REACTIONS OF 2-, 3-, 4-PYRIDINE-2-PROPENOATES AND 2-, 3-, 4-QUINOLINE-2-PROPENOATES WITH DIAZOMETHANE*

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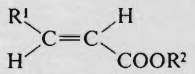
Cycloaddition reactions of esters of *trans*-pyridine-2-propenoic acids, *Ia—Id*, and methyl *trans*-quinoline-2-propenoates *Ie—Ig* with diazomethane gave 4-pyridyl-2-pyrazoline-3-carboxylates *IIa—IId* and 4-quinolyl-2-pyrazoline-3-carboxylates *IIe—IIg*, respectively.

Cycloaddition reactions of diazomethane with esters of 2-propenoic acids, having an aromatic or heteroaromatic substituent at position 3, have been described. These reactions give rise to esters of 4-aryl-2-pyrazoline-3-carboxylic acids[1–3] or 4-heteroaryl-2-pyrazoline-3-carboxylic acids[4,5]. We thought it worth while to study the reactions of diazomethane with methyl esters of *trans*-2-pyridine-, 3-pyridine- and 4-pyridine-2-propenoic acids (*Ia*, *Ic*, *Id*), with ethyl 2-pyridine-2-propenoate (*Ib*), as well as with methyl *trans*-2-quinoline-2-propenoate (*Ie*) and its isomers I*f*, I*g*. Only one of these reactions has been described[4], *viz.* the addition of diazomethane to *Ia*; the reaction product was converted into its N-acetyl derivative, identified as methyl 1-acetyl-4-(2-pyridyl)-2-pyrazoline-3-carboxylate.



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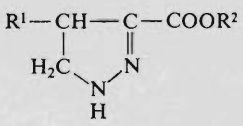

II

Ia, IIa, R^1 = 2-pyridyl, $R^2 = CH_3$
Ib, IIb, R^1 = 2-pyridyl, $R^2 = C_2H_5$
Ic, IIc, R^1 = 3-pyridyl, $R^2 = CH_3$
Id, IId, R^1 = 4-pyridyl, $R^2 = CH_3$
Ie, IIe, R^1 = 2-quinolyl, $R^2 = CH_3$
If, IIf, R^1 = 3-quinolyl, $R^2 = CH_3$
Ig, IIg, R^1 = 4-quinolyl, $R^2 = CH_3$

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Reactions of esters *Ia–Ig* with an ethereal solution of diazomethane invariably gave one product only. On the basis of analytical and spectral data these products were identified as esters of 4-pyridyl- or 4-quinolyl-2-pyrazoline-3-carboxylic acids *IIa–IIg*. The cycloaddition of diazomethane to the esters *Ia–Ig* evidently proceeds as the analogous reactions of esters of cinnamic[1-3] and 2-furan-2-propenoic[5] acids *i.e.* diazoalkanes add to activated unsaturated systems in only one direction, yielding pyrazolines with nitrogen β to the activating group[6].

EXPERIMENTAL

IR spectra were measured with an apparatus Perkin Elmer 325, mass spectra with an apparatus LKB 9 000, ^{1}H-NMR spectra with an apparatus Varian XL-100-15 (10·1 MHz) at 37°C, tetramethylsilane being used as internal standard. The temperature data are not corrected.

Methyl *trans*-2-Pyridine-2-propenoate (*Ia*)

To a solution of *trans*-2-pyridine-2-propenoic acid[7] (9·3 g, 0·066 mol) in methanol (50 ml) was added dropwise conc. sulphuric acid (15·4 ml) and the mixture was refluxed on a water bath. After 4 h it was poured on ice and neutralized with potassium carbonate. The product was taken into ether and the solution was worked up in the usual manner; yield 8·5 g (83·5%), m.p. 28 to 30°C. For $C_9H_9NO_2$ (163·2) calculated: 66·25% C, 5·56% H, 8·58% N; found: 66·96% C, 5·83% H, 8·46% N. ^{1}H-NMR spectrum (C^2HCl_3, ppm): 3·80 (s, 3 H) CH_3; 6·94 (d, 1 H, 16 Hz) =CH; 7·15—7·50 (m, 2 H) positions 3 and 5; 7·67 (m, 1 H) position 4; 7·66 (d, 1 H, 16 Hz) —CH=; 8·65 (m, 1 H, 5 Hz) position 6.

Methyl *trans*-2-Quinoline-2-propenoate (*Ie*)

The esterification was carried out analogously; 20·4 g (0·102 mol) of 2-quinoline-2-propenoic acid[8] afforded 17 g (78%) of *Ie*, m.p. 79—80°C (methanol). For $C_{13}H_{11}NO_2$ (213·2) calculated: 73·22% C, 5·20% H, 6·57% N; found: 73·35% C, 5·35% H, 6·44% N. ^{1}H-NMR spectrum (C^2HCl_3, ppm): 3·84 (s, 3 H) CH_3; 6·98 (d, 1 H, 16 Hz) =CH(α); 7·4—8·2 (m, 7 H; 8·04, d, 16 Hz) 6 H arom., CH=(β).

Methyl *trans*-3-Quinoline-2-propenoate (*If*)

The ester, m.p. 120—121°C (methanol) was prepared as described[9], except that triphenylphosphine was used instead of tri-*o*-tolylphosphine; yield 30%. For $C_{13}H_{11}NO_2$ (213·2) calculated: 73·22% C, 5·20% H, 6·57% N; found: 73·39% C, 5·37% H, 6·36% N. ^{1}H-NMR spectrum ($C_6{}^2H_6$, ppm): 3·53 (s, 3 H) CH_3; 6·41 (d, 1 H, 16 Hz) =CH; 7·64 (d, 1 H, 16 Hz) CH= 7·1—8·9 (m, 6 H) arom. protons.

Methyl *trans*-4-Quinoline-2-propenoate (*Ig*)

In analogy to the preparation of *Ia*, 19·9 g of 4-quinoline-2-propenoic acid[10] gave 12·0 g (56·3%) of *Ig*, m.p. 59—60°C. For $C_{13}H_{11}NO_2$ (213·2) calculated: 73·22% C, 5·20% H, 6·57% N; found: 73·50% C, 5·47% H, 6·57% N. ^{1}H-NMR spectrum (C^2HCl_3, ppm): 3·9 (s, 3 H) CH_3; 6·65 (d, 1 H, 16 Hz) =CH(α); 7·5—8·3 (m, 5 H) arom. protons, =CH(β); 8·96 (d, 1 H, 4 Hz) C_2.

Methyl 4-(2-Pyridyl)-2-pyrazoline-3-carboxylate (*IIa*)

Diazomethane, prepared from 15·7 g of N-methyl-N-nitroso-*p*-toluenesulphonamide[11], was distilled into a solution of *Ia* (3·2 g, 0·02 mol) in diethyl ether (60 ml). The mixture was stirred and cooled with ice, then left standing for 24 h. The separated crystals were recrystallized from methanol, m.p. 141—143°C, yield 2·15 g (53·5%). For $C_{10}H_{11}N_3O_2$ (205·2) calculated: 58·53% C, 5·40% H, 20·48% N; found: 58·64% C, 5·54% H, 20·76% N. IR spectrum ($CHCl_3$, cm^{-1}): 1 710 ν(C=O); 3 410 (m) ν(NH). Mass spectrum: M^+ 205. ^{1}H-NMR spectrum (C^2HCl_3, ppm): 3·71 (s, 3 H) CH_3; 3·9—4·2 (m, 2 H) N—CH_2C; 4·58 (ddd, 1 H, 12 Hz) C—CH; 6·0—6·8 (m, 1 H) NH; 7·1—7·32 (m, 2 H) protons on $C_{(3)}$ and $C_{(5)}$; 7·5—7·72 (m, 1 H) protons on $C_{(4)}$; 8·56 (d, 1 H, 5 Hz) protons on $C_{(6)}$ of the pyridine ring.

Ethyl 4-(2-Pyridyl)-2-pyrazoline-3-carboxylate (*IIb*)

3·54 g (0·02 mol) of *Ib* (ref.[12]) gave 2·16 g (50·3%) of the product, m.p. 95—97°C (ethanol). For $C_{11}H_{13}N_3O_2$ (219·2) calculated: 60·26% C, 5·98% H, 19·17% N; found: 60·41% C, 6·08% H, 19·17% N. IR spectrum ($CHCl_3$, cm^{-1}): 1 710 (s) (C=O); 3 405 (w) (NH). ^{1}H-NMR spectrum ($C_6{}^2H_6$, ppm): 0·88 (t, 3 H, 6 Hz) CH_3; 3·20—3·72 (m, 2 H) N—CH_2C; 3·76—4·12 (m, 2 H) O—CH_2—C; 4·4 (dd, 1 H, 12 Hz) C—CH<; 5·4—6·2 (m, 1 H) NH; 6·48—7·1 (m, 3 H) protons on $C_{(3)}$, $C_{(5)}$; 8·4 (d, 1 H, 5 Hz) protons on $C_{(6)}$ of the pyridine ring.

Methyl 4-(3-Pyridyl)-2-pyrazoline-3-carboxylate (*IIc*)

3·4 g (0·061 mol) of *Ic* (ref.[13]) gave 2 g (50%) of the product, m.p. 114—116°C (methanol). For $C_{10}H_{11}N_3O_2$ (205·2) calculated: 58·53% C, 5·40% H, 20·48% N; found 58·65% C, 5·24% H, 20·65% N. ^{1}H-NMR spectrum (C^2HCl_3, ppm): 2·96 (m, 1 H) CH; 2·99 (s, 3 H) OCH_3; 3·40 (m, 2 H) CH_2; 5·78 (m, 1 H) proton on $C_{(5)}$; 6·06 (m, 1 H) proton on $C_{(4)}$; 6·83 (m, 2 H) proton on $C_{(6)}$ of the pyridine ring and one exchangeable proton (NH).

Methyl 4-(4-Pyridyl)-2-pyrazoline-3-carboxylate (*IId*)

2·0 g (0·012 mol) of *Id* (ref.[14]) gave 1·3 g (52%) of the product, m.p. 137—139°C (methanol). For $C_{10}H_{11}N_3O_2$ (205·2) calculated: 58·53% C, 5·40% H, 20·48% N; found: 58·58% C, 5·69% H, 20·68% N. IR spectrum ($CHCl_3$, cm^{-1}): 1 715 (vs) ν(C=O); 3 410 (m) ν(NH). Mass spectrum: M^+ 205. ^{1}H-NMR spectrum ($C_6{}^2H_6$, ppm): 2·7—3·2 (m, 2 H) N—CH_2C; 3·33 (s, 3 H) CH_3; 3·8 (dd, 1 H, 12 Hz) C—CH; 5·2—5·4 (m, 1 H) NH; 6·74—6·86 (m, 2 H) protons on $C_{(3)}$ and $C_{(5)}$; 8·4—8·6 (m, 2 H) protons on $C_{(2)}$ and $C_{(6)}$ of the pyridine ring.

Methyl 4-(2-Quinolyl)-2-pyrazoline-3-carboxylate (*IIe*)

2·13 g (0·01 mol) of *Ie* gave 1·3 g (51%) of *IIe*, yellow crystals, m.p. 129—132°C (methanol). For $C_{14}H_{13}N_3O_2$ (255·3) calculated: 65·87% C, 5·13% H, 16·46% N; found: 65·63% C, 5·10% H, 16·36% N. IR spectrum ($CHCl_3$, cm^{-1}): 1 720 (s) ν(C=O); 3 410 (w) ν(NH). ^{1}H-NMR spectrum (hexadeuterodimethyl sulphoxide, ppm): 3·52 (s, 3 H) CH_3; 3·66—4·2 (m, 2 H) N—CH_2—C; 3·66—4·2 (band, 1 H) NH; 4·68 (dd, 1 H, 12 Hz) C—CH; 7·3—8·5 (m, 6 H) aromatic protons.

Methyl 4-(3-Quinolyl)-2-pyrazoline-3-carboxylate (*IIf*)

2·56 g (0·012 mol) of *If* gave 1·0 g (32·7%) of the product, m.p. 142—144°C (methanol). For $C_{14}H_{13}N_3O_2$ (255·3) calculated: 65·87% C, 5·13% H, 16·46% N; found: 65·64% C, 5·33% H,

16·22% N. Mass spectrum: M^+ 255. IR spectrum ($CHCl_3$, cm^{-1}): 1 710 (s) ν(C=O); 3 410 (m) ν(NH). ^{1}H-NMR spectrum (C^2HCl_3, ppm): 3·76 (s, 3 H) CH_3; 3·8—4·36 (m, 2 H) N—CH_2—C; 4·5 (dd, 1 H, 12 Hz) C—CH<; 6·3—6·6 (band, 1 H) NH; 7·2—8·96 (m, 6 H) aromatic protons.

Methyl 4-(4-Quinolyl)-2-pyrazoline-3-carboxylate (*IIg*)

4·26 g (0·02 mol) of *Ig* gave 1·7 g (33%) of the product, m.p. 155—156°C (methanol). For C_{14}·.$H_{13}N_3O_2$ (255·3) calculated: 65·87% C, 5·13% H, 16·46% N; found: 65·70% C, 5·27% H, 16·62% N. Mass spectrum: M^+ 255. IR spectrum ($CHCl_3$, cm^{-1}) 1 718 (vs) ν(C=O); 3 410 (m) ν(NH). ^{1}H-NMR spectrum (C^2HCl_3, ppm): 3·74 (s, 3 H); 3·4—4·36 (m, 2 H) N—CH_2—C; 5·08 (dd, 1 H, 12 Hz) C—CH; 6·4—6·7 (band, 1 H) NH; 7·0—8·84 (m, 6 H) aromatic protons.

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