# Studies on Naphthyridines. Part 2 [1]. Synthesis of 4-Substituted and 6-Substituted 1,6-Naphthyridin-5(6*H*)-ones



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Ethyl 4-substituted 2-methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates **3a-h** were synthetized in a one-step reaction from diethyl 2,6-dimethylpyridine-3,5-dicarboxylates **1a-h** by aminomethinylation with 1,3,5-triazine (**2**). The 6-substitued derivatives **6a-z,aa-ff** could be obtained from diethyl 2-[2-(dimethylamino)-vinyl]-6-methylpyridine-3,5-dicarboxylate (**4**) either directly or *via* the isolated intermediate 2-[2-(arylamino)-vinyl]pyridine compounds **5a-i**.

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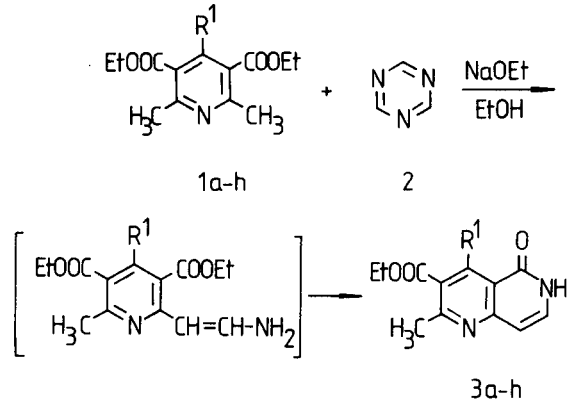
We earlier reported the one-step synthesis of pyrido-[4,3-*d*]pyrimidin-5(6*H*)-one by using 1,3,5-triazine as the ring-closure agent [2]. This aminomethinylation reaction was extended to the synthesis of the 1,6-naphthyridin-5(6*H*)-one skeleton (**3a**, $R^1$ = H), which could readily be formed from diethyl 2,6-dimethylpyridine-3,5-dicarboxylate (**1a**, $R^1$ = H) [1].

1,6-Naphthyridin-5(6*H*)-ones are increasingly being subjected to study because of their biological properties, *e.g.* their anti-inflammatory, anticonvulsant [3,4], insecticidal [5], antibacterial, antifungal [6,7] and Ca antagonistic activities [8,9]. Several methods are known for their synthesis from 2,3-disubstituted pyridines. Ikekawa [10] and Wibberley [11] started from ethyl 2-methylpyridine-3-carboxylate and obtained 1,6-naphthyridin-5(6*H*)-one in several steps in an overall yield of 3%.

Baldwin *et al.* [12] treated 2-methylpyridine-3-carbonitrile with *N,N*-dimethylformamide dimethyl acetal, and cyclized the product with hydrogen bromide in acetic acid to obtain a mixture of 1,6-naphthyridin-5(6*H*)-one and 5-bromo-1,6-naphthyridine. *N*-Substituted 2-methylpyridine-3-carboxamides were lithiated and cyclized with aromatic carboxylic esters [3,4], or they were condensed with benzaldehyde and the intermediate 2-styryl derivatives were subjected to cyclization in polyphosphoric acid to give 7-substituted naphthyridones in 33-83% yields [13,14].

Scheme 1




We report here a one-step procedure for the synthesis of ethyl 4-substituted 2-methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates **3b-h** (Scheme 1) and a two-step procedure for the preparation of the 6-substituted deriva-

Scheme 2

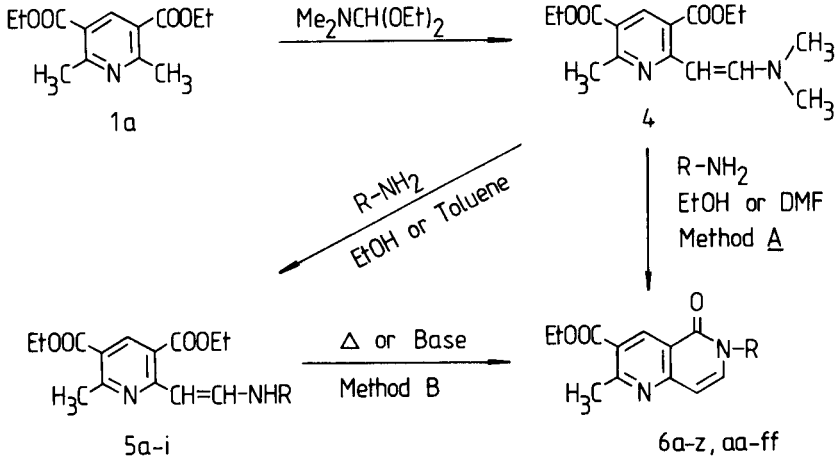
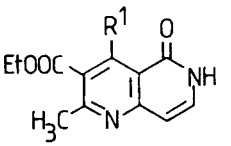


Table 1. Ethyl 4-Substitued 2-methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates and their UV and IR Data



3 a-h

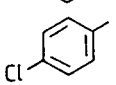
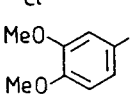
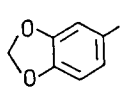
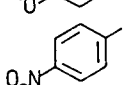
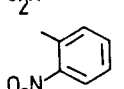
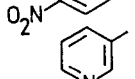
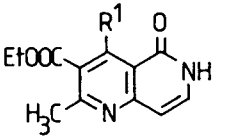
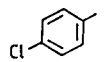
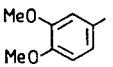
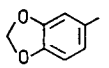
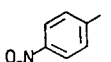
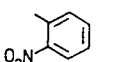
| Compound No. | $R^1$ | Reaction Time (h) | Yield (%) | Mp °C Solvent | Molecular Formula M.W. | Analysis % Calcd./Found C | H | N | Cl | UV $\lambda_{max}$ nm/log ε | | IR cm$^{-1}$ $\nu$C=O (ester) | $\nu$C=O (ring) | $\nu$ NH |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 3a | H [2] | 2 | 80 | 260 (MeOH) | $C_{12}H_{12}N_2O_3$ 232.241 | 62.06 62.30 | 5.21 5.33 | 12.06 11.83 | | 320 (4.12) | 250 (3.97) | 1730 | 1665 | 3175 |
| 3b |  | 3 | 97 | 235-236 (EtOH) | $C_{18}H_{16}N_2O_3$ 308.339 | 70.12 70.10 | 5.23 5.32 | 9.08 9.21 | | 304 (4.07) | 244 (4.08) | 1730 | 1670 | |
| 3c |  | 6 | 42 | 227 (MeOH) | $C_{18}H_{15}ClN_2O_3$ 342.784 | 63.07 62.85 | 4.41 4.55 | 8.17 8.30 | 10.34 10.70 | 305 (4.08) | 244 (4.09) | 1725 | 1660 | 3190 |
| 3d |  | 6 | 91 | 210-211 (MeOH) | $C_{20}H_{20}N_2O_5$ 368.392 | 65.21 65.48 | 5.47 5.24 | 7.60 7.96 | | 304 (4.15) | | 1720 | 1660 | 3190 |
| 3e |  | 5 | 96 | 226-227 (EtOH) | $C_{19}H_{16}N_2O_5$ 352.349 | 64.77 64.64 | 4.58 4.46 | 7.95 8.28 | | 303 (4.18) | 242 (4.16) | 1730 | 1670 | 3190 |
| 3f |  | 5 | 21 | 244-245 (MeOH) | $C_{18}H_{15}N_3O_5$ 353.337 | 61.19 61.07 | 4.28 4.25 | 11.89 11.88 | | 300 (4.19) | 252 (3.91) | 1730 | 1670 | 3180 |
| 3g |  | 3 | 25 | 206 (EtOH) | $C_{18}H_{15}N_3O_5$ 353.337 | 61.19 60.95 | 4.28 4.31 | 11.89 11.76 | | 305 (4.04) | 252 (4.10) | 1725 | 1665 | 3320 |
| 3h |  | 4 | 74 | 215-216 (EtOH) | $C_{17}H_{15}N_3O_3$ 309.326 | 66.01 65.83 | 4.89 4.87 | 13.58 13.31 | | 307 (3.99) | 250 (4.00) | 1725 | 1670 | 3200 |

Table 2. $^1$H-NMR Data of Ethyl 4-Substituted 2-methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates



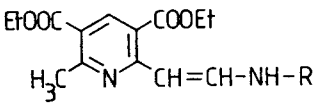
3 a-h

| Compound No. | $R^1$ | Solvent | 7-H | 8-H | 6-H | 3-COOCH$_2$CH$_3$ | 2-CH$_3$ | 3-COOCH$_2$CH$_3$ | 4-$R^1$ |
|---|---|---|---|---|---|---|---|---|---|
| 3a | H | DMSO-$d_6$ | 7.60d (J=8Hz) | 6.62dd (J=8Hz) (J=1Hz) | 11.65br.s | 4.43q (J=7Hz) | 2.90s | 1.47t (J=7Hz) | 8.87d (J=1Hz) |
| 3b |  | $CDCl_3$ | 6.85d [a] (J=7.5Hz) | 6.64d (J=7.5Hz) | 10.45br.s | 3.96q (J=7Hz) | 2.67s | 0.92t (J=7Hz) | 7.05-7.45m |
| 3c |  | DMSO-$d_6$ | 7.00-7.55m | 6.56d (J=7.5Hz) | 11.30br.s | 3.97q (J=7Hz) | 2.55s | 0.90t (J=7Hz) | 7.00-7.55m |
| 3d |  | $CDCl_3$ | 7.04d [a] (J=7Hz) | 6.71d (J=7Hz) | 10.38br.s | 4.03q (J=7Hz) | 2.66s | 1.00t (J=7Hz) | 6.60-7.10m 3.82s -OCH$_3$ 3.92s -OCH$_3$ |
| 3e |  | DMSO-$d_6$ | 7.40d [a] (J=7Hz) | 6.32-7.00m | 11.20br.s | 4.00q (J=7Hz) | 2.53s | 0.95t (J=7Hz) | 6.32-7,00m 6.01s -O-CH$_2$-O- |
| 3f |  | $CDCl_3$ | 7.12d [a] (J=8Hz) | 6.77d (J=8Hz) | 10.15br.s | 4.03q (J=7Hz) | 2.72s | 1.00t (J=7Hz) | 7.42d (J=9Hz) 8.27d (J=9Hz) |
| 3g |  | $CDCl_3$ | 7.12d (J=8Hz) | 6.76d (J=8Hz) | 10.54br.s | 3.97q (J=7Hz) | 2.69s 2.77s | 0.95t (J=7Hz) | 6.95-7.30m 7.40-7.75m 8.10-8.37m |
| 3h |  | $CDCl_3$ | 7.02d (J=7Hz) | 6.70d (J=7Hz) | 11.05br.s | 4.01q (J=7Hz) | 2.68s | 0.97t (J=7Hz) | 7.20-7.40m 5'-H 7.48-7.66m 4'-H 8.40-8.70m {2'-H 6'-H |

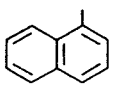
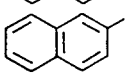
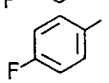
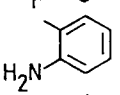
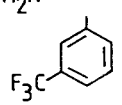
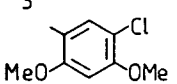
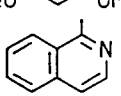
s= singlet, br.s= broad singlet, d= doublet, dd= doublet of doublets, t= triplet, q= quartet, m= multiplet

[a] After $D_2O$ addition.

Table 3. Diethyl 2-[2-(Arylamino)vinyl]-6-methylpyridine-3,5-dicarboxylates and their UV and IR Data

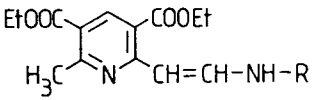



5a-i

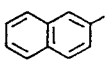
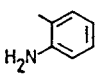
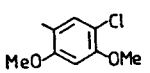
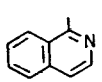
| Compound No. | R | Solvent | Reaction Time (h) | Yield (%) | Mp °C Solvent | Molecular Formula M.W. | Analysis % Calcd./Found C | H | N | X | UV $\lambda_{max}$ nm/log ε | | | IR cm$^{-1}$ $\nu$C=O (ester) | $\nu$C=C |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 5a |  | EtOH | 14 [a] | 62 | 156-157 | $C_{20}H_{22}N_2O_4$ | 67.78 | 6.26 | 7.90 | | 410 | | 260 | 1710 | 1640 |
| | | Toluene | 5 | 60 | (EtOAc) | 354.409 | 68.02 | 6.42 | 8.01 | | (4.58) | | (4.09) | | |
| 5b |  | Toluene | 11 | 62 | 145-146 | $C_{24}H_{24}N_2O_4$ | 71.27 | 5.98 | 6.93 | | 420 | 334 | 305 | 252 | 1715 | 1645 |
| | | | | | (Acetone) | 404.469 | 71.35 | 5.77 | 6.97 | | (4.55) | (3.98) | (4.02) | (4.22) | | |
| 5c |  | Toluene | 4 | 57 | 138-139 | $C_{24}H_{24}N_2O_4$ | 71.27 | 5.98 | 6.93 | | 420 | | 288 | 248 | 1710 | 1640 |
| | | EtOH | 20 | 20 | (EtOH) | 404.469 | 70.96 | 5.90 | 6.97 | | (4.72) | | (4.10) | (4.39) | | |
| | | Pyridine | 6 | 35 | | | | | | | | | | | | |
| 5d |  | EtOH | 33 | 62 | 170-171 | $C_{20}H_{21}FN_2O_4$ | 64.51 | 5.68 | 7.52 | 5.10 | 405 | | | 248 | 1720 | 1645 |
| | | | | | (DMF) | 372.399 | 64.15 | 5.50 | 7.19 | 5.00 | | | | | 1710 | |
| 5e |  | Toluene | 7 | 43 | 154-155 | $C_{20}H_{21}FN_2O_4$ | 64.51 | 5.68 | 7.52 | 5.10 | 408 | 318 | | 258 | 1725 | 1640 |
| | | | | | (EtOH) | 372.399 | 64.14 | 5.67 | 7.40 | 5.20 | (4.60) | (3.48) | | (4.04) | | |
| 5f |  | Toluene | 7 | 54 | 154-155 | $C_{20}H_{23}N_3O_4$ | 65.03 | 6.28 | 11.37 | | 418 | 316 | 287 | 257 | 1710 | 1645 |
| | | | | | (EtOAc) | 369.424 | 64.87 | 6.24 | 11.23 | | (4.33) | (3.72) | (3.76) | (4.00) | | |
| 5g |  | EtOH | 24 | 17 | 145-146 | $C_{21}H_{21}F_3N_2O_4$ | 59.71 | 5.01 | 6.63 | 13.49 | 402 | | | 262 | 1715 | 1650 |
| | | | | | (EtOH) | 422.407 | 60.10 | 4.83 | 6.60 | 13.68 | (4.64) | | | (4.01) | | |
| 5h |  | EtOH | 12 | 49 | 170-171 | $C_{22}H_{25}ClN_2O_6$ | 58.87 | 5.61 | 6.24 | 7.90 | 430 | | | 265 | 1710 | 1630 |
| | | Toluene | 6 | 47 | (DMF) | 448.898 | 59.08 | 5.65 | 6.42 | 7.99 | (4.55) | | | (4.19) | | |
| 5i |  | Toluene | 6 | 25 | 152-153 | $C_{23}H_{23}N_3O_4$ | 68.13 | 5.72 | 10.36 | | 412 | | 303 | | 1715 | 1645 |
| | | | | | (EtOH) | 405.457 | 68.50 | 5.88 | 10.32 | | (4.60) | | (3.80) | | | |

[a] At room temperature.

Table 4. $^1$H-NMR Data of Diethyl 2-[2-(Arylamino)vinyl]-6-methylpyridine-3,5-dicarboxylates

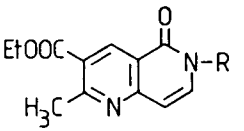



5 a-i

| Compound No. | R | Solvent | 2-CH=CH-NH- | 4-H | 2-CH=CH- | 2-CH=CH- | 3,5-COOCH$_2$CH$_3$ | 6-CH$_3$ | 3,5-COOCH$_2$CH$_3$ | -R |
|---|---|---|---|---|---|---|---|---|---|---|
| 5a |  | $CDCl_3$ | 12.25d [a] (J=12Hz) | 8.70s | 6.85-7.50 m | 6.50d (J=9Hz) | 4.40q (J=7Hz) | 2.92s | 1.42t (J=7Hz) | 6.85-7.50m |
| 5b |  | $CDCl_3$ | 12.65d [a] (J=12Hz) | 8.65s | 8.05-8.30 m | 6.55d (J=9Hz) | 4.36q 4.38q (J=7Hz) | 3.00s | 1.42t (J=7Hz) | 7.05-7.90m |
| 5c |  | $CDCl_3$ | 12.32d [a] (J=12Hz) | 8.65s | 7.05-7.85 m | 6.50d (J=9Hz) | 4.35q 4.36q (J=7Hz) | 2.95s | 1.42t (J=7Hz) | 7.05-7.85m |
| 5d |  | $CDCl_3$ | 12.37d [a] (J=12Hz) | 8.66s | 6.80-7.45 m | 6.57d (J=9Hz) | 4.38q (J=7Hz) | 2.90s | 1.40t (J=7Hz) | 6.80-7.45m |
| 5e |  | $CDCl_3$ | 12.19d (J=12Hz) | 8.65s | 7.17dd (J=9Hz) (J=12Hz) | 6.44d (J=9Hz) | 4.36q (J=7Hz) | 2.87s | 1.40t (J=7Hz) | 6.93s 7.00d (J=2Hz) |
| 5f |  | $CDCl_3$ | 11.90d (J=11.8Hz) | 8.77s | 7.35dd (J=8.7Hz) (J=11.8Hz) | 6.60d (J=8.7Hz) | 4.42q 4.44q (J=7Hz) | 2.94s | 1.42t (J=7Hz) | 6.70-7.25m 3.70s -NH$_2$ [a] |
| 5g |  | $CDCl_3$ | 12.30d [a] (J=12Hz) | 8.70s | 7.00-7.55 m | 6.55d (J=9Hz) | 4.40q (J=7Hz) | 2.92s | 1.42t (J=7Hz) | 7.00-7.55m |
| 5h |  | $CDCl_3$ | 12.02d [a] (J=12Hz) | 8.55s | 7.10dd (J=9Hz) (J=12Hz) | 6.41d (J=9Hz) | 4.32q (J=7Hz) | 2.90s | 1.40t (J=7Hz) | 3.83s, 3.90s } -OCH$_3$ 6.48s, 7.00s } 3'-H, 6'-H |
| 5i |  | $CDCl_3$ | 13.00d [a] (J=12Hz) | 8.75s | 8.00-8.45 m | 6.76d (J=9Hz) | 4.442 (J=7Hz) | 3.10s | 1.45t (J=7Hz) | 7.24d 3'-H (J=6Hz) 7.50-7.90m 8.00-8.45m |

[a] Broad signal

Table 5. Ethyl 6-Substituted 2-methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates and their UV and IR Data




6 a-z , aa-ff

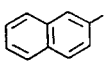
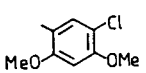
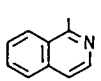
| Compound No. | R | Method | Solvent | Reaction Time (h) | Yield (%) | Mp °C Solvent | Molecular Formula M.W. | Analysis % Calcd./Found C | H | N | X | UV $\lambda_{max}$ nm/log ε | | | IR cm$^{-1}$ $\nu$C=O (ester | $\nu$C=O (ring) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6a |  | A | EtOH | 8 | 76 | 160-161 | $C_{18}H_{16}N_2O_3$ | 70.12 | 5.23 | 9.08 | | 312 | 257 | | 1725 | 1670 |
| | | B | EtOH [a] | 5 | 71 | (EtOAc) | 308.339 | 70.24 | 5.10 | 9.39 | | (4.16) | (4.05) | | | |
| | | | EtOH [b] | 40 | 91 | | | | | | | | | | | |
| 6b |  | A | DMF | 7 | 70 | 167-168 | $C_{22}H_{18}N_2O_3$ | 73.73 | 5.06 | 7.82 | | 316 | 250 | 220 | 1720 | 1670 |
| | | | | | | (EtOH) | 358.399 | 73.52 | 5.32 | 7.59 | | (4.12) | (4.03) | (4.97) | | |
| 6c |  | A | DMF | 10 | 67 | 141-142 | $C_{22}H_{18}N_2O_3$ | 73.73 | 5.06 | 7.82 | | 325 | 258 | 220 | 1715 | 1670 |
| | | B | DMF | 10 | 56 | (Acetone) | 358.399 | 73.57 | 4.96 | 7.81 | | (4.16) | (4.23) | (4.91) | | |
| 6d |  | A | DMF | 7 | 64 | 162-163 | $C_{18}H_{15}FN_2O_3$ | 66.25 | 4.63 | 8.58 | 5.82 | 318 | 255 | | 1730 | 1670 |
| | | | | | | (EtOH) | 326.329 | 66.52 | 4.74 | 8.25 | 5.64 | (4.07) | (4.03) | | | |
| 6e |  | A | EtOH | 8 | 55 | 152-153 | $C_{18}H_{15}FN_2O_3$ | 66.25 | 4.63 | 8.58 | 5.82 | 322 | 257 | | 1725 | 1675 |
| | | | | | | (EtOH) | 326.329 | 66.60 | 4.42 | 8.76 | 6.20 | (4.16) | (4.12) | | | |
| 6f |  | A | EtOH | 18 | 62 | 175-176 | $C_{18}H_{17}N_3O_3$ | 66.86 | 5.30 | 13.00 | | 316 | | | 1715 | 1665 |
| | | | | | | (EtOH) | 323.354 | 66.47 | 5.08 | 12.84 | | (4.14) | | | | |
| 6g |  | A | DMF | 6 | 66 | 130-131 | $C_{19}H_{15}F_3N_2O_3$ | 60.64 | 4.02 | 7.44 | 15.14 | 322 | 258 | | 1720 | 1680 |
| | | | | | | (EtOH) | 376.337 | 60.91 | 4.33 | 7.63 | 15.21 | | | | | |
| 6h |  | B | EtOH [b] | 0.5 | 75 | 230-231 | $C_{20}H_{19}ClN_2O_5$ | 59.63 | 4.75 | 6.95 | 8.80 | 318 | 298 | | 1725 | 1675 |
| | | | | | | (DMF) | 402.837 | 60.01 | 4.86 | 7.08 | 8.99 | (4.05) | (4.05) | | | |
| 6i |  | A | EtOH | 36 | 14 | 246-247 | $C_{21}H_{17}N_3O_3$ | 70.18 | 4.77 | 11.69 | | 322 | | | 1720 | 1670 |
| | | | DMF | 8 | 55 | (EtOH) | 359.384 | 70.49 | 4.78 | 11.72 | | (4.19) | | | | |
| | | B | EtOH [b] | 1.5 [c] | 95 | | | | | | | | | | | |

Table 5. (continued)[1]

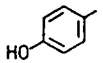
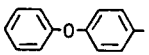
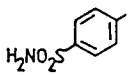
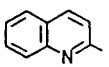
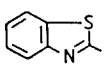
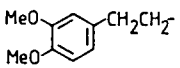
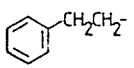
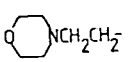
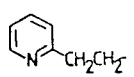
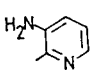
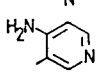
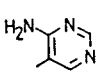
| Compound No. | R | Method | Solvent | Reaction Time (h) | Yield (%) | Mp °C Solvent | Molecular Formula M.W. | Analysis % Calcd./Found C | H | N | X | UV $\lambda_{max}$ nm/log ε | | | IR ν C=O (ester) | IR ν C=O (ring) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6j |  | A | EtOH | 6 | 53 | 228-229 | $C_{18}H_{16}N_2O_4$ | 66.66 | 4.97 | 8.64 | | 328 | 278 | | 1728 | 1645 |
| | | | | | | (EtOH) | 324.339 | 66.33 | 5.00 | 8.67 | | (4.12) | (4.07) | | | |
| 6k |  | A | DMF | 11 | 69 | 118-120 | $C_{24}H_{20}N_2O_4$ | 71.99 | 5.03 | 7.00 | | 325 | 258 | | 1715 | 1680 |
| | | | | | | (EtOH | 400.437 | 71.90 | 4.99 | 7.04 | | (4.12) | (4.09) | | | |
| 6l |  | A | EtOH | 65 | 31 | 274-275 | $C_{18}H_{17}N_3O_5S$ | 55.80 | 4.42 | 10.85 | 8.28 | 320 | 259 | | 1740 | 1660 |
| | | | DMF | 4 | 57 | (DMF) | 387.417 | 55.68 | 4.37 | 10.75 | 8.38 | (4.18) | (4.08) | | | |
| 6m |  | A | EtOH | 17 | 48 | 148-149 | $C_{17}H_{15}N_3O_3$ | 66.01 | 4.89 | 13.58 | | 320 | 258 | | 1725 | 1690 |
| | | | m-Xylene | 15 | 26 | (EtOH) | 309.326 | 66.35 | 4.93 | 13.43 | | (4.19) | (4.05) | | | |
| 6n |  | A | DMF | 8 | 58 | 230-231 | $C_{21}H_{17}N_3O_3$ | 70.18 | 4.77 | 11.69 | | 323 | 231 | | 1730 | 1680 |
| | | | | | | (DMF) | 359.387 | 70.50 | 4.71 | 11.70 | | (4.46) | (4.76) | | | |
| 6o |  | A | EtOH | 6 | 74 | 243-244 | $C_{14}H_{13}N_5O_3$ | 56.18 | 4.38 | 23.40 | | 390 | 314 | | 1715 | 1665 |
| | | | Toluene | 7 | 67 | (DMF) | 299.290 | 55.90 | 4.30 | 23.23 | | (2.63) | (4.15) | | | |
| 6p |  | A | EtOH | 1.5 | 50 | 249-250 | $C_{19}H_{15}N_3O_3S$ | 62.45 | 4.14 | 11.50 | 8.77 | | | | 1720 | 1680 |
| | | | | | | (DMF) | 365.413 | 62.38 | 4.08 | 11.17 | 8.63 | | | | | |
| 6q | $-NH_2$ | A | EtOH | 4.5 [c] | 94 | 191 | $C_{12}H_{13}N_3O_3$ | 58.29 | 5.30 | 16.99 | | 328 | 259 | | 1720 | 1645 |
| | | | | 1.5 | 92 | (DMF) | 247.255 | 58.01 | 5.06 | 16.96 | | | | | | |
| 6r | $CH_3NH-$ | A | EtOH | 8 [c] | 60 | 146-147 | $C_{13}H_{15}N_3O_3$ | 59.76 | 5.79 | 16.08 | | 325 | 258 | 210 | 1725 | 1670 |
| | | | | 1 | 76 | (EtOAc) | 261.282 | 59.75 | 5.98 | 16.19 | | (4.03) | (4.08) | (4.50) | | |
| 6s |  | A | EtOH | 10 | 74 | 194-195 | $C_{18}H_{17}N_3O_3$ | 66.86 | 5.30 | 13.00 | | 318 | 249 | | 1730 | 1660 |
| | | | | | | (EtOH) | 323.354 | 66.53 | 5.52 | 13.10 | | (4.13) | (4.06) | | | |
| 6t |  | A | EtOH | 6 | 90 | 152-153 | $C_{22}H_{24}N_2O_5$ | 66.65 | 6.10 | 7.07 | | 324 | 285 | 253 | 1720 | 1665 |
| | | | | | | (EtOH) | 396.446 | 66.69 | 6.02 | 7.03 | | (4.09) | (3.75) | (4.05) | | |
| 6u | $Me_2NCH_2CH_2-$ | A | EtOH | 6.5 | 66 | 120-121 | $C_{16}H_{21}N_3O_3$ | 63.35 | 6.98 | 13.85 | | 325 | | 252 | 1720 | 1665 |
| | | | | | | (Acetone) | 303.363 | 63.57 | 6.92 | 13.72 | | (4.11) | | (4.06) | | |
| 6v | $HOCH_2CH_2-$ | A | EtOH | 5 | 80 | 143-144 | $C_{14}H_{16}N_2O_4$ | 60.86 | 5.84 | 10.14 | | 322 | | 252 | 1725 | 1670 |
| | | | | | | (EtOAc) | 276.294 | 60.42 | 5.82 | 9.90 | | (4.06) | | (4.01) | | |

Table 5. (continued)[2]

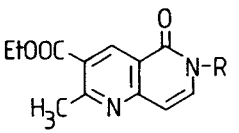
| Compound No. | R | Method | Solvent | Reaction Time (h) | Yield (%) | Mp °C Solvent | Molecular Formula M.W. | Analysis % Calcd./Found C | H | N | UV $\lambda_{max}$ nm/log ε | | IR ν C=O (ester) | IR ν C=O (ring) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 6w | D,L $HOCH_2\overset{*}{C}H(CH_2CH_3)$- | A | EtOH | 8 | 58 | 125-126 (Acetone) | $C_{16}H_{20}N_2O_4$ 304.348 | 63.14 63.09 | 6.62 6.61 | 9.20 9.38 | 325 (4.12) | 252 (4.06) | 1725 | 1660 |
| 6x | D $HOCH_2\overset{*}{C}H(CH_2CH_3)$- | A | EtOH | 8 | 45 | 110-112 (Acetone) | $C_{16}H_{20}N_2O_4$ 304.348 | 63.14 63.01 | 6.62 6.62 | 9.20 9.21 | 325 (4.10) | 252 (4.04) | 1725 | 1660 |
| 6y | $HOCH_2CH_2NH$- | A | EtOH | 1 | 82 | 155-156 (EtOAc) | $C_{14}H_{17}N_3O_4$ 291.309 | 57.72 57.92 | 5.88 6.01 | 14.42 14.67 | 325 (4.17) | 258 (4.22) | 1720 | 1680 |
| 6z | $Me_2NCH_2CH_2CH_2$- | A | EtOH | 12 | 57 | 74-75 (Hexane) | $C_{17}H_{23}N_3O_3$ 317.390 | 64.33 63.95 | 7.30 7.07 | 13.24 13.44 | 323 (4.04) | 252 (3.99) | 1730 | 1675 |
| 6aa |  | A | EtOH | 4 | 68 | 103-104 (EtOH) | $C_{20}H_{20}N_2O_3$ 336.393 | 71.41 71.42 | 5.99 6.03 | 8.33 8.54 | 322 (4.10) | 252 (4.07) | 1725 | 1680 |
| 6bb |  | A | EtOH | 6 | 87 | 122-123 (EtOH) | $C_{18}H_{23}N_3O_4$ 345.402 | 62.59 62.88 | 6.71 6.59 | 12.17 12.14 | 324 (4.10) | 252 (4.03) | 1720 | 1665 |
| 6cc |  | A | EtOH | 8 | 55 | 145-146 (EtOH) | $C_{19}H_{19}N_3O_3$ 337.381 | 67.64 67.55 | 5.68 5.54 | 12.45 12.45 | 322 (4.10) | 255 (4.15) | 1720 | 1660 |
| 6dd |  | A | EtOH | 25 | 60 | 227-228 (EtOH) | $C_{17}H_{16}N_4O_3$ 324.341 | 62.96 63.25 | 4.97 4.73 | 17.27 17.24 | 315 (4.25) | | 1730 | 1660 |
| 6ee |  | A | EtOH | 100 | 48 | 247-248 (EtOH) | $C_{17}H_{16}N_4O_3$ 324.341 | 62.96 62.85 | 4.97 4.89 | 17.27 17.08 | 318 (3.95) | 240 (4.14) | 1750 | 1670 |
| | | | DMF | 8 | 62 | | | | | | | | | |
| 6ff |  | A | EtOH | 60 | 62 | 238-239 (EtOH) | $C_{16}H_{15}N_5O_3$ 325.328 | 59.07 58.88 | 4.65 4.54 | 21.53 21.42 | 318 (4.05) | | 1740 | 1660 |
| | | | DMF | 8 | 70 | | | | | | | | | |

[a] Triethylamine was used as catalyst

[b] Sodium ethoxide was used as catalyst

[c] At room temperature

Table 6. $^1$H-NMR Data of Ethyl 6-Substituted 2-methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates




6a-z, aa-ff

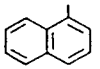
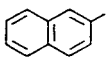
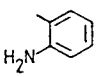
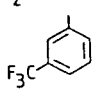
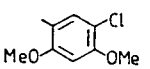
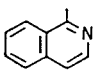
| Compound No. | R | Solvent | 4-H [a] | 7-H | 8-H [a] | 3-COOCH$_2$CH$_3$ | 2-CH$_3$ | 3-COOCH$_2$CH$_3$ | 6-R |
|---|---|---|---|---|---|---|---|---|---|
| 6a |  | $CDCl_3$ | 9.17d (J=1Hz) | 7.50d (J=7.5Hz) | 6.76dd (J=7.5Hz) (J=1Hz) | 4.41q (J=7Hz) | 2.98s | 1.40t (J=7Hz) | 7.47s |
| 6b |  | $CDCl_3$ | 9.17s | 7.25-7.70 m | 6.83dd (J=8Hz) (J=1Hz) | 4.40q (J=7Hz) | 3.00s | 1.40t (J=7Hz) | 7.25-7.70m 7.75-8.05m |
| 6c |  | $CDCl_3$ | 9.15s | 7.35-7.68 m | 6.79dd (J=8Hz) (J=1Hz) | 4.40q (J=7Hz) | 2.98s | 1.41t (J=7Hz) | 7.35-7.68m 7.72-8.05m |
| 6d |  | DMSO-$d_6$ | 8.88s | 7.85d (J=8Hz) | 6.80dd (J=8Hz) (J=1Hz) | 4.42q (J=7Hz) | 2.93s | 1.44t (J=7Hz) | 7.30-7.80m |
| 6e |  | $CDCl_3$ | 9.11s | 7.05-7.50 m | 6.74d (J=8Hz) | 4.40q (J=7Hz) | 2.96s | 1.41t (J=7Hz) | 7.05-7.50m |
| 6f |  | $CDCl_3$ | 9.12s | 7.35d (J=8Hz) | 6.75d (J=8Hz) | 4.40q (J=7Hz) | 2.95s | 1.40t (J=7Hz) | 3.78s -$NH_2$ [b] 6.55-7.45m |
| 6g |  | $CDCl_3$ | 9.17s | 7.45d (J=8Hz) | 6.80dd (J=8Hz) (J=1Hz) | 4.40q (J=7Hz) | 2.97s | 1.42t (J=7Hz) | 7.00-7.85m |
| 6h |  | DMSO-$d_6$ | 8.83s | 7.63d (J=8Hz) | 6.65dd (J=8Hz) (J=0.8Hz) | 4.34q (J=7Hz) | 2.84s | 1.35t (J=7Hz) | 3.79s } -$OCH_3$ 3.95s } 6.95s 6'-H 7.50s 3'-H |
| 6i |  | DMSO-$d_6$ | 8.95s | 7.65-8.30 m | 6.94dd (J=8Hz) (J=0.8Hz) | 4.45q (J=7Hz) | 3.00s | 1.46t (J=7Hz) | 8.60d (J=6Hz) 7.65-8.30m |

Table 6. (continued)[1]

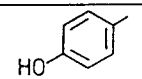
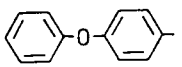
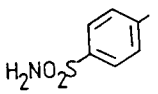
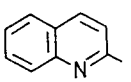
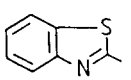
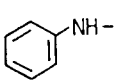
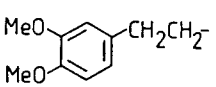
| Compound No. | R | Solvent | 4-H | 7-H | 8-H | 3-COOCH$_2$CH$_3$ | 2-CH$_3$ | 3-COOCH$_2$CH$_3$ | 6-R |
|---|---|---|---|---|---|---|---|---|---|
| 6j |  | $CDCl_3$ | 9.15s | 7.50d (J=8Hz) | 6.78d (J=8Hz) | 4.42q (J=7Hz) | 2.98s | 1.42t (J=7Hz) | 6.96d (J=9Hz)<br>7.24d (J=9Hz)<br>9.10s -OH [b] |
| 6k |  | $CDCl_3$ | 9.12s | 6.90-7.55 m | 6.75d (J=8Hz) | 4.40q (J=7Hz) | 2.98s | 1.42t (J=7Hz) | 6.90-7.55m |
| 6l |  | DMSO-$d_6$ | 8.92s | 7.95d (J=8Hz) | 6.82d (J=8Hz) | 4.40q (J=7Hz) | 2.89s | 1.38t (J=7Hz) | 7.55s -$NH_2$ [b]<br>7.77d (J=8Hz)<br>8.06d (J=8Hz) |
| 6m |  | $CDCl_3$ | 9.22s | 8.15d (J=8Hz) | 6.85dd (J=8Hz) (J=1Hz) | 4.44q (J=7Hz) | 2.99s | 1.44t (J=7Hz) | 7.25-7.50m 5'-H<br>7.75-8.30m 3',4'-H<br>8.50-8.70m 6'-H |
| 6n |  | $CDCl_3$ | 9.21s | 7.50-8.40 m | 6.89dd (J=7.9Hz) (J=0.8Hz) | 4.43q (J=7Hz) | 3.00s | 1.44t (J=7Hz) | 7.50-8.40m |
| 6o |  | DMSO-$d_6$ | 8.90s | 7.93d (J=8Hz) | 6.80dd (J=8Hz) (J=1Hz) | 4.42q (J=7Hz) | 2.92s | 1.43t (J=7Hz) | 8.67s 5'-H |
| 6p |  | $CDCl_3$ | 9.28s | 9.12d (J=8Hz) | 7.00dd (J=8Hz) (J=1Hz) | 4.44q (J=7Hz) | 3.00s | 1.45t (J=7Hz) | 7.35-7.70m<br>7.80-8.20m |
| 6q | $-NH_2$ | DMSO-$d_6$ | 8.97s | 7.97d (J=8Hz) | 6.73d (J=8Hz) | 4.47q (J=7Hz) | 2.92s | 1.47t (J=7Hz) | 6.16s [b] |
| 6r | $CH_3NH-$ | $CDCl_3$ | 9.14s | 7.60d (J=8Hz) | 6.72d (J=8Hz) | 4.42q (J=7Hz) | 2.95s | 1.42t (J=7Hz) | 2.85s -$NHCH_3$ [c]<br>6.00s -$NH$-$CH_3$ [b] |
| 6s |  | $CDCl_3$ | 9.10s | 7.62d (J=8Hz) | 6.71d (J=8Hz) | 4.36q (J=7Hz) | 2.95s | 1.38t (J=7Hz) | 6.60-7.40m |
| 6t |  | $CDCl_3$ | 9.20s | 7.08d (J=8Hz) | 6.59dd (J=8Hz) (J=1Hz) | 4.44q (J=7Hz) | 2.96s | 1.44t (J=7Hz) | 3.05t (J=7Hz) N-$CH_2CH_2$<br>3.80s } -$(OCH_3)_2$<br>3.87s }<br>4.22t (J=7Hz) N-$CH_2CH_2$<br>6.50-6.90m |

Table 6. (continued)$_2$

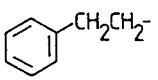
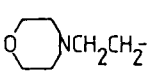
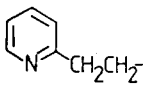
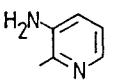
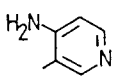
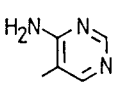
| Compound No. | R | Solvent | 4-H | 7-H | 8-H | 3-COOCH$_2$CH$_3$ | 2-CH$_3$ | 3-COOCH$_2$CH$_3$ | 6-R |
|---|---|---|---|---|---|---|---|---|---|
| 6u | $Me_2NCH_2CH_2$- | $CDCl_3$ | 9.15s | 7.45d (J=8Hz) | 6.67dd (J=8Hz) (J=1Hz) | 4.41q (J=7Hz) | 2.95s | 1.43t (J=7Hz) | 2.30s N-$CH_2CH_2$N ($CH_3$)$_2$<br>2.68t (J=6.5Hz) N-$CH_2CH_2$N<br>4.10t (J=6.5Hz) N-$CH_2CH_2$N |
| 6v | $HOCH_2CH_2$- | $CDCl_3$ | 9.12s | 7.48d (J=8Hz) | 6.72d (J=8Hz) | 4.44q (J=7Hz) | 2.93s | 1.44t (J=7Hz) | 2.65-3.10m N-$CH_2CH_2OH$<br>3.90-4.30m N-$CH_2CH_2OH$ |
| 6w | $HOCH_2CH(CH_3CH_2)$- D,L | $CDCl_3$ | 9.08s | 7.48d (J=7.9Hz) | 6.68d (J=7.9Hz) | 4.40q (J=7Hz) | 2.93s | 1.42t (J=7Hz) | 0.93t (J=7Hz) N-$CHCH_2OH$<br>1.88qi(J=7Hz) $CH_2CH_3$<br>3.10 [b] N-$CHCH_2OH$<br>3.92d (J=5Hz) N-$CHCH_2OH$<br>4.88m N-$CHCH_2OH$ |
| 6x | $HOCH_2C^*H(CH_3CH_2)$- D | $CDCl_3$ | 9.08s | 7.48d (J=7.9Hz) | 6.68d (J=7.9Hz) | 4.40q (J=7Hz) | 2.93s | 1.42t (J=7Hz) | 0.93t (J=7Hz) N-$CHCH_2OH$<br>1.88qi(J=7Hz) $CH_2CH_3$<br>3.10t (J=5Hz) N-$CHCH_2OH$<br>3.92dd(J=7Hz) (J=5Hz) N-$CHCH_2OH$<br>4.88m N-$CHCH_2OH$ |
| 6y | $HOCH_2CH_2NH$- | $CDCl_3$ | 9.10d (J=0.9Hz) | 7.60d (J=8Hz) | 6.75dd (J=8Hz) (J=0.9Hz) | 4.41q (J=7Hz) | 2.95s | 1.42t (J=7Hz) | 3.05-3.40m N-$NHCH_2CH_2OH$<br>3.45-3.70m N-$NHCH_2CH_2OH$<br>6.25t (J=6Hz) N-$NHCH_2CH_2OH$ |
| 6z | $Me_2NCH_2CH_2CH_2$- | $CDCl_3$ | 9.15d (J=1Hz) | 7.45d (J=8Hz) | 6.65dd (J=8Hz) (J=1Hz) | 4.40q (J=7Hz) | 2.94s | 1.41t (J=7Hz) | 1.70-2.45m N-$CH_2CH_2CH_2N$ ($CH_3$)$_2$<br>2.22s N-$CH_2CH_2CH_2N$ ($CH_3$)$_2$<br>4.07t(J=6.5Hz) N-$CH_2CH_2CH_2N$ ($CH_3$)$_2$ |
| 6aa |  | $CDCl_3$ | 9.20s | 7.04d (J=7.5Hz) | 6.54d (J=7.5Hz) | 4.41q (J=7Hz) | 2.94s | 1.42t (J=7Hz) | 3.08t (J=7Hz) N-$CH_2CH_2$<br>4.21t (J=7Hz) N-$CH_2CH_2$<br>6.90-7.40m N-$CH_2CH_2C_6H_5$ |
| 6bb |  | $CDCl_3$ | 9.19s | 7.45d (J=8Hz) | 6.70d (J=8Hz) | 4.42q (J=7Hz) | 2.95s | 1.42t (J=7Hz) | 2.52t (J=5Hz) 2',6'-$CH_2$<br>2.72t(J=6.5Hz) N-$CH_2CH_2$<br>3.70t (J=5Hz) 3',5'-$CH_2$<br>4.13t(J=6.5Hz) N-$CH_2CH_2$ |

Table 6. (continued)[3]

| Compound No. | R | Solvent | 4-H | 7-H | 8-H | 3-COOCH$_2$CH$_3$ | 2-CH$_3$ | 3-COOCH$_2$CH$_3$ | 6-R |
|---|---|---|---|---|---|---|---|---|---|
| 6cc |  | $CDCl_3$ | 9.22s | 7.25d (J=7.5Hz) | 6.55d (J=7.5Hz) | 4.43q (J=7Hz) | 2.95s | 1.44t (J=7Hz) | 3.30t (J=7Hz) N-CH$_2$CH$_2$<br>4.49t (J=7Hz) N-CH$_2$CH$_2$<br>7.00-7.37m 3'-H,5'-H<br>7.60ddd (J=8Hz) (J=8Hz) (J=2Hz) 4'-H<br>8.62dd (J=5Hz) (J=2Hz) 6'-H |
| 6dd |  | $CDCl_3$ [d] | 9.14d (J=0.7Hz) | 7.66d (J=7.8Hz) | 6.82dd (J=7.8Hz) (J=0.7Hz) | 4.38q (J=7Hz) | 2.93s | 1.39t (J=7Hz) | 7.26dd (J=9.5Hz) (J=1.3Hz) 4'-H<br>7.23dd (J=9.5Hz) (J=4.8Hz) 5'-H<br>8.00dd (J=4.8Hz) (J=1.3Hz) 6'-H<br>4.12 [b] 3'-NH$_2$ |
| 6ee |  | $CDCl_3$ [d] | 9.03d (J=0.7Hz) | 7.33d (J=7.6Hz) | 6.78dd (J=7.6Hz) (J=0.7Hz) | 4.37q (J=7Hz) | 2.93s | 1.39t (J=7Hz) | 6.68d (J=5.8Hz) 5'-H<br>8.21d (J=5.8Hz) 6'-H<br>8.17s 2'-H<br>4.59 [b] 4'-NH$_2$ |
| 6ff |  | $CDCl_3$ [d] | 9.12d (J=0.7Hz) | 7.30d (J=7.7Hz) | 6.86dd (J=7.7Hz) (J=0.7Hz) | 4.40q (J=7Hz) | 2.97s | 1.42t | 8.64s 2'-H<br>8.27s 6'-H<br>5.23 [b] 4'-NH$_2$ |

qi= quintet

[a] The coupling of $^5J_{4,8}$= 0.7-1.0 Hz can not be determined in some cases

[b] Broad signal

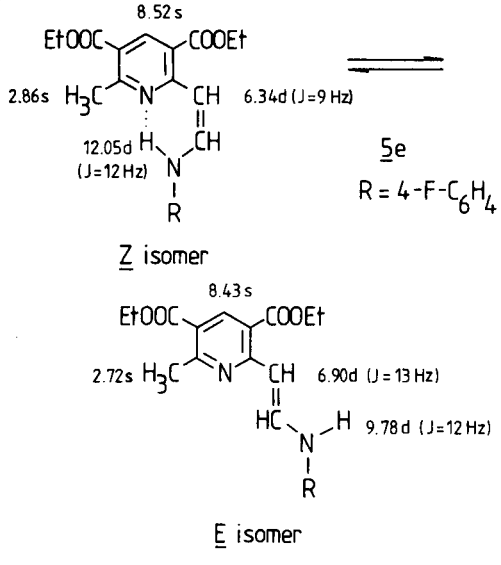
[c] After $D_2O$ addition

[d] The spectrum was recorded at 400 MHz.

tives **6a-z,aa-ff** (Scheme 2). When the diethyl 2,6-dimethylpyridine-3,5-dicarboxylates **1a-h** [15] were treated with 1,3,5-triazine (**2**) in the presence of ethanolic sodium ethoxide at reflux temperature, 4-substituted 1,6-naphthyridin-5(6*H*)-ones **3a-h** ($R^1$ = phenyl, substituted phenyl, 3-pyridyl) were isolated in 21-97% yields (see Table 1). The intermediate aminomethylene compounds could not be isolated. The structures of the new 1,6-naphthyridines **3b-h** were characterized by uv ir, and $^1H$ nmr spectroscopy (see Tables 1 and 2). Recently, 1,3,5-triazine was used in DMF in the presence of sodium hydride for the aminomethinylation of 1,4-dihydropyridines [16].

As shown in Scheme 2, the active methyl group of compound **1a** was caused to react with *N,N*-dimethylformamide diethyl acetal to yield diethyl 2-[2-(dimethylamino)-vinyl]-6-methylpyridine-3,5-dicarboxylate (**4**) [1], which was cyclized to the 6-substituted derivatives of the 1,6-naphthyridin-5(6*H*)-one, **6a-z,aa-ff**, by treatment with primary aliphatic, aromatic or heterocyclic amines or hydrazines, either in ethanol or in DMF (see Table 5, Method *A*). When the reaction was carried out in refluxing toluene, or in the case of less reactive or sterically hindered aromatic amines, only diethyl 2-[2-(arylamino)vinyl]-6-methylpyridine-3,5-dicarboxylates **5a-i** could be isolated (see Table 3). Compounds **5a-i** could readily be cyclized to 1,6-naphthyridine ring compounds **6a-i** at higher temperature (in refluxing DMF) or in the presence of a basic catalyst (*e.g.* triethylamine or sodium ethoxide) (Method *B*). In the presence of sodium ethoxide in ethanol, the ring-closure took place at room temperature in a few minutes, even under heterogeneous conditions.

The *Z*/*E* isomer ratio for compounds **5a-i** was examined in chloroform, DMSO and ethanol by $^1H$ nmr spectroscopy. In chloroform, only the *Z* isomer (chelated *via* an intramolecular hydrogen-bond) could be detected (see Table 4).



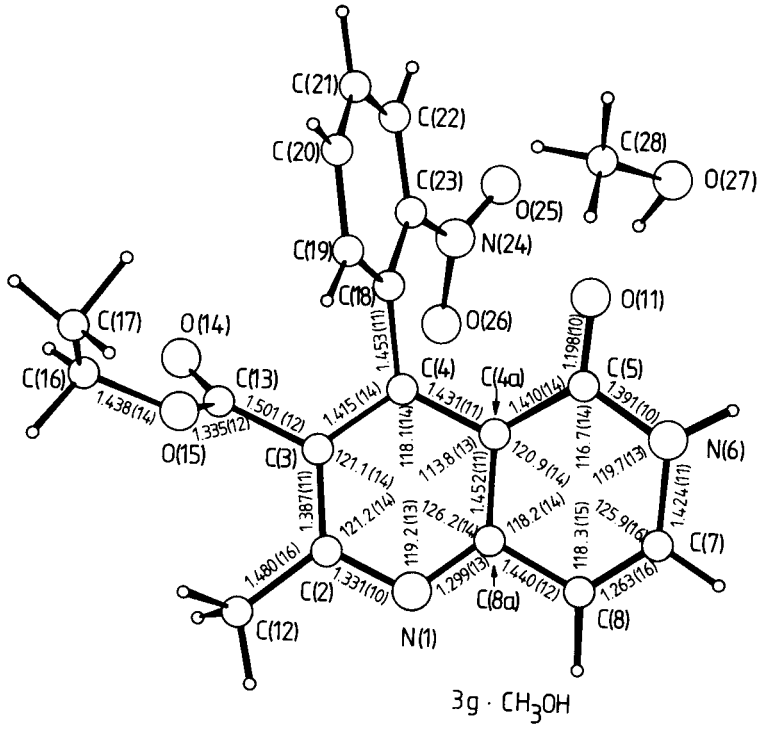




Figure 1. View of compound **3g**. $CH_3OH$ with atomic numbering, char acteristic bond lengths (Å) and angles (°). Estimated standard deviations are in the range 0.01-0.02 Å, 1-2°, respectively.

The signals of the NH, C(4)-H or C(6)-$CH_3$ groups are suitable for determination of the *Z*/*E* isomer ratio (see Table 7).

Table 7. Z/E Isomer Ratio for Compounds 5

| Compound No. | DMSO-$d_6$ Z | DMSO-$d_6$ E | EtOH-$d_6$ Z | EtOH-$d_6$ E |
|---|---|---|---|---|
| 5a | 50 | 50 | insoluble | |
| 5b | 75 | 25 | 100 | 0 |
| 5c | 45 | 55 | 100 | 0 |
| 5d | 100 | 0 | 100 | 0 |
| 5e | 50 | 50 | 75 | 25 |
| 5f | 70 | 30 | 90 | 10 |
| 5g | 48 | 52 | 77 | 23 |
| 5h | 100 | 0 | 100 | 0 |
| 5i | 44 | 56 | 100 | 0 |

The structure of 1,6-naphthyridin-5(6*H*)-one (**3g**) was characterized by X-ray analysis. Selected bond lengths and angles for compound **3g**. $CH_3OH$ are given in Figure 1. The relative positions of the substituents are described by the torsion angles: O(15)-C(13)-C(3)-C(4) −107°, C(3)-C(4)-C(18)-C(23) −117°, and O(26)-N(24)-C(23)-C(18) 26°. Compound **3g** and the methanol molecule are connected by the hydrogen-bonds N(6)-H(6)...O(27) (1-x,-y,1-z) and O(27)-H(27)...O(11) (x,y,z). The N(6)...O(27) and O(27)-...O(11) distances are 2.74(1) and 2.73(1) Å, respectively. Potential energy calculations were performed by using the EENYC program of Motherwell [17], where the constants were those given by Giglio [18]. The analysis of the rotation of the 2-nitrophenyl and ethoxycarbonyl groups is given in Figure 2. The ethoxycarbonyl group can rotate quite freely, while a higher barrier hinders the rotation around the C(4)-C(18) bond.

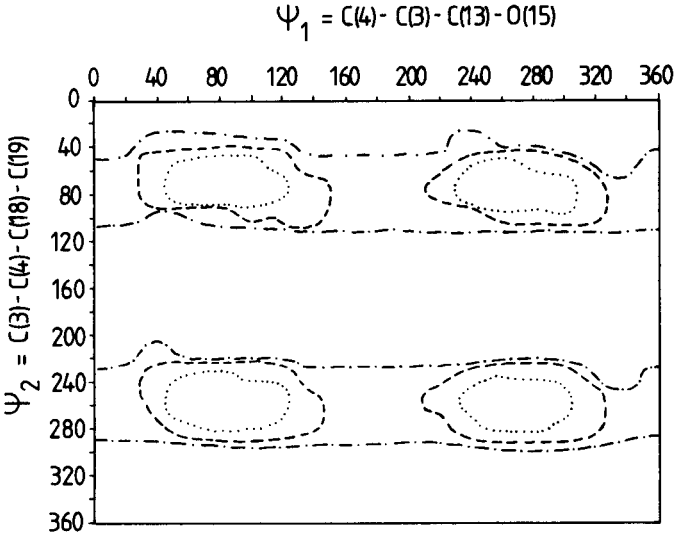



Figure 2. Potential energy map, horizontal axis $\psi_1$: C(4)-C(3)-C(13)-O(15), vertical axis $\psi_2$: C(3)-C(4)-C(18)-C(19). Boudaries for · · · U > 0 kcal mol$^{-1}$ (0 kJ mol$^{-1}$), - - - U > 10 kcal mol$^{-1}$ (42 kJ mol$^{-1}$), - · - · - · - U > 50 kcal mol$^{-1}$ (210 kJ mol$^{-1}$).

Table 8.

Fractional coordinates and averaged temperature factor ($B_{eq}$) with their estimated standard deviations in parentheses for compound 3g.$CH_3OH$.

| | X/A | Y/B | Z/C | $B_{eq}$ |
|---|---|---|---|---|
| N1 | -0.1694 ( 8 ) | 0.8783 ( 6 ) | 0.4231 ( 5 ) | 4.38(34) |
| C2 | -0.2484 (11 ) | 0.9120 ( 7 ) | 0.3393 ( 6 ) | 4.37(43) |
| C3 | -0.1855 (10 ) | 0.9521 ( 7 ) | 0.2715 ( 6 ) | 3.92(40) |
| C4 | -0.0350 (11 ) | 0.9592 ( 7 ) | 0.2894 ( 6 ) | 4.18(40) |
| C4a | 0.0508 (11 ) | 0.9275 ( 6 ) | 0.3814 ( 6 ) | 3.84(39) |
| C5 | 0.2009 (10 ) | 0.9350 ( 8 ) | 0.4130 ( 6 ) | 4.41(43) |
| N6 | 0.2657 ( 8 ) | 0.8978 ( 6 ) | 0.5040 ( 5 ) | 4.79(35) |
| C7 | 0.1797 (13 ) | 0.8585 ( 7 ) | 0.5617 ( 7 ) | 5.39(45) |
| C8 | 0.0451 (11 ) | 0.8514 ( 7 ) | 0.5373 ( 7 ) | 4.50(46) |
| C8a | -0.0315 (11 ) | 0.8892 ( 7 ) | 0.4448 ( 6 ) | 3.88(39) |
| O11 | 0.2732 ( 8 ) | 0.9688 ( 5 ) | 0.3648 ( 5 ) | 6.17(30) |
| C12 | -0.4060 (13 ) | 0.9046 ( 9 ) | 0.3181 ( 9 ) | 7.50(58) |
| C13 | -0.2768 (11 ) | 0.9867 ( 7 ) | 0.1760 ( 7 ) | 5.17(45) |
| O14 | -0.2887 ( 8 ) | 0.9504 ( 6 ) | 0.0973 ( 4 ) | 7.49(36) |
| O15 | -0.3418 ( 8 ) | 1.0648 ( 5 ) | 0.1895 ( 5 ) | 7.14(32) |
| C16 | -0.4376 (15 ) | 1.1064 (11 ) | 0.1059 ( 9 ) | 12.10(70) |
| C17 | -0.4214 (25 ) | 1.1930 (14 ) | 0.1007 (14 ) | 25.16(99) |
| C18 | 0.0239 (10 ) | 1.0103 ( 7 ) | 0.2204 ( 6 ) | 3.48(38) |
| C19 | -0.0088 (11 ) | 1.1011 ( 7 ) | 0.2061 ( 7 ) | 4.04(42) |
| C20 | 0.0473 (13 ) | 1.1517 ( 7 ) | 0.1370 ( 8 ) | 6.54(49) |
| C21 | 0.1252 (11 ) | 1.1117 ( 8 ) | 0.0819 ( 7 ) | 5.47(51) |
| C22 | 0.1574 (11 ) | 1.0222 ( 8 ) | 0.0959 ( 7 ) | 5.38(48) |
| C23 | 0.1106 (10 ) | 0.9724 ( 7 ) | 0.1624 ( 6 ) | 4.04(40) |
| N24 | 0.1546 ( 9 ) | 0.8766 ( 6 ) | 0.1737 ( 5 ) | 5.47(37) |
| O25 | 0.2569 ( 8 ) | 0.8479 ( 5 ) | 0.1509 ( 5 ) | 7.32(37) |
| O26 | 0.0760 ( 8 ) | 0.8214 ( 5 ) | 0.2051 ( 5 ) | 6.06(31) |
| O27 | 0.4504 ( 9 ) | 1.1178 ( 6 ) | 0.4018 ( 6 ) | 8.61(38) |
| C28 | 0.3723 (15 ) | 1.1923 (10 ) | 0.3656 (10 ) | 11.39(70) |
| H6 | 0.372 | 0.901 | 0.530 | 5.33 |
| H7 | 0.227 | 0.836 | 0.629 | 5.65 |
| H8 | -0.014 | 0.815 | 0.582 | 5.17 |
| H12A | -0.457 | 0.853 | 0.271 | 6.95 |
| H12B | -0.465 | 0.963 | 0.290 | 6.95 |
| H12C | -0.446 | 0.890 | 0.381 | 6.95 |
| H16A | -0.547 | 1.112 | 0.119 | 10.82 |
| H16B | -0.458 | 1.071 | 0.044 | 10.82 |
| H17A | -0.400 | 1.228 | 0.166 | 17.00 |
| H17B | -0.463 | 1.227 | 0.038 | 16.99 |
| H17C | -0.300 | 1.190 | 0.085 | 16.99 |
| H19 | -0.075 | 1.132 | 0.245 | 5.48 |
| H20 | 0.032 | 1.223 | 0.132 | 7.00 |
| H21 | 0.161 | 1.149 | 0.029 | 7.09 |
| H22 | 0.220 | 0.993 | 0.056 | 5.81 |
| H27 | 0.380 | 1.070 | 0.390 | 8.93 |
| H28A | 0.420 | 1.260 | 0.350 | 9.74 |
| H28B | 0.313 | 1.212 | 0.412 | 9.74 |
| H28C | 0.305 | 1.178 | 0.300 | 9.74 |

## EXPERIMENTAL

All melting points are uncorrected. The UV spectra were taken in ethanol with a Unicam SP 800 spectrophotometer, the ir spectra were recorded on a Zeiss UR 20 spectrophotometer in potassium bromide disks. The nmr spectra were recorded with a Brucker WP-80 DS spectrometer. Chemical shifts were determin-

ed on the δ scale with tetramethylsilane (δ = 0) as internal standard.

Ethyl 4-Substituted 2-Methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates (**3b-h**) (Scheme 1).

General Procedure.

To ethanolic sodium ethoxide [prepared from sodium (2.3 g, 0.1 g-atom) and ethanol (200 ml)] were added the pyridinedicarboxylates **1b-h** [15] (0.1 mole) and 1,3,5-triazine [19,20] (8.11 g, 0.1 mole). The mixture was stirred and heated under reflux for 2-6 hours. After evaporation of the ethanol at atmospheric pressure, water (200-250 ml) was added, and the *p*H was adjusted to 7 with 10% hydrochloric acid. The 1,6-naphthyridines **3b,d,e** were isolated by suction, and washed with water. For the isolation of compounds **3c,f,g,h** the neutral aqueous mixture was extracted with chloroform (3 x 150 ml). Compound **3g** was purified by column chromatography on silica gel using chloroform:methanol (10:1) as eluant.

For the analytical, physical and spectroscopical data of the obtained esters **3a-h** see Tables 1 and 2.

Diethyl 2-[2-(Arylamino)vinyl]-6-methylpyridine-3,5-dicarboxylates (**5a-i**) (Scheme 2).

General Procedure.

A mixture of diethyl 2-[2-(*N,N*-dimethylamino)vinyl]-6-methylpyridine-3,5-dicarboxylate (**4**) [1] (3.06 g, 0.01 mole). aromatic or heterocyclic amines (0.01-0.015 mole) and solvent (ethanol, toluene or pyridine) (20-50 ml) was stirred and heated under reflux for 4-33 hours. The arylaminovinyl compounds (**5a-i**) were filtered off from the cold reaction mixture.

For the reaction time, solvents, analytical, physical and spectroscopical data see Tables 3 and 4.

Ethyl 6-Substituted 2-methyl-5-oxo-5,6-dihydro-1,6-naphthyridine-3-carboxylates **6a-z,aa-ff**.

Method *A*.

A mixture of 2-[2-(*N,N*-dimethylamino)vinyl]-6-methylpyridine-3,5-dicarboxylate (**4**) (3.06 g, 0.01 mole), amines or hydrazines (0.01-0.015 mole) and solvent (ethanol, DMF) (15-50 ml) was stirred and refluxed for 1-65 hours. Compounds thus obtained, **6a-z,-aa-ff**, were precipitated at cooling or were isolated after solvent evaporation.

For the reaction time, solvents used, analytical, physical and spectroscopical data see Table 5 and 6.

Method *B*.

To ethanolic sodium ethoxide [prepared from sodium (2.3 g, 0.1 g-atom) and ethanol (40 ml)] 2-[2-(arylamino)vinyl]pyridine (**5**) (0.01 mole) was added. The mixture was stirred at room temperature for 0.5-10 hours, was diluted with water (40 ml) and the *p*H was adjusted to 7 with 10% hydrochloric acid. The products **6a,c,h,i** were filtered off, washed with water (2 x 10 ml).

For the reaction conditions, analytical, physical and spectroscopical data see Tables 5 and 6.

Crystallography.

The crystal data of **3g** is as follows: monoclinic, a = 9.662(1), b = 14.546(5), c = 14.147(8) Å, β = 104.66 (3)°, determined from the angular setting of 25 reflections, V = 1923.5 Å$^3$, $D_x$ = 1.379 g, cm$^{-3}$, Z = 4, μ(Mo$K\bar{\alpha}$ = 0.7107 Å) 1.12 cm$^{-1}$, space group $P2_1/c$ from systematic abscences; 1713 independent reflections were collected on an ENRAF-NONIUS CAD-4 four-circle diffractometer using monochromated Mo-$K\bar{\alpha}$ radiation. The intensity data were corrected for crystal decay using the intensity data of three standard reflections, the minimal decay correction factor was 0.977, while maximal 1.418. After conventional data reduction, 995 reflections with $I > 2\theta(I)$ were taken observed. The structure was solved by the routine application of direct methods and refined by the ENRAF-NONIUS SDP program package. After two cycles of anisotropic refinement the hydrogen atom positions were determined from difference Fourier map, but their positions were not refined. The final R-values for the 995 observed reflections are R = 0.081, $R_w$ = 0.083 (fudge factor, p = 0.01). The final coordinates are given in Table 8.

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