlorides on TEA treatment is unprecedented. The reaction tolerates a wide range of substituents including alkyl, halogenated alkyl, alkoxyl and halide groups on the aryl substituent. It can be triggered by H-5 capture, and involves cleavage of the N-O and C_3-C_4 bonds (Scheme 2). We were unable to isolate the other product of 2-isoxazoline ring fragmentation, pyruvic acid chloride, *e.g.* as an anilide **7** formed with *p*-methoxyaniline, in a pure state. However, proton NMR spectrum of an impure fraction from column chromatography of products obtained from reaction of **3f** acyl chloride contained signals which could be ascribed to 4-methoxypyruvanilide **7** (singlets at 2.22 and 3.81 ppm). The yield of unstable pyruvamide was low. It is conceivable that initially formed acyl chloride undergoes cyclisation to 3-methyl-oxiranone-2 prone to anionic polymerization or copolimerization with ketenes formed in a competitive reaction from 2-isoxazoline acyl chlorides.

Scheme 2



Introduction of a second substituent, such as methyl group, into the position -5 of isoxazoline acyl chloride **3g** resulted in formation in the expected reaction of 3-(4-trifluoromethylphenyl)-5-methylisoxazole (**5c**) (13%) together with oligomeric compounds. In the case of an electron donating substituent, such as ethyl group, fragmentation of the corresponding acyl chloride **3h** afforded *inter alia* isoxazole **5d**. In both cases no aryl nitrile was detected underlying the role of H-5 acidity. Other tertiary amines are also acceptable as bases. When TEA was replaced by diisopropylethylamine (DIPEA) the yield of arylnitrile produced from acyl chloride **3e** was increased (from 49 to 61%). Inorganic bases such as sodium hydride proved less appropriate for this transformation, probably due to heterogenous reaction conditions. 3-(2-Methoxyphenyl)isoxazole was isolated as only non-oligomeric product apart from parent carboxylic acid **2e**.

A similar fragmentation reaction was reported previously for 3-aryl-5-acyl-2-isoxazolines [5].

3-Aryl-2-isoxazolines **6a** and **6b** could be formed by hydrolysis of acyl chlorides followed by decarboxylation. The amount of these products was increased substantially when the TEA was dried over KOH pellets.

More unusual is formation in relatively mild conditions of 3-aryl isoxazoles. Hydro-chloroformyl elimination from acyl halides is a known reaction requiring usually high temperatures and presence of rhodium or palladium catalyst [6-9]. Acyl chlorides containing a β hydrogen atom are converted to olefins with loss of HCl and CO. A driving force in the observed transformation could be formation of a stable conjugated aromatic-heteroaromatic system.

Further studies are under way to examine closer this reaction.

EXPERIMENTAL

Reagent grade chemicals were used without further purification unless otherwise noted. Elemental analyses were performed at Microanalysis Laboratory of Institute of Organic Chemistry, Polish Academy of Sciences, Warsaw. Melting points were determined in capillary tubes and are uncorrected. Spectra were obtained as follows: IR spectra on JASCO FTIR-420 spectrometer, ^{1}H NMR spectra on Varian 500 UNITY plus-500 and Varian 200 UNITY plus 200 spectrometers in deuterated chloroform using TMS as internal standard, EI mass spectra on AMD M-40. Flash-chromatography was carried out using silica gel S 230-400 mesh (Merck).

Hydroximinoyl acid chlorides were prepared from the corresponding aryl aldehyde oximes and NCS in DMF [10]. The corresponding nitrile oxides were generated *in situ* by dehydrohalogenation with triethylamine.

General Procedure for the Cycloaddition Reactions of Hydroximinoyl Acid Chlorides with Ethyl Acrylate.

A solution of chloro oxime (13 mmol) in anhydrous toluene (15 mL) was added dropwise over 30 min. to a stirred mixture of anhydrous toluene, anhydrous NEt_3 (6 mL), $MgSO_4$ (2 g) and ethyl acrylate (8 mL, 80 mmol). The reaction mixture was stirred overnight at room temperature, diluted with toluene (50 mL), washed with water (5 x 100 mL) and evaporated *in vacuo*.

Ethyl 3-phenyl-4,5-dihydroisoxazole-5-carboxylate (**1a**).

This compound was obtained as an oil, (91%); 3070, 761, 692 (Ph), 1739 (CO) cm^{-1}; ^{1}H nmr ($CDCl_3$, 200 MHz): δ 7.7-7.65 (m, 2H), 7.44-7.38 (m, 3H), 5.16 (dd, J = 10.0; 8.2 Hz, 1H, H-5), 4.26 (q, J = 7.1 Hz, 2H, OCH_2), 3.64 (dd, J = 10.0; 8.2 Hz, 2H, H-4), 1.32 (t, J = 7.1 Hz, 3H).

Ethyl 3-(4-ethylphenyl)-4,5-dihydroisoxazole-5-carboxylate (**1b**).

This compound was obtained as a white powder, (87%), mp 33-35 °C; ir (KBr) 3040, 828 (Ph), 1758 (CO) cm^{-1}; ^{1}H nmr ($CDCl_3$, 200 MHz): δ 7.60 (dm, J = 8.3 Hz, 2H, H-2', H-6'), 7.23 (dm, J = 8.3 Hz, 2H, H-3', H-5'), 5.14 (dd, J = 10.0; 8.4 Hz, 1H, H-5), 4.26 (q, J = 7.2 Hz, 2H, CH_2), 3.63 (d, J = 8.4 Hz, 1H, H-4), 3.625 (d, J = 10.0 Hz, 1H, H-4), 2.67 (q, J = 7.6 Hz, 2H, CH_2-Ph), 1.32 (t, J = 7.2 Hz, 3H, CH_3CH_2O), 1.24 (t, J = 7.6 Hz,

3H, Aryl$CH_2\underline{CH_3}$). eims: m/z (%) 247 (M^+, 19), 174 (M^+-$COOC_2H_5$, 100), 146(M^+ -$COOC_2H_5$ -C_2H_4, 52).

Anal. Calcd. For $C_{14}H_{17}NO_3$: C, 67.99; H, 6.93. Found: C, 68.01; H, 6.97.

Ethyl 3-(4-isopropylphenyl)-4,5-dihydroisoxazole-5-carboxylate (**1c**).

This compound was obtained as a yellow oil, (90%); ir (neat) 3040, 834 (Ph), 1739 (CO) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.61 (dd, J = 8.3; 1.9 Hz, 2H, H-5', H-3'), 7.26 (dd, J = 8.3; 1.7 Hz, 2H, H-6', H-2'), 5.15 (dd, J = 10.0; 8.2 Hz, 1H, H-5), 4.26 (q, J = 7.0 Hz, 2H, -O-CH_2), 3.63 (d, J = 8.2 Hz, 1H, H-4), 3.62 (d, J = 10.0 Hz, 1H, H-4), 2.92 (septuplet, J = 7.2 Hz, 1H, CH iPr), 1.32 (t, J = 7.2 Hz, 3H, CH_3 Et), 1.26 (d, J = 7.2 Hz, 6H, CH_3 iPr).

Anal. Calcd. For $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33. Found: C, 69.09; H, 7.25.

Ethyl 3-(4-trifluoromethylphenyl)-4,5-dihydroisoxazole-5-carboxylate (**1d**).

This compound was obtained as a oil (81%); ir (neat) 3040, 841 (Ph), 1741 (CO) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.79 (d, J = 8.5 Hz, 2H, H-3', H-5'), 7.67 (d, J = 8.5 Hz, 2H, H-2', H-6'), 5.22 (dd, J = 11.0; 8.5 Hz, 1H, H-5), 4.28 (q, J = 7.0 Hz, 2H, CH_2), 3.67 (d, J = 8.5 Hz, 1H, H-4), 3.65 (d, J = 11.0 Hz, 1H, H-4), 1.33 (t, J = 7.0 Hz, 3H, CH_3); eims: m/z (%) 287 (M^+, 10), 268 (M^+-F, 5), 214 (M^+-CO_2Et, 100), 186 (M^+- CO_2Et-C_2H_4, 80), 145 ($C_6H_5CF_3$, 60).

Anal. Calcd. For $C_{13}H_{12}NO_3F_3$: C, 54.36; H, 4.21. Found: C, 54.51; H, 4.36.

Ethyl 3-(2-methoxyphenyl)-4,5-dihydroisoxazole-5-carboxylate (**1e**).

This compound was obtained as a oil, (88%); ir (neat) 3040, 1602, 1491, 755 (Ph), 1740 (CO) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.76 (m, 1H, H-3'), 7.36 (m, 1H, H-5'), 7.02-6.84 (m, 2H, H-4', H-6'), 5.11 (dd, J = 10.6; 8.0 Hz, 1H, H-5), 4.27 (q, J = 7.1 Hz, 2H, OCH_2), 3.86 (s, 3H, OCH_3), 3.75 (d, J = 10.6, 1H, H-4), 3.74 (d, J = 8.0 Hz, 1H, H-4), 1.32 (t, J = 7.1 Hz, 3H, Et).

Ethyl 3-(2,3,6-trichlorophenyl)-4,5-dihydroisoxazole-5-carboxylate (**1f**).

This compound was obtained as a dense oil (74%); ir (neat) 3080, 820 (Ph), 1741 (CO), 580, 520 cm^{-1} (Cl); ^1H NMR ($CDCl_3$, 200 MHz): δ 7.49 (d, J = 8.8 Hz, 1H, H-4'), 7.33 (d, J = 8.8 Hz, 1H, H-5'), 5.26 (dd, J = 10.0; 8.0 Hz, 1H, H-5), 4.30 (q, J = 7.2 Hz, 2H, CH_2), 3.58 (d, J = 8.0 Hz, 1H, H-4), 3.57 (d, J = 10.0 Hz, 1H, H-4), 1.35 (t, J = 7.2 Hz, 3H).

Anal. Calcd. For $C_{12}H_{10}NO_3Cl_3$: C, 44.68; H, 3.12. Found: C, 44.49; H, 3.02.

Ethyl 3-(4-trifluoromethylphenyl)-5-methyl-4,5-dihydroisoxazole-5-carboxylate (**1g**).

This compound was obtained similarly starting from ethyl methacrylate as a dense yellowish oil, (86%); ir (KBr) 3040, 835 (Ph), 1736 (CO) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.78 (d, J = 8.4 Hz, 2H, H-3', H-5'), 7.67 (d, J = 8.4 Hz, 2H, H-2', H-6'), 4.27 (q, J = 7.2 Hz, 2H,-OCH_2), 3.91 (d, J = 17.0 Hz, 1H, H-4), 3.22 (d, J = 17.0 Hz, 1H, H-4), 1.74 (s, 3H, CH_3), 1.33 (t, J = 7.1 Hz, 3H, Et); eims: m/z (%) 301 (M^+ , 6), 282 (M^+-F, 6), 228 (M^+-CO_2Et, 64), 145 ($C_6H_4CF_3$).

Anal. Calcd. For $C_{14}H_{14}NO_3F_3$: C, 55.81; H, 4.68. Found: C, 55.56; H, 4.51.

Methyl 3-(4-ethylphenyl)-4,5-dihydroisoxazole-5-methyl-5-carboxylate (**1h**).

This compound was obtained as an oil (87%); ir (neat) 3040, 834 (Ph), 1741 (CO) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.58 (dm, J = 8.4 Hz, 2H, H-2', H-6'), 7.23 (dm, J = 8.4 Hz, 2H, H-3', H-5'), 3.88 (d, J = 17.0 Hz, 1H, H-4), 3.81 (s, 3H, OCH_3), 3.21 (d, J = 17.0 Hz, 1H, H-4), 2.67 (q, J = 7.6 Hz, 2H, CH_2-Ph), 1.71 (s, 3H, C-CH_3), 1.24 (t, J = 7.6 Hz, 3H, EtO).

Anal. Calcd. For $C_{14}H_{15}NO_3$: C, 68.55; H, 6.16. Found: C, 68.73; H, 6.03.

General Procedure for Hydrolysis of Ethyl Esters **1a-h**.

To a suspension of an ethyl ester in mixture of ethanol and water 1:1 was added a solution of sodium hydroxide (2.5-3 eq.) in water and the mixture was heated at reflux for 1.5-3 hours. The solution was cooled, extracted with ether and the ethereal extracts were discarded. The aqueous layer was acidified with dilute hydrochloric acid and the product, which separated, was extracted with methylene chloride. The combined extracts were washed with water, dried (magnesium sulfate) and evaporated *in vacuo* to yield a solid, which was used directly in the next step. An analytical sample was prepared by recrystallization.

3-Phenyl-4,5-dihydroisoxazole-5-carboxylic acid (**2a**).

This compound was obtained as a white powder (87%), mp 124-127 °C; ir (KBr) 3600-2600 1728 (COOH), 3050, 755, 692(Ph) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.70-7.65 (m, 2H, H-2', H-6'), 7.47-7.39 (m, 3H, H-3'-H-5'), 5.24 (dd, J = 10.0; 7.8 Hz, 1H, H-5), 3.73 (d, J = 10.0 Hz, 1H, H-4), 3.72 (d, J = 7.8 Hz, 1H, H-4).

3-(4-Ethylphenyl)-4,5-dihydroisoxazole-5-carboxylic acid (**2b**).

This compound was obtained as a white powder (89%), mp 105-107 °C; ir (KBr) 3500-2800, 1730 (COOH) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.97 (d, J = 8.4 Hz, 2H, H-3', H-5'), 7.76 (d, J = 8.4 Hz, 2H, H-2', H-6'), 7.29 (s, 1H, H-4), 2.68 (q, J = 7.0 Hz, 2H, CH_2), 1.45 (t, J = 7.0 Hz, 3H, CH_3); eims: m/z (%) 285 (M^+, 18), 266 M^+-F, 4), 212 (M^+-CO_2Et, 100), 184 (M^+- CO_2Et-C_2H_4, 18), 145 ($C_6H_5CF_3$, 21).

Anal. Calcd. For $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98. Found: C, 65.78; H, 6.00.

3-(4-Isopropylphenyl)-4,5-dihydroisoxazole-5-carboxylic acid (**2c**).

This compound was obtained as a glass (95%), ir (KBr) 3500-2800, 1730 (COOH) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 9.19 (s, 1H, OH), 7.60 (dd, J = 6.6; 1.8 Hz, 2H, H-3', H-5'), 7.27 (dd, J = 6.6; 1.8 Hz, 2H, H-2', H-6'), 5.21 (dd, J = 9.8; 7.9 Hz, 1H, H-5), 3.70 (d, J = 9.8 Hz, 1 H, H-4), 3.69 (d, J = 7.9 Hz, 1H, H-4), 2.93 (septuplet, J = 6.8 Hz, 1H, CH iPr), 1.25 (d, J = 6.8 Hz, 6H, CH_3 iPr).

Anal. Calcd. For $C_{13}H_{15}NO_3$ x ½ H_2O: C, 64.44; H, 6.66. Found: C, 64.54; H, 6.47.

3-(Trifluoromethylphenyl)-4,5-dihydroisoxazole-5-carboxylic acid (**2d**).

This compound was obtained as a white powder (87%), mp 139-141 °C; ir (KBr) 3600-2800, 1729 (COOH), 1336 (CF_3) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.80 (d, J = 8.4 Hz, 2H, H-3',

H-5'), 7.69 (d, J = 8.4 Hz, 2H, H-2', H-6'), 5.30 (dd, J = 9.5; 8.2 Hz, 1H, H-5), 3.74 (d, J = 9.5 Hz, 1 H, H-4), 3.73 (d, J = 8.2 Hz, 1H, H-4).

Anal. Calcd. For $C_{11}H_8NO_3F_3$: C, 50.97; H, 3.11. Found: C, 51.22; H, 3.26.

3-(2-Methoxyphenyl)-4,5-dihydroisoxazole-5-carboxylic acid (**2e**).

This compound was obtained as a white powder (79%), mp 74-77 °C; ir (KBr) 3600-2400, 1737 (COOH), 1602, 1491, 755 (Ph) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz) δ 7.73 (m, 1H, H-6'), 7.40 (m, 1H, H-4'), 7.03-6.86 (m, 2H, H-3', H-5'), 5.17 (dd, J = 10.4; 7.3 Hz, 1H, H-5), 3.80 (d, J = 10.4 Hz, 1H, H-4), 3.79 (d, J = 7.3 Hz, 1H, H-4).

Anal. Calcd. For $C_{11}H_{11}NO_4$ x ½ H_2O: C, 57.38; H, 5.26. Found: C, 57.07; H, 4.87.

3-(2,3,6-Trichlorophenyl)-4,5-dihydroisoxazole-5-carboxylic acid (**2f**).

This compound was obtained as a white powder (87%), mp 88-90 °C; ir (KBr) 3600-2500, 1731 (COOH), 819, 523 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.50 (d, J = 8.6 Hz, 1H, H-4'), 7.34 (d, J = 8.6 Hz, 1H, H-5'), 5.33 (dd, J = 11.2; 6.8 Hz, 1H, H-5), 4.30 (q, J = 7.2 Hz, 2H, CH_2), 3.66 (d, J = 11.2 Hz, 1H, H-4), 3.62 (d, J = 6.8 Hz, 1H, H-4).

Anal. Calcd. For $C_{10}H_6NO_3Cl_3$: C, 40.78; H, 2.05. Found: C, 40.62; H, 2.11.

3-(Trifluoromethylphenyl)-5-methyl-4,5-dihydroisoxazole-5-carboxylic acid (**2g**).

This compound was obtained as a white powder (87%), mp 164-166 °C; ir (KBr) 3422, 1716 (COOH), 838 cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.77 (d, J = 8.4 Hz, 2H, H-3', H-5'), 7.68 (d, J = 8.8 Hz, 2H, H-2', H-6'), 3.91 (d, J = 17.3 Hz, 1H, H-4), 3.31 (d, J = 17.3 Hz, 1H, H-4), 1.80 (s, 3H, CH_3-C-); eims: m/z (%) 273 (M^+, 10), 254 (M^+-F, 7), 228 (M^+-CO_2H, 48), 186 (76), 145 ($C_6H_4CF_3$, 22).

Anal. Calcd. For $C_{12}H_{10}NO_3F_3$: C, 52.75; H, 3.69. Found: C, 52.73; H, 3.84.

3-(4-Ethylphenyl)-4,5-dihydroisoxazole-5-methyl-5-carboxylic acid (**2h**).

This compound was obtained as a white powder (95%), mp 84-87 °C; ir (KBr) 3300-2500, 1699 (COOH), 833 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.56 (dm, J = 8.2 Hz, 2H, H-2', H-6'), 7.24 (dm, J = 8.2 Hz, 2H, H-3', H-5'), 3.88 (d, J = 17.3 Hz, 1H, H-4), 3.29 (d, J = 17.3 Hz, 1H, H-4), 2.68 (q, J = 7.6 Hz, 2H, CH_2-CH_3), 1.77 (s, 3H, CH_3), 1.24 (t, J = 7.6 Hz, 3H, CH_3).

Anal. Calcd. For $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48. Found: C, 67.07; H, 6.37.

General Procedure for Preparation of Acid Chlorides and Reaction with Triethylamine.

To a solution of 3-aryl-4,5-dihydroisoxazole-5-carboxylic acid (2 mmol) in dry benzene (15 mL) was added with stirring oxalyl chloride (10 mmol). The solution was heated at reflux for 1.5 hour. Benzene and excess of oxalyl chloride were removed *in vacuo*. Dry benzene and TEA (10-30 mmol) were added and the solution was heated at reflux for 1 hour and stirred at room temperature overnight. The reaction mixture was washed with water, dried (magnesium sulfate), evaporated *in vacuo* and the residue was separated by column chromatography on silica gel using hexane – ethyl acetate gradient (from 20:1 to 1:1, v/v).

Benzonitrile (**4a**).

This compound was obtained as an oil (28%); ir (neat) 3037, 1492, 757, 688 (Ph), 2230 (CN) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.67 (m, 2H, H-2, H-6), 7.51 (m, 3H, H-3-5).

4-Ethylbenzonitrile (**4b**).

This compound was obtained as an oil (33%); ir (neat) 2228 (CN) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.57 (dm, J = 8.5 Hz, 2H, H-2, -H-6), 7.29 (dm, J = 8.5 Hz, 2H, H-3, H-5), 2.71 (q, J = 7.5 Hz, 2H), 1.25 (t. J = 7.5 Hz, 3H); ^{13}C nmr ($CDCl_3$, 50.3 MHz): δ 149.8 (C-4), 132.2 (C-3, C-5), 128.6 (C-2, C-6), 119.2 (CN), 109.5 (C-1), 29.0 (CH_2), 15.0 (CH_3).

4-Isopropylbenzonitrile (**4c**).

This compound was obtained as an oil (12%); ir (neat) 3020, 1609, 1504, 835 (Ph), 2228 (CN) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.58 (dm, J = 8.3 Hz, 2H, H-2', H-6'), 7.32 (dm, J = 8.3 Hz, 2H, H-3', H-5'), 2.96 (septuplet, J = 6.8 Hz, 1H), 1.26 (d, J = 6.8 Hz, 6H).

2-Methoxybenzonitrile (**4d**).

This compound was obtained as an oil (49%); ir (neat) 3042, 1599, 1495, 760 (Ph), 2227 (CN) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.6-7.5 (m, 2H, H-4, H-6), 7.05-6.91 (m, 2H, H-3, H-5), 3.94 (s, 3H, CH_3).

2,3,6-Trichlorobenzonitrile (**4e**).

This compound was obtained as an oil (51%); ir (neat) 2227 (CN) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.65 (d, J = 8.8 Hz, 1H, H-4), 7.40 (d, J = 8.8 Hz, 1H, H-5).

3-(4-Trifluoromethylphenyl)isoxazole (**5a**).

This compound was obtained as an oil (0.3%); ^1H nmr ($CDCl_3$, 200 MHz): δ 8.52 (d, J = 1.8 Hz, 1H, H-5), 7.96 (dm, J = 8.2 Hz, 2H, H-2', H-6'), 7.74 (dm, J = 8.2 Hz, 2H, H-3', H-5'), 6.72 (d, J = 1.8 Hz, 1H, H-4).

Anal. Calcd. For $C_{10}H_6ONF_3$: C, 56.34; H, 2.84. Found: C, 56.16; H, 2.93.

3-(2-Methoxyphenyl)isoxazole (**5b**).

This compound was obtained as an oil (2%); ir (neat) 3070, 800 (Ph), 1259 (OMe) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 8.44 (d, J = 1.6 Hz, 1H, H-5), 7.72 (m, 1H, H-3'), 7.43 (m, 1H, H-5'), 7.00 (m, 2H, H-4', H-6'), 6.87 (d, J = 1.6 Hz, 1H, H-4), 3.91 (s, 3H).

Anal. Calcd. For $C_{10}H_9NO_2$: C, 68.55; H, 5.18. Found: C, 68.83; H, 5.34.

3-(4-Trifluoromethylphenyl)-5-methylisoxazole (**5c**).

This compound was obtained as an oil (13%); ir (neat) 3120, 1610, 1332 (CF_3), 849, 820 cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.91 (d, J = 8.8 Hz, 2H, H-2', H-6'), 7.71 (d, J = 8.8 Hz, 2H, H-3', H-5'), 6.27 (q, J = 0.6 Hz, 1H, H-4), 2.51 (d, J = 0.6 Hz, 3H, CH_3-C=).

Anal. Calcd. For $C_{11}H_8NOF_3$: C, 58.15; H, 3.55. Found: C, 58.28; H, 3.71.

3-(4-Ethylphenyl)-5-methylisoxazole (**5d**).

This compound was obtained as an oil (2.9%); ir (neat) 3110, 1610, 1332, 849, 820 cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.70 (d, J = 8.1 Hz, 2H, H-2', H-6'), 7.28 (d, J = 8.1 Hz, 2H, H-3', H-

5'), 6.27 (q, J = 0.8 Hz, 1H, H-4), 2.69 (q, J = 7.6 Hz, 2H, CH_2), 2.47 (d, J = 0.8 Hz, 3H, CH_3-C=), 1.26 (t, J = 7.6 Hz, 3H, CH_3-CH_2).

Anal. Calcd. For $C_{12}H_{13}NO$: C, 76.97; H, 6.70. Found: C, 76.71; H, 6.86.

Isoxazolines: 3-(4-Ethylphenyl)-2-isoxazoline (**6a**).

This compound was obtained as an oil (1.6%); ir (neat) 3040, 834 (Ph), 1600 (C=N) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.61 (dm, J = 8.4 Hz, 2H, H-2', H-6'), 7.24 (dm, J = 8.4 Hz, 2H, H-3', H-5'), 4.48 (t, J = 10.1 Hz, 2H, H-5), 3.33 (t, J = 10.1 Hz, 2H, H-4), 2.68 (q, J = 7.5 Hz, 2H), 1.25 (t. J = 7.8 Hz, 3H); eims: m/z (%) 175 (M^+, 100), 160 (M^+-CH_3, 90), 132 (M^+- CH_3-C_2H_4, 30).

Anal. Calc. For $C_{11}H_{13}ON$: C, 75.39; H, 7.48. Found: C, 75.58; H, 7.61.

3-(4-Isopropylphenyl)-2-isoxazoline (**6b**).

This compound was obtained as an oil (5.3%); ir (neat) 3040, 837 (Ph), 1605 (C=N) cm^{-1}; ^1H nmr ($CDCl_3$, 200 MHz): δ 7.62 (dm, J = 8.2 Hz, 2H, H-2', H-6'), 7.27 (dm, J = 8.2 Hz, 2H, H-3', H-5'), 4.74 (t, J = 10.0 Hz, 2H, H-5), 3.33 (t, J = 10.0 Hz, 2H, H-4), 2.94 (septuplet, J = 6.8 Hz, 1H), 1.23 (d, J = 6.8 Hz, 6H); eims: m/z (%) 189 (M^+, 45), 174 (M^+-CH_3, 100).

Anal. Calc. For $C_{12}H_{15}ON$: C, 76.15; H, 7.99. Found: C, 75.99; H, 8.11.

Acknowledgements.

This work was supported in part by the Polish State Committee for Scientific Research (Grant E-142/S/2004), what is gratefully acknowledged.

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