Tetrahedron Vol. 49, No. 36, pp. 8147-8158, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00

THE CHEMISTRY OF 5-OXODIHYDROISOXAZOLES VII[1]
CONVERSION OF HETEROCYCLYLISOXAZOL-5(2H)-ONES TO IMIDAZOLES BY FLASH VACUUM PYROLYSIS

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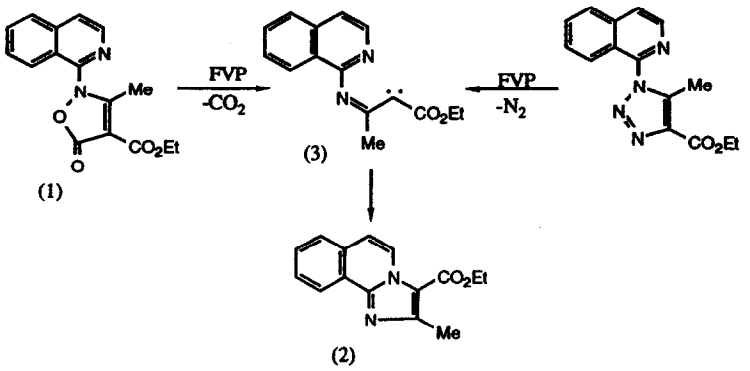
(*Received in USA* 30 *March* 1993; *accepted* 10 *May* 1993)

Keywords: Isoxazolones, flash vacuum pyrolysis, imino carbenes, annelated imidazoles

Abstract - A number of 5-oxo-2,5-dihydroisoxazoles, substituted with nitrogen heterocycles at N-2, have been subjected to flash vacuum pyrolysis. Annelated imidazoles are obtained in excellent yields, and are presumed to arise by intramolecular cyclisation of an imino carbene intermediate. The heterocycles annelated in this manner include isoquinoline, quinoline, benzothiazole, quinazoline, phenanthridine, pyrimidine and pyridine.

INTRODUCTION

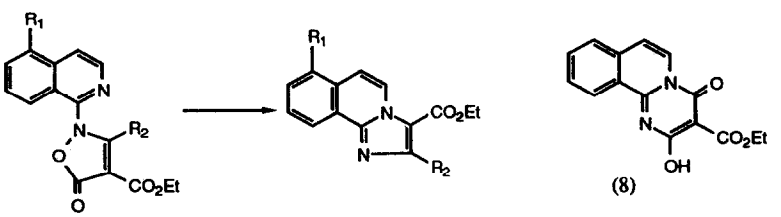
We have recently reported the flash vacuum pyrolysis (fvp) of the isoquinolin-1-ylisoxazolone (**1**)[2], in which the major product was the imidazo[2,1-a]isoquinoline (**2**). It was suggested that this reaction proceeded essentially via the intermediate imino carbene (**3**), with a minor pathway involving diradicals. There is therefore a clear similarity between the decomposition of triazoles and isoxazolones (Scheme 1), although the triazoles do not generally undergo clean cyclization on pyrolysis.[3] Wentrup and co-workers[4-6] have previously studied fvp of some isoxazolones, but the structures of the products predicated different reaction pathways to those reported in the present work. In this communication we extend our previous observation[2], and report a new general synthesis of annelated imidazoles.



Scheme 1

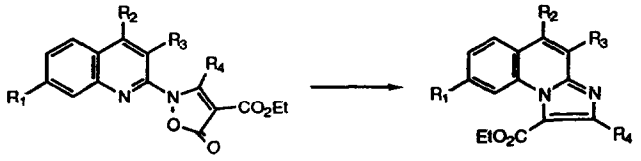
DISCUSSION

The study of the fvp of the simple isoxazolones (**4**) and (**5**)[7] helped define an important parameter. At 530°/0.01 mm, these compounds rearranged almost quantitatively to the respective imidazoles (**6**) and (**7**), with only traces of other compounds, provided that the sublimation temperature was maintained about 25° below the melting point. If the isoxazolones were allowed to melt during the fvp, or if the pyrolysis was carried out in the condensed phase, a number of products was obtained, in which a hydroxypyrimidine was a major component (e.g. (**8**) from (**4**)): the latter could be isolated in 72% yield when (**4**) was heated for 30 minutes at 160° under nitrogen. These compounds are the product of base-catalysed rearrangement.[8] The presence of substituents at C-3 of the isoxazolone, as in (**1**), did not prevent the formation of side products during pyrolysis in the condensed phase, our earlier work[2] showing that radical pathways, leading to hydrogen abstraction, occurred to the extent of 13%.



	R_1	R_2	
(1)	H	Me	(2)
(4)	H	H	(6)
(35)	NO_2	Me	(36)

In view of our belief that the formation of the imidazoles involved intramolecular capture of a carbene by the nitrogen of the heterocycle, a number of substituted quinolines and isoquinolines were synthesised to determine whether the carbene could be intercepted by alkyl or aryl groups, and to what extent the yield of imidazole was affected by the presence of electron-donating or -withdrawing groups in the quinoline or isoquinoline ring.

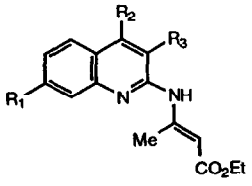


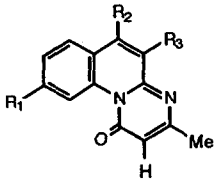
	R_1	R_2	R_3	R_4	
(5)	H	H	H	H	(7)
(9)	H	H	H	Me	(10)
(13)	H	Me	H	H	(16)
(14)	H	H	Me	H	(17)
(15)	MeO	H	Me	H	(18)
(19)	H	H	Me	Me	(22)
(20)	H	Me	H	Me	(23)
(21)	MeO	H	Ph	Me	(24)
(31)	MeO	H	Me	Me	(33)
(32)	Cl	H	Me	Me	(34)

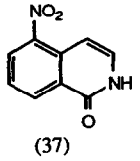
Fvp of (9) at 560°/0.01 mm gave the expected imidazole (10) in 92% yield, with the reduction products (11) 1%, and (12) 5%, which we have previously rationalised as arising from radical pathways.[2] The amino butenoates were compared with authentic samples prepared by hydrogenolysis of the corresponding isoxazolone, and these compounds were, in turn, smoothly converted into the pyrimidines by fvp. The stereochemistry of the butenoates was suggested to be (*E*) by the lack of hydrogen bonding between the NH and ester carbonyl group, and the long range coupling between the methyl group and the vinyl hydrogen.

Fvp of the quinoline derivatives (13)-(15) at 530°/0.01 mm gave the respective imidazoles (16)-(18) almost exclusively, and no by-products could be isolated. The presence of a methyl group at C-3 of the isoxazolone, as in (19)-(21), led to the formation of the expected imidazoles (22)-(24)

(ca. 95%), together with the butenoates (25)-(27) (ca. 1%) and the corresponding pyrimidines (28)-(30) (ca. 5%), except in the cases of (31) and (32) which again gave only the respective imidazoles.



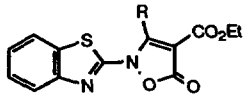




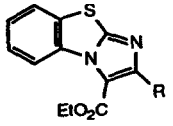
(37)

	R_1	R_2	R_3	
(11)	H	H	H	(12)
(25)	H	H	Me	(28)
(26)	H	Me	H	(29)
(27)	MeO	H	Ph	(30)

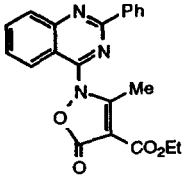
It is interesting to note that the presumed carbene intermediate did not insert into either a methyl or a phenyl group placed at C-3 of the quinoline. The above reaction has been extended to compounds with a number of other heterocyclic substituents placed on the isoxazolone nitrogen. The 5-nitroisoquinolinyl isoxazolone (35) gave the expected imidazole (36) in 85% yield, with 15% of 5-nitroisocarbostyryl (37), the origin of which is not clear at this stage. The benzothiazole derivatives (38) and (39) gave the expected imidazoles (40) and (41) in 97% and 94% yields respectively. Similarly, the quinazolinyl, phenanthridinyl and pyrimidinyl derivatives (42), (43) and (44) gave the corresponding imidazoles (45)-(47) exclusively. The only unexpected observation came with the pyrolysis of the nitropyridinyl analogue (48), which gave 87% of the expected imidazole (49) and 11% of its isomer (50). The structures of (49) and (50) were determined by comparison of their ^{1}H and ^{13}C n.m.r. spectra, and with the chemical shifts expected from the literature[9]. In particular H-5 of (49) resonated at 10.24 ppm compared to 9.97 ppm in (50). The later compound had H-3 at 5.84 ppm attached to the most upfield carbon[9] at 85.92 ppm. This represents the first example in our work where rearrangement of the first formed imino carbene has occurred, presumably facilitated by the relatively low nucleophilic character of the pyridine nitrogen (Scheme 2).



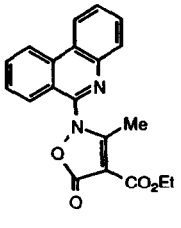
(38) R = H
(39) R = Me



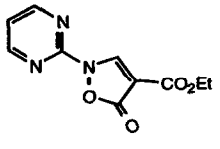
(40) R = H
(41) R = Me



(42)



(43)



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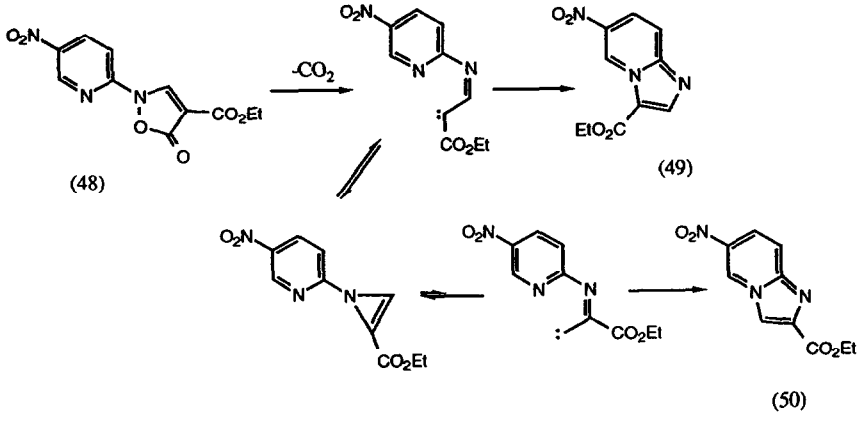

(48) (49) (50)

Scheme 2

In conclusion, flash vacuum pyrolysis of 2-heterocyclyl isoxazolones leads predominantly to imino carbene intermediates which almost exclusively undergo direct cyclisation to produce annelated imidazoles in excellent yields. The carbene tends not to insert into C-H or C=C bonds.

EXPERIMENTAL

Pyrolysis conditions have been described previously[2]: sublimation temperatures were ca. 25° below the melting points respectively. General experimental and instrumental conditions were as before.[2]

The pyrolysis condensate was chromatographed on alumina in light petroleum/dichloromethane in each case to yield the following pure products.

Ethyl imidazo[2,1-a]isoquinoline-3-carboxylate (6), pale yellow solid, 95% yield, m.p. 115-117° (Found: C, 70.0; H, 5.1; N, 12.0; $M^{+\cdot}$ 240.0905. $C_{14}H_{12}N_2O_2$ requires C, 70.0; H, 5.0; N, 11.7%; $M^{+\cdot}$ 240.0899). ν_{max} 1684, 1522, 1489, 1361, 1333, 1205 cm^{-1}; δ_H 1.46 (3H, t, J 7 Hz), 4.44, (2H, q, J 7 Hz), 7.27 (1H, d, J 8 Hz, H-6), 7.65-7.72 (2H, m), 7.77-7.81 (1H, m, H-7), 8.28 (1H, s, H-2), 8.68-8.72 (1H, m, H-10), 9.07 (1H, d, J 8 Hz, H-5); δ_C 14.48 (CH_3), 60.66 (CH_2), 114.58, 117.79, 123.13, 123.72, 124.10, 126.88, 128.49, 129.55, 130.25, 139.33, 146.28, 160.74; λ_{max} (EtOH) 216 ($1.86x10^4$), 250 ($3.36x10^4$), 264 ($3.36x10^4$), 280 ($1.58x10^4$), 294 ($1.18x10^4$), 308 ($4.27x10^3$), 320 ($5.60x10^3$), 336 nm ($5.40x10^3$).

Ethyl imidazo[1,2-a]quinoline-1-carboxylate (7), pale yellow solid, 96% yield, m.p. 100-101° (from ethyl acetate/light petroleum) (Found: C, 69.8; H, 5.1; N, 11.7; $M^{+\cdot}$ 240.0903. $C_{14}H_{12}N_2O_2$ requires C, 70.0; H, 5.0; N, 11.7%; $M^{+\cdot}$ 240.0899). ν_{max} 1684, 1615, 1525, 1488, 1361, 1324, 1268, 1221 cm^{-1}; δ_H 1.38 (3H, t, J 7 Hz), 4.36 (2H, q, J 7 Hz), 7.25-7.31 (1H, m, H-7), 7.38-7.48 (3H, m), 7.54 (1H, dd, J 2, 9 Hz, H-6), 8.23 (1H, s, H-2), 8.84 (1H, dd, J 1, 9 Hz, H-9); δ_C 13.96 (CH_3), 60.62 (CH_2), 116.29, 119.24, 120.17, 123.90, 124.86, 128.01, 128.14, 129.47, 133.16, 143.09, 148.12, 160.33

Ethyl 2-methylimidazo[1,2-a]quinoline-1-carboxylate (10), colourless solid, 92% yield, m.p. 84-85° (from ethyl acetate/light petroleum) (Found: C, 71.0; H, 5.8; N, 11.2; $M^{+\cdot}$ 254.1049. $C_{15}H_{14}N_2O_2$ requires C, 70.9; H, 5.6; N, 11.0%; $M^{+\cdot}$ 254.1055). ν_{max} 1683, 1522, 1412, 1361, 1340, 1271, 1218, 1182 cm^{-1}; δ_H 1.44 (3H, t, J 7 Hz), 2.67 (3H, s), 4.47 (2H, q, J 7 Hz), 7.25-7.31 (1H, m, H-7), 7.36 (1H, d, J 9 Hz, H-5), 7.41-7.48 (2H, m), 7.55 (1H, dd, J 2, 9 Hz, H-6), 8.19 (1H, dd, J 1, 9 Hz, H-9); δ_C 13.74 (CH_3), 15.70 (CH_3), 60.15 (CH_2), 115.20, 115.98, 118.30, 123.45, 123.99, 127.37, 127.94, 128.93, 132.35, 145.54, 150.98, 161.13

Ethyl 3-[(Quinolin-2-yl)amino]but-2-enoate (11), colourless needles, 0.5% yield, m.p. 73-74° (from ethanol), (Found: C, 70.5; H, 6.4; N, 10.7%; $M^{+\cdot}$ 256.1213. $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.3; N, 10.9%; $M^{+\cdot}$ 256.1212).

ν_{max} 3292, 3220, 1660, 1638, 1615, 1606, 1569, 1515, 1392, 1312, 1283, 1228 cm^{-1}; δ_H 1.31 (3H, t, J 7 Hz), 2.69 (3H, d, J 1 Hz), 4.19 (2H, q, J 7 Hz), 4.87 (1H, q, J 1 Hz, H-2), 6.91 (1H, d, J 9 Hz), 7.36 (1H, m), 7.60 (1H, m), 7.67 (1H, dd, J 1, 8 Hz), 7.80 (1H, dd, J 1, 8 Hz), 7.96 (1H, d, J 9 Hz), 11.20 (1H, s, NH); δ_C 14.47 (CH_3), 23.05 (CH_3), 59.21 (CH_2), 91.23, 114.86, 124.29, 124.68, 127.34, 127.78, 129.69, 137.77, 147.04, 152.09, 158.01, 170.12.

3-Methyl-1H-pyrimido[1,2-a]quinolin-1-one (12), colourless needles, 5% yield, m.p. 133-134° (lit.[10] 132-133°) (Found: $M^{+\cdot}$ 210.0791. $C_{13}H_{10}N_2O$ requires $M^{+\cdot}$ 210.0793). ν_{max} 1673, 1634, 1522, 1444, 1362, 1140, 1131 cm^{-1}; δ_H 2.34 (3H, s), 6.32 (1H, s, H-2), 7.18 (1H, d, J 9 Hz, H-5), 7.43 (1H, m, H-8), 7.53-7.59 (2H, m), 7.67 (1H, d, J 9 Hz, H-6), 9.78 (1H, dd, J 1, 9 Hz, H-10); δ_C 23.35 (CH_3), 109.10, 122.17, 124.13, 124.65, 126.65, 127.92, 129.53, 135.32, 136.36, 150.89, 161.56, 163.04.

Ethyl 5-methylimidazo[1,2-a]quinoline-1-carboxylate (16), colourless needles, 96% yield, m.p. 123-125° (from ethyl acetate/light petroleum) (Found: C, 71.0; H, 5.8; N, 10.9; $M^{+\cdot}$ 254.1061. $C_{15}H_{14}N_2O_2$ requires C, 70.9; H, 5.6; N, 11.0%; $M^{+\cdot}$ 254.1055). ν_{max} 1683, 1518, 1487, 1331, 1282, 1258, 1221, 1180 cm^{-1}; δ_H 1.41 (3H, t, J 7 Hz), 2.53 (3H, d, J 1 Hz,) 4.39 (2H, q, J 7 Hz), 7.34 (1H, q, J 1 Hz, H-4), 7.39-7.45 (1H, m, H-7), 7.52-7.59 (1H, m, H-8), 7.79 (1H, dd, J 1, 8 Hz, H-6), 8.23 (1H, s, H-2), 8.96 (1H, ddd, J 0.6, 1, 8 Hz, H-9); δ_C 14.27 (CH_3), 19.19 (CH_3), 60.87 (CH_2), 116.32, 119.90, 120.16, 124.60, 124.89, 125.18, 128.26, 133.34, 137.05, 143.62, 148.56, 160.85.

Ethyl 4-methylimidazo[1,2-a]quinoline-1-carboxylate (17), pale yellow needles, 97% yield, m.p. 103-104° (from ethyl acetate/light petroleum) (Found: C, 71.2; H, 5.4; N, 11.0; $M^{+\cdot}$ 254.1051. $C_{15}H_{14}N_2O_2$ requires C, 70.9; H, 5.6; N, 11.0%; $M^{+\cdot}$ 254.1055). ν_{max} 1688, 1522, 1489, 1362, 1327, 1266, 1225, 1186 cm^{-1}; δ_H 1.42 (3H, t, J 7 Hz), 2.58 (3H, s), 4.42 (2H, q, J 7 Hz), 7.34-7.40 (2H, m), 7.47-7.53 (1H, m, H-8), 7.61 (1H, dd, J 1, 8 Hz, H-6), 8.26 (1H, s, H-2), 8.87 (1H, dd, J 1, 8 Hz, H-9); δ_C 14.31 (CH_3), 17.25 (CH_3), 61.01 (CH_2), 119.38, 120.94, 124.69, 125.25, 125.93, 127.41, 127.82, 128.04, 132.72, 142.88, 149.18, 160.95.

Ethyl 8-methoxy-4-methylimidazo[1,2-a]quinoline-1-carboxylate (18), pale yellow solid, 89% yield, m.p. 105-107° (from ethyl acetate/light petroleum) (Found: C, 67.9; H, 5.6; N, 10.1; $M^{+\cdot}$ 284.1157. $C_{16}H_{16}N_2O_3$ requires C, 67.6; H, 5.7; N, 9.9%; $M^{+\cdot}$ 284.1161). ν_{max} 1690, 1522, 1489, 1337, 1205 cm^{-1}; δ_H 1.44 (3H, t, J 7 Hz), 2.61 (3H, s), 3.95 (3H, s), 4.43 (2H, q, J 7 Hz), 7.06

(1H, dd, J 2, 9 Hz, H-7), 7.40 (1H, s, H-5), 7.58 (1H, d, J 9 Hz, H-6), 8.33 (1H, s, H-2), 8.73 (1H, d, J 2 Hz, H-9); δ_C 14.40 (CH_3), 17.20 (CH_3), 55.73 (OCH_3), 61.10 (CH_2), 102.52, 115.27, 118.80, 120.63, 123.02, 128.12, 128.99, 134.26, 143.57, 149.84, 159.21, 161.09.

Ethyl 2,4-dimethylimidazo[1,2-a]quinoline-1-carboxylate (22), white solid, 92% yield, m.p. 95-96° (from ethyl acetate/light petroleum) (Found: C, 71.8; H, 6.1; N, 10.4; $M^{+\cdot}$ 268.1181. $C_{16}H_{16}N_2O_2$ requires C, 71.6; H, 6.0; N, 10.4%; $M^{+\cdot}$ 268.1212). ν_{max} 1694, 1528, 1424, 1361, 1342, 1276, 1205, 1184 cm^{-1}; δ_H 1.44 (3H, t, J 7 Hz), 2.58 (3H, s), 2.65 (3H, s), 4.41 (2H, q, J 7 Hz), 6.86 (1H, s, H-5), 6.94-7.01 (1H, m, H-7), 7.09-7.20 (2H, m), 7.82 (1H, dd, J 1, 8 Hz, H-9); δ_C 13.83 (CH_3), 15.67 (CH_3), 16.63 (CH_3), 60.24 (CH_2), 116.31, 118.00, 123.76, 123.93, 124.46, 126.30, 127.03, 127.17, 131.42, 146.18, 150.44, 161.40.

Ethyl 2,5-dimethylimidazo[1,2-a]quinoline-1-carboxylate (23), colourless solid, 94% yield, m.p. 138-139° (from ethyl acetate/light petroleum) (Found: C, 71.8; H, 6.1; N, 10.4; $M^{+\cdot}$ 268.1187. $C_{16}H_{16}N_2O_2$ requires C, 71.6; H, 6.0; N, 10.4%; $M^{+\cdot}$ 268.1212). ν_{max} 1689, 1630, 1528, 1412, 1348, 1293, 1182 cm^{-1}; δ_H 1.44 (3H, t, J 7 Hz), 2.61 (3H, d, J 1 Hz), 2.64 (3H, s),4.47, (2H, q, J 7 Hz), 7.32 (1H, q, J 1 Hz, H-4), 7.44-7.50 (1H, m, H-7), 7.55-7.62 (1H, m, H-8), 7.89 (1H, dd, J 2, 8 Hz, H-6), 8.28 (1H, dd, J 1, 8 Hz, H-9); δ_C 14.43 (CH_3), 16.34 (CH_3), 19.33 (CH_3), 60.88 (CH_2), 115.74, 116.31, 119.44, 124.68, 124.83, 125.21, 128.12, 132.06, 137.09, 146.62, 152.11, 162.16.

Ethyl 8-methoxy-2-methyl-4-phenylimidazo[1,2-a]quinoline-1-carboxylate (24), colourless solid, 94% yield, m.p. 153-155° (from ethyl acetate/light petroleum) (Found: C, 73.6; H, 5.5; N, 7.8; $M^{+\cdot}$ 360.1480. $C_{22}H_{20}N_2O_3$ requires C, 73.3; H, 5.6; N, 7.8%; $M^{+\cdot}$ 360.1474). ν_{max} 1685, 1620, 1597, 1520, 1338, 1252, 1205 cm^{-1}; δ_H 1.48 (3H, t, J 7 Hz), 2.72 (3H, s), 3.92 (3H, s), 4.52 (2H, q, J 7 Hz), 7.02 (1H, dd, J 2, 9 Hz, H-7), 7.38-7.54 (3H, m), 7.63 (1H, s, H-5), 7.64 (1H, d, J 9 Hz, H-6), 7.76 (1H, d, J 2 Hz, H-9), 7.92-7.96 (2H, m); δ_C 14.38 (CH_3), 16.65 (CH_3), 55.44 (OCH_3), 60.90 (CH_2), 102.01, 114.35, 116.50, 118.55, 126.00, 127.89, 128.00, 128.31, 129.07, 129.93, 133.68, 136.29, 146.11, 152.12, 159.39, 162.15.

Ethyl 3-[(3-methylquinolin-2-yl)amino]but-2-enoate (25), pale yellow needles, 0.8% yield, m.p. 123-124° (from ethanol) (Found: C, 71.0; H, 6.6; N, 10.4; $M^{+\cdot}$ 270.1374. $C_{16}H_{18}N_2O_2$ requires C, 71.1; H, 6.7; N, 10.4%; $M^{+\cdot}$ 270.1368). ν_{max} 1640, 1620, 1569, 1513, 1429, 1411, 1392, 1356, 1323, 1281, 1235, 1213, 1179 cm^{-1}; δ_H 1.32 (3H, t, J 7 Hz), 2.50 (3H, s), 2.74 (3H, d, J 1 Hz), 4.20

(2H, q, J 7 Hz), 4.92 (1H, q, J 1 Hz, H-2), 7.30-7.37 (1H, m,), 7.52-7.58 (1H, m), 7.62 (1H, dd, J 1.3, 8 Hz, H-9), 7.77-7.80 (2H, m), 11.22 (1H, s, NH); δ_C 14.52 (CH_3), 18.05 (CH_3), 23.32 (CH_3), 59.22 (CH_2), 92.28, 122.36, 124.16, 125.14, 126.56, 127.38, 128.64, 136.79, 145.80, 151.66, 158.29, 170.22.

Ethyl 3-[(4-methylquinolin-2-yl)amino]but-2-enoate (26), colourless needles, 1% yield, m.p. 59-61° (from ethyl acetate/light petroleum) (Found: $M^{+\cdot}$ 270.1361. $C_{16}H_{18}N_2O_2$ requires $M^{+\cdot}$ 270.1368). ν_{max} 1664, 1640, 1609, 1572, 1519, 1389, 1320, 1257, 1201 cm^{-1}; δ_H 1.32 (3H, t, J 7 Hz), 2.57 (3H, d, J 1 Hz), 2.68 (3H, d, J 1 Hz), 4.19 (2H, q, J 7 Hz), 4.85 (1H, q, J 1 Hz, H-2), 6.75 (1H, q, J 1 Hz), 7.33-7.40 (1H, m), 7.55-7.61 (1H, m), 7.77-7.83 (2H, m), 11.14 (1H, s, NH); δ_C 14.45 (CH_3), 18.51 (CH_3), 22.99 (CH_3), 59.13 (CH_2), 91.26, 115.03, 123.43, 124.00, 124.99, 128.28, 129.34, 145.78, 147.00, 151.90, 158.19, 170.11.

3,5-Dimethyl-1H-pyrimido[1,2-a]quinolin-1-one (28), colourless needles, 5% yield, m.p. 138-139° (from ethyl acetate) (Found: $M^{+\cdot}$ 224.0956. $C_{14}H_{12}N_2O$ requires $M^{+\cdot}$ 224.0950). ν_{max} 1674, 1636, 1523, 1442, 1364, 1144, 1132 cm^{-1}; δ_H 2.34 (3H, s), 2.37 (3H, s), 6.32 (1H, s, H-2), 7.33-7.48 (4H, m), 9.66 (1H, dd, J 1, 9 Hz, H-10); δ_C 18.93 (CH_3), 23.50 (CH_3), 108.82, 121.79, 124.36, 126.26, 126.91, 128.03, 131.32, 134.20, 134.51, 150.45, 160.99, 163.50.

3,6-Dimethyl-1H-pyrimido[1,2-a]quinolin-1-one (29), colourless needles, 4% yield, m.p. 135-137° (from ethyl acetate) (Found: C, 75.2; H, 5.1; N, 12.7; $M^{+\cdot}$ 224.0967. $C_{14}H_{12}N_2O$ requires C, 75.0; H, 5.4; N, 12.5%; $M^{+\cdot}$ 224.0950). ν_{max} 1675, 1634, 1523, 1443, 1362, 1146, 1134 cm^{-1}; δ_H 2.34 (3H, s), 2.43 (3H, d, J 1 Hz), 6.28 (1H, s, H-2), 6.92 (1H, q, J 1 Hz, H-5), 7.30-7.75 (3H, m), 9.72 (1H, dd, J 1, 9 Hz, H-10).

9-Methoxy-3-methyl-5-phenyl-1H-pyrimido[1,2-a]quinolin-1-one (30), pale yellow solid , 5% yield, m.p. 148-150° (from ethyl acetate) (Found: $M^{+\cdot}$ 316.1207. $C_{20}H_{16}N_2O_2$ requires $M^{+\cdot}$ 316.1212). ν_{max} 1672, 1612, 1516, 1338, 1282, 1254, 1162 cm^{-1}; δ_H 2.33 (3H, s), 3.97 (3H, s), 6.39 (1H, s, H-2), 7.15 (1H, dd, J 2, 9 Hz, H-8), 7.40-7.50 (3H, m), 7.61 (1H, d, J 9 Hz, H-7), 7.63-7.68 (2H, m), 7.75 (1H, s, H-2), 9.47 (1H, d, J 2 Hz, H-10); δ_C 23.63 (CH_3), 55.76 (OCH_3), 105.64, 108.39, 116.14, 118.76, 127.88, 127.90, 129.07, 130.13, 132.27, 135.95, 136.54, 137.58, 150.21, 160.14, 161.74, 164.15.

Ethyl 8-methoxy-2,4-dimethylimidazo[1,2-a]quinoline-1-carboxylate (33), colourless needles, 98% yield, m.p. 100-101° (from ethyl acetate/light petroleum) (Found: C, 68.7; H, 5.8; N, 9.2; $M^{+\cdot}$ 298.1324. $C_{17}H_{18}N_2O_3$ requires

C, 68.4; H, 6.1; N, 9.4%; $M^{+\cdot}$ 298.1317). ν_{max} 1701, 1627, 1535, 1406, 1346, 1278, 1245, 1180 cm^{-1}; δ_H 1.37 (3H, t, J 7 Hz), 2.47 (3H, s), 2.61 (3H, s), 3.79 (3H, s), 4.39 (2H, q, J 7 Hz), 6.86 (1H, dd, J 2, 9 Hz, H-7), 7.16 (1H, s, H-5), 7.37 (1H, d, J 9 Hz, H-6), 7.65 (1H, d, J 2 Hz, H-9); δ_C 14.08 (CH_3), 16.32 (CH_3), 16.76 (CH_3), 54.99 (OCH_3), 60.47 (CH_2), 101.54, 113.61, 116.23, 118.09, 121.71, 127.21, 128.46, 132.96, 147.05, 151.14, 158.28, 161.71.

Ethyl 8-chloro-2,4-dimethylimidazo[1,2-a]quinoline-1-carboxylate (34), pale yellow solid, 94% yield, m.p. 117-119° (from ethyl acetate) (Found: C, 63.7; H, 5.1; N, 9.1; $M^{+\cdot}$ 302.0794. $C_{16}H_{15}ClN_2O_2$ requires C, 63.6; H, 5.0; N, 9.3%; $M^{+\cdot}$ 302.0822). ν_{max} 1697, 1627, 1534, 1406, 1346, 1280, 1245, 1180 cm^{-1}; δ_H 1.41 (3H, t, J 7 Hz), 2.46 (3H, d, J 1 Hz), 2.59 (3H, s), 3.79 (3H, s), 4.43 (2H, q, J 7 Hz), 7.14 (1H, q, J 1 Hz, H-5), 7.19 (1H, dd, J 2, 9 Hz, H-7), 7.37 (1H, d, J 9 Hz, H-6), 8.16 (1H, d, J 2 Hz, H-9); δ_C 14.20 (CH_3), 16.22 (CH_3), 17.14 (CH_3), 61.00 (CH_2), 116.93, 118.65, 122.72, 125.03, 125.50, 126.81, 128.70, 132.38, 132.56, 146.74, 151.61, 161.66.

Ethyl 2-methyl-7-nitroimidazo[2,1-a]isoquinoline-3-carboxylate (36), pale brown needles, 85% yield, m.p. 173-174° (from ethanol) (Found: C, 60.1; H, 4.1; N, 13.8; $M^{+\cdot}$ 299.0896. $C_{15}H_{13}N_3O_4$ requires C, 60.2; H, 4.4; N, 14.0%; $M^{+\cdot}$ 299.0906). ν_{max} 1694, 1520, 1410, 1348, 1251, 1210, 1141, 1109, 1026 cm^{-1}; δ_H 1.46 (3H, t, J 7 Hz), 2.73 (3H, s), 4.45 (2H, q, J 7 Hz), 7.69 (1H, dd, J 8, 9 Hz, H-9), 7.91 (1H, d, J 8 Hz, H-6), 8.33 (1H, dd, J 0.6, 8 Hz, H-8), 8.92 (1H, dd, J 0.6, 9 Hz, H-10), 9.14 (1H, d, J 8 Hz, H-5); δ_C 14.14 (CH_3), 16.35 (CH_3), 60.80 (CH_2), 107.80, 114.76, 123.02, 124.02, 126.21, 126.98, 127.11, 130.02, 143.03, 145.33, 151.21, 161.05.

5-Nitroisocarbostyryl (37), pale yellow solid, 15% yield, m.p. 220°(dec.) (Found: $M^{+\cdot}$ 190.0381. $C_9H_6N_2O_3$ requires $M^{+\cdot}$ 190.0378). ν_{max} 1688, 1633, 1610, 1520, 1351, 1326, 1238 cm^{-1}; δ_C ($CDCl_3/CD_3SOCD_3$) 97.32, 123.69, 124.57, 126.64, 129.76, 131.10, 131.69, 143.02, 159.18.

Ethyl imidazo[2,1-b]benzothiazole-3-carboxylate (40), white solid, 97% yield, m.p. 115-116° (from ethyl acetate/light petroleum) (Found: C, 58.6; H, 4.0; N, 11.1; $M^{+\cdot}$ 246.0470. $C_{12}H_{10}N_2O_2S$ requires C, 58.5; H, 4.1; N, 11.4%; $M^{+\cdot}$ 246.0463). ν_{max} 1715, 1517, 1471, 1425, 1330, 1314, 1298, 1254, 1160, 1126 cm^{-1}; δ_H 1.39 (3H, t, J 7 Hz), 4.36 (2H, q, J 7 Hz), 7.25-7.30 (1H, m , H-7), 7.34-7.40 (1H, m, H-6), 7.59 (1H, dd, J 1, 8 Hz, H-8), 7.97 (1H, s, H-2), 8.95 (1H, dd, J 1, 8 Hz, H-5); δ_C 14.27 (CH_3), 60.70 (CH_2), 117.53, 121.72, 123.36, 125.13, 126.15, 129.79, 133.19, 143.11, 153.08, 159.50.

Ethyl 2-methylimidazo[2,1-b]benzothiazole-3-carboxylate (41), white solid, 95% yield, m.p. 82-83° (from ethyl acetate) (Found: C, 59.8; H, 4.9; N, 10.8; $M^{+\cdot}$ 260.0624. $C_{13}H_{12}N_2O_2S$ requires C, 60.0; H, 4.7; N, 10.8%; $M^{+\cdot}$ 260.0619). ν_{max} 1706, 1518, 1472, 1340, 1298, 1260, 1170, 1152, 1132 cm^{-1}; δ_H 1.43 (3H, t, J 7 Hz), 2.62 (3H, s), 4.41 (2H, q, J 7 Hz), 7.27-7.33 (1H, m, H-7), 7.37-7.44 (1H, m, H-6), 7.62 (1H, dd, J 1, 8 Hz, H-8), 8.93 (1H, dd, J 1, 8 Hz, H-5); δ_C 14.27 (CH_3), 16.91 (CH_3), 60.52 (CH_2), 117.43, 118.26, 123.26, 124.66, 125.94, 129.42, 133.73, 151.26, 153.91, 160.40.

Ethyl 2-methyl-5-phenylimidazo[1,2-c]quinazoline-3-carboxylate (45), colourless needles, 96% yield, m.p. 165-167° (from ethyl acetate/light petroleum) (Found: C, 72.8; H, 5.2; N, 12.8; $M^{+\cdot}$ 331.1294. $C_{20}H_{17}N_3O_2$ requires C, 72.5; H, 5.2; N, 12.7%; $M^{+\cdot}$ 331.1321). ν_{max} 1705, 1608, 1549, 1407, 1347, 1325, 1268, 1236 cm^{-1}; δ_H 0.90 (3H, t, J 7 Hz), 2.62 (3H, s), 3.60 (2H, q, J 7 Hz), 7.42-7.46 (3H, m), 7.47-7.53 (1H, m, H-9), 7.56-7.62 (1H, m, H-8), 7.75-7.79 (2H, m), 7.86 (1H, dd, J 1.5, 8 Hz, H-7), 8.44 (1H, dd, J 1.5, 8 Hz, H-10); δ_C 13.64 (CH_3), 14.62 (CH_3), 60.72 (CH_2), 116.04, 117.01, 122.92, 126.30, 127.81, 127.96, 128.57, 130.18, 130.85, 136.30, 141.71, 146.50, 146.90, 150.14, 160.06.

Ethyl 2-methylimidazo[1,2-f]phenanthridine-3-carboxylate (46), white solid, 96% yield, m.p. 85-86° (from ethyl acetate/light petroleum) (Found: C, 75.0; H, 5.1; N, 9.4; $M^{+\cdot}$ 304.1124. $C_{19}H_{16}N_2O_2$ requires C, 75.0; H, 5.3; N, 9.2%; $M^{+\cdot}$ 304.1212). ν_{max} 1705, 1598, 1538, 1404, 1347, 1338, 1278, 1188 cm^{-1}; δ_H 1.45 (3H, t, J 7 Hz), 2.70 (3H, s), 4.49 (2H, q, J 7 Hz), 7.40-7.66 (4H, m), 8.01 (1H, dd, J 1, 8 Hz), 8.29 (1H, dd, J 2, 8 Hz), 8.35 (1H, dd, J 2,8 Hz), 8.63 (1H, m); δ_C 14.42 (CH_3), 15.98 (CH_3), 61.04 (CH_2), 117.66, 119.79, 122.06, 122.39, 122.47, 123.69, 124.97, 125.21, 127.89, 128.35, 128.88, 129.65, 131.82, 145.50, 151.07, 162.12.

Ethyl imidazo[1,2-a]pyrimidine-3-carboxylate (47), pale yellow needles, 96% yield, m.p. 116-117° (from ethanol) (Found: C, 56.7; H, 4.9; N, 22.0; $M^{+\cdot}$ 191.0687. $C_9H_9N_3O_2$ requires C, 56.5; H, 4.7; N, 22.0%; $M^{+\cdot}$ 191.0695). ν_{max} 1708, 1517, 1405, 1314, 1288, 1241 cm^{-1}; δ_H 1.34 (3H, t, J 7 Hz), 4.34 (2H, q, J 7 Hz), 7.08 (1H, dd, J 4, 7 Hz, H-6), 8.35 (1H, s, H-2), 8.65 (1H, dd, J 2, 4 Hz, H-7), 9.48 (1H, dd, J 2, 7 Hz, H-5); δ_C 14.23 (CH_3), 60.73 (CH_2), 110.32, 114.27, 135.31, 142.38, 150.69, 152.04, 160.06.

Ethyl 6-nitroimidazo[1,2-a]pyridine-3-carboxylate (49), pale yellow needles, 87% yield, m.p. 172-174° (from ethyl acetate) (Found: C, 51.1; H, 3.9;

N, 18.0; $M^{+\cdot}$ 235.0601. $C_{10}H_9N_3O_4$ requires C, 51.1; H, 3.9; N, 17.9%; $M^{+\cdot}$ 235.0593). ν_{max} 1694, 1638, 1552, 1521, 1481, 1350, 1318, 1298, 1212 cm^{-1}; δ_H 1.38 (3H, t, J 7 Hz), 4.39 (2H, q, J 7 Hz), 7.73 (1H, d, J 9 Hz,H-8), 8.11 (1H, dd, J 2, 9 Hz, H-7), 8.36 (1H, s, H-2), 10.24 (1H, d, J 2 Hz, H-5).

Ethyl 6-nitroimidazo[1,2-a]pyridine-2-carboxylate (50), pale yellow needles, 11% yield, m.p. 120-122° (from ethyl acetate) (Found: $M^{+\cdot}$ 235.0587. $C_{10}H_9N_3O_4$ requires $M^{+\cdot}$ 235.0593). ν_{max} 1701, 1640, 1551, 1518, 1480, 1348, 1319, 1298, 1216 cm^{-1}; δ_H 1.44 (3H, t, J 7 Hz), 4.41 (2H, q, J 7 Hz), 5.84 (1H, s, H-3), 7.54 (1H, d, J 10 Hz, H-8), 8.37 (1H, dd, J 2.5, 10 Hz, H-7), 9.97 (1H, d, J 2.5 Hz, H-5).

ACKNOWLEDGEMENTS

The authors are gratetul to the Australian Research Council for support of this work.

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