v-Triazolines. Part 41.[1] A new synthesis of 2-alkylquinazolines and 2,9-dialkylpyrimido[4,5-*b*]indoles

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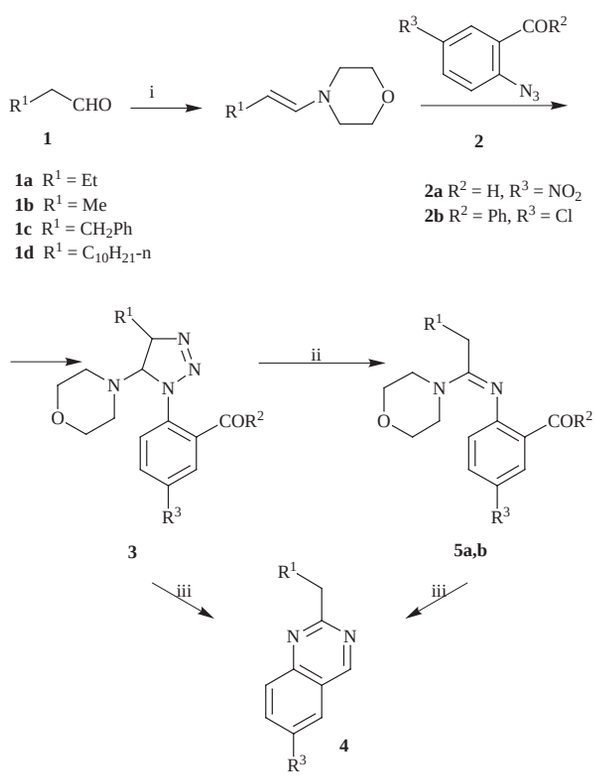
2-Alkylquinazolines were obtained from amidines by reaction with ammonia. The synthesis has been applied to the preparation of 2,9-dialkylpyrimido[4,5-*b*]indoles, in a one pot reaction, from 1-alkyl-2-azidoindole-3-carbaldehydes, a secondary amine and aldehydes and reaction with ammonia.

For a long time the interest of our research group has been focused on the possibilities offered by 4,5-dihydro-*v*-triazoles (*v*-triazolines), by way of their transformations as a direct or indirect synthetic tool for the preparation of nitrogen-containing heterocycles.[1–6] As a general rule, 5-amino-*v*-triazolines are readily accessible compounds and their conversion into functionalized tertiary amidines through thermal nitrogen elimination and rearrangement is a well established reaction.[7]

Previous and recent work has explored several synthetic procedures directed to quinoxalines,[2] quinolines,[3] oxopyridines,[4] benzimidazoles,[5] aminoquinazolines[6] and phenanthridines[1] starting from 5-amino-*v*-triazolines.

The quinazoline ring is of general interest owing to its presence in several compounds of high pharmacological importance as sedatives, diuretics and antimicrobials.[8] Moreover, recent preliminary pharmacological tests[9] carried out on some representatives of the pyrimido[4,5-*b*]indole series aroused interest because of the ability of these compounds to inhibit arterial smooth cell proliferation which is known to play an important role in the processes involved in the formation of atherosclerotic lesions.[10] Accordingly, it was considered of importance to develop new synthetic strategies directed to this class of heterocycles for further studies. The construction of the pyrimidine ring in quinazolines has been described in the literature according to several schemes, among them including the simultaneous formation of the 2,3 and 3,4 bonds, for example by heating *o*-acylaminobenzaldehydes with ammonia.[11] However, to the best of our knowledge, the amidine group as a precursor of the N1–C2 atoms has not been used thus far. The pyrimido[4,5-*b*]indole ring is rare in itself and general synthetic methods are lacking.[12]

The present paper is concerned with a new synthetic approach to 2-alkylquinazolines and 2-alkylpyrimido[4,5-*b*]-indoles.



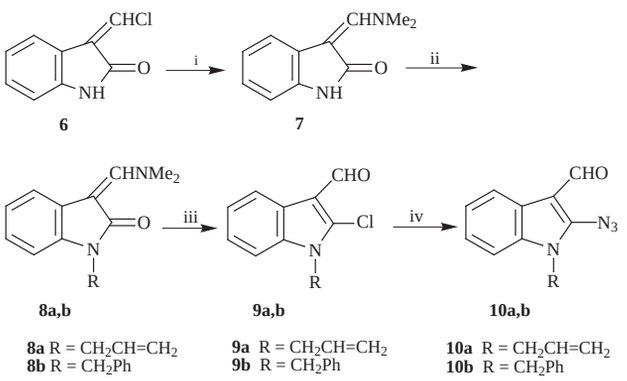
Scheme 1 *Reagents and conditions*: i, morpholine, MePh, rt; ii, MePh, reflux; iii, NH_3, EtOH, 150 °C or $MeCOONH_4$, MePh, reflux.

Results and discussion

In a three-component reaction, aldehydes **1a**–**d** readily reacted with morpholine and aryl azides **2a**,**b** in toluene solution at room temperature affording *trans*-triazolines **3a**–**e**[13] in acceptable yields (Scheme 1). Products **3** are formed through the 1,3-dipolar cycloaddition reaction of the azides **2** to intermediate enamines derived from aldehyde **1** and morpholine. On reaction with a saturated solution of ammonia in ethanol in a sealed vessel at 150 °C or with ammonium acetate in boiling toluene, compounds **3a**–**d** were transformed in a short time (about 30 minutes) into the corresponding 2-alkylquinazolines **4a**–**d**. No quinazoline product could be obtained from **3e**, and only the amidine **5b** was isolated as a rearrangement product of the starting triazoline accompanied by nitrogen elimination. This rearrangement is an expected process[14] and the formation of products **4** from **3** is fairly explained by amidine intermediates which undergo condensation of the formyl group with ammonia and ring closure by nucleophilic attack of the resulting imine on the amidine carbon. This pathway was easily confirmed by heating **3a** in toluene solution. Amidine **5a** was produced and could be transformed in a separate step into **4a** by reaction with ethanolic ammonia. Compound **5b** resisted cyclization under a variety of conditions.

The synthetic scheme was applied to the preparation of 2,9-dialkylpyrimido[4,5-*b*]indoles. 1-Allyl- and 1-benzyl-2-azido-

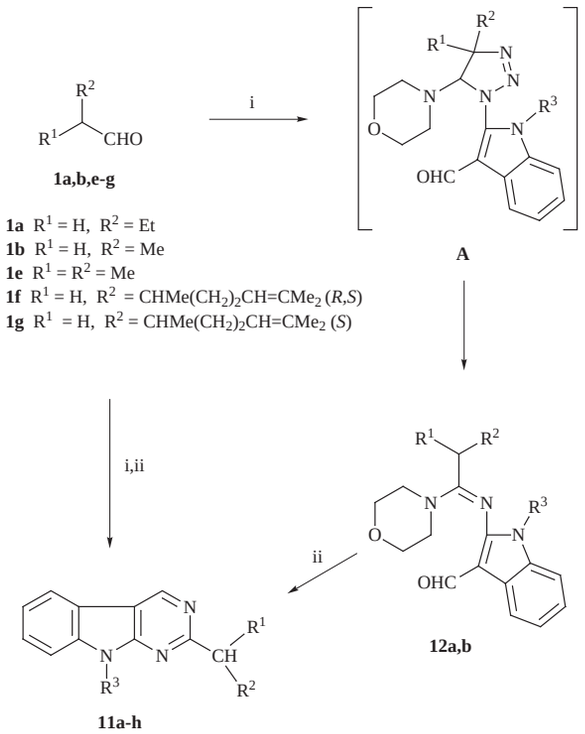
indole-3-carbaldehydes **10a**,**b** were prepared by the reaction sequence depicted in Scheme 2, *i.e.* from 3-chloromethylene-



Scheme 2 *Reagents and conditions*: i, Me_2NH, 33% in EtOH, CH_2Cl_2, rt; ii, NaH, THF, $BrCH_2CH{=}CH_2$ or $ClCH_2Ph$; iii, $POCl_3$, $CHCl_3$, reflux; iv, NaN_3, DMSO, rt.

indol-2-one **6** which was reacted with dimethylamine yielding the corresponding 3-dimethylaminomethylene compound **7**. *N*-Alkylation of the corresponding anion, produced by reaction with sodium hydride, with allyl bromide or benzyl chloride, respectively, afforded compounds **8a**,**b**, readily transformed into the corresponding aldehydes **9a**,**b** with phosphorus oxychloride. Reaction of the latter with sodium azide yielded the final products **10a**,**b**. Azide **10b** was also prepared from the 2-bromoindole-3-carbaldehyde, through benzylation and reaction with sodium azide by a modification of existing procedures. A one-pot procedure was found satisfactory for the preparation of pyrimido[4,5-*b*]indoles **11a**–**h**. Aldehydes **1a**,**b**,**e**–**g** were reacted with morpholine and azides **10a**,**b** at room temperature in toluene, then ammonium acetate was added and the reaction mixture refluxed for a short time, affording the final products in acceptable yields. The reaction pathway is depicted in Scheme 3. The intermediate compounds are triazolines **A** and amidines **12**. The former could never be isolated, probably owing to their thermal instability as a result both of the electron-withdrawing effect of the N-1 substituent and of steric crowding, whereas amidines **12** are stable compounds which were obtained pure in the case of compounds **12a**,**b** by stopping the reaction before addition of ammonium acetate. Further reaction with ammonia or ammonium acetate afforded the corresponding pyrimido[4,5-*b*]indoles **11a**,**b**. Catalytic reduction of **11g** afforded **11i**.

Thus a facile synthesis of 2-alkyl-quinazolines and -pyrimido[4,5-*b*]indoles has been found, starting from readily available materials and through simple operative procedures.



1a R^1 = H, R^2 = Et
1b R^1 = H, R^2 = Me
1e R^1 = R^2 = Me
1f R^1 = H, R^2 = $CHMe(CH_2)_2CH{=}CMe_2$ (*R*,*S*)
1g R^1 = H, R^2 = $CHMe(CH_2)_2CH{=}CMe_2$ (*S*)

11a, 12a R^1 = H, R^2 = Me, R^3 = CH_2Ph
11b,12b R^1 = H, R^2 = Me, R^3 = $CH_2CH{=}CH_2$
11c R^1 = H, R^2 = Et, R^3 = CH_2Ph
11d R^1 = R^2 = Me, R^3 = CH_2Ph
11e R^1 = H, R^2 = Et, R^3 = $CH_2CH{=}CH_2$
11f R^1 = H, R^2 = $CHMe(CH_2)_2CH{=}CMe_2$ (*R*,*S*), R^3 = $CH_2CH{=}CH_2$
11g R^1 = H, R^2 = $CHMe(CH_2)_2CH{=}CMe_2$ (*R*,*S*), R^3 = CH_2Ph
11h R^1 = H, R^2 = $CHMe(CH_2)_2CH{=}CMe_2$ (*S*), R^3 = CH_2Ph
11i R^1 = H, R^2 = $CHMe(CH_2)_2CH_2CHMe_2$, R^3 = CH_2Ph

Scheme 3 *Reagents and conditions*: i, morpholine, **10a** or **10b**, MePh, rt; ii, $AcONH_4$, MePh, reflux.

Experimental

Mps were determined by a Büchi 510 (capillary) apparatus. IR spectra were measured with a JASCO IR Report 100 instrument (Nujol; ν_{max}/cm^{-1}). NMR spectra were obtained with Bruker AC 200 and Varian Gemini 200 instruments at 200 MHz. *J* Values are given in Hz for solutions in $CDCl_3$. 2-Azido-5-nitrobenzaldehyde **2a**[15] and 2-azido-5-chlorobenzaldehyde **2b**[16] are known compounds.

3-Dimethylaminomethylene-2,3-dihydro-1*H*-indol-2-one 7

3-Chloromethylene-2,3-dihydro-1*H*-indol-2-one **6**[17] (14.37 g, 80 mmol) was dissolved in CH_2Cl_2 and a 37% solution of dimethylamine in EtOH (27.7 ml, 160 mmol) was added slowly in 10 min. The solution was stirred for 3 h at room temperature, then evaporated at reduced pressure and extracted with CH_2Cl_2. The extracts were washed with water, dried with Na_2SO_4 then evaporated and the residue recrystallized with CH_2Cl_2–Pr^i_2O (77%); mp 198 °C (Found: C, 70.0; H, 6.5; N, 14.7. $C_{11}H_{12}N_2O$ requires C, 70.2; H, 6.4; N, 14.9%); ν_{max} 1650 (CO); δ_H 3.20–3.65 (6H, m, CH_3), 6.83–7.59 (5H, m, ArH and CH), 8.58 and 9.19 (1H, br s, NH).

1-Allyl-3-dimethylaminomethylene-2,3-dihydro-1*H*-indol-2-one 8a

3-Dimethylaminomethylene-2,3-dihydro-1*H*-indol-2-one **7** (10.26 g, 54 mmol) was suspended in anhydrous THF in an N_2 atmosphere. NaH (60% in oil; 4.26 g, 100 mmol) was added at room temperature. After 30 min, allyl bromide was added and the mixture was refluxed for 3 h. The solvent was evaporated at reduced pressure, the residue taken up with water–CH_2Cl_2 and acidified with 5% HCl. The extracts were dried with Na_2SO_4 and evaporated at reduced pressure. The crude residue was chromatographed with ethyl acetate–cyclohexane (1 : 4) and crystallized with Pr^i_2O to afford **8a** (92%); mp 86 °C (Found: C, 73.4; H, 7.3; N, 11.9. $C_{14}H_{16}N_2O$ requires C, 73.7; H, 7.0; N, 12.3%); ν_{max} 1640 (CO); δ_H 3.20–3.70 (6H, m, $2CH_3$), 4.42–4.48 (2H, m, CH_2), 5.11–5.20 (2H, m, NCH_2), 5.78–5.95 (1H, m, –CH=), 6.78–7.28 (3H, m, ArH), 7.43 (1H, d, *J* 8.2, 4-H), 7.63 (1H, s, =CH–N).

1-Benzyl-3-dimethylaminomethylene-2,3-dihydro-1*H*-indol-2-one 8b

The title compound was obtained in 50% yield by the same method as for **8a** starting from **7** (11.0 g, 60 mmol), 60% NaH (2.95 g, 120 mmol) and benzyl chloride (15.18 g, 120 mmol); mp 127 °C (Et_2O) (Found: C, 77.5; H, 6.8; N, 9.8. $C_{18}H_{18}N_2O$ requires C, 77.7; H, 6.5; N, 10.1%); ν_{max} 1620 (CO); δ_H 3.32–3.37

(6H, m, $2CH_3$), 5.04 (2H, s, CH_2Ph), 6.69–7.40 (8H, m, ArH), 7.49 (1H, d, H-4), 7.68 (1H, s, CH).

1-Allyl-2-chloro-1*H*-indole-3-carbaldehyde 9a

Ketone **8a** (9.29 g, 40 mmol) was dissolved in $CHCl_3$ (100 ml) and $POCl_3$ (11.45 ml, 127 mmol) was added. The mixture was refluxed for 3 h until disappearance of the starting material (TLC ethyl acetate–cyclohexane, 3:7). The organic layer was washed with a solution of $NaHCO_3$ and extracted with CH_2Cl_2. The extracts were dried with Na_2SO_4 and evaporated at reduced pressure. The crude residue was purified by chromatography with ethyl acetate–cyclohexane (1:1) affording pure **9a** (57%); mp 59 °C (Found: C, 65.4; H, 4.9; N, 4.95. $C_{12}H_{10}ClNO$ requires C, 65.6; H, 4.55; N, 5.0%); ν_{max} 1645 (CHO); δ_H 4.80–4.95 (2H, m, CH_2), 4.96–5.45 (2H, m, CH_2N), 5.85–6.10 (1H, m, CH), 7.15–7.42 (3H, m, ArH), 8.25–8.38 (1H, m, 4-H), 10.13 (1H, s, CHO).

1-Benzyl-2-chloro-1*H*-indole-3-carbaldehyde 9b

The title compound was obtained in 68% yield by the same method as for **9a** starting from **8b** (7.5 g, 27 mmol) and $POCl_3$ (12.7 g, 80 mmol); mp 136 °C (Et_2O) (Found: C, 71.0; H, 4.6; N, 4.95. $C_{16}H_{12}ClNO$ requires C, 71.2; H, 4.45; N, 5.2%); ν_{max} 1640 (CHO); δ_H 5.46 (2H, s, CH_2), 7.11–7.33 (8H, m, ArH), 8.30–8.34 (1H, m, 4-H), 10.17 (1H, s, CHO).

1-Allyl-2-azido-1*H*-indole-3-carbaldehyde 10a

Compound **9a** (2.81 g, 12.8 mmol) was suspended in DMSO (17 ml) and NaN_3 (1.25 g, 19.2 mmol) was added. The mixture was stirred at room temperature for 24 h and the reaction was monitored by ^1H NMR spectroscopy until disappearance of the starting chloro derivative. The solution was taken up with H_2O and extracted with Et_2O. The organic layer, dried with Na_2SO_4, was evaporated at reduced pressure and afforded **10a** (89%) sufficiently pure for direct use; mp 68 °C; ν_{max} 2115 (N_3), 1647 (CHO); δ_H 4.68–4.70 (2H, m, CH_2), 4.99–5.25 (2H, m, CH), 5.84–5.98 (1H, m, CH), 7.27–7.32 (3H, m, ArH), 8.01–8.05 (1H, m, 4-H), 10.32 (1H, s, CHO).

1-Benzyl-2-azido-1*H*-indole-3-carbaldehyde 10b

The title compound was obtained either starting from **9b** (4 g, 15.0 mmol) and NaN_3 (1.055 g, 16 mmol) by the procedure described for **10a** (yield 90%), or starting from 2-bromo-3-formylindole which was prepared according to a known method,[18] modified by reducing the reaction time to 3 h and crystallizing directly from Et_2O (50%). 2-Bromo-3-formylindole (1.5 g, 6.7 mmol) was alkylated with benzyl chloride (1.64 g, 13 mmol) and NaH (60% in oil, 0.52 g, 13 mmol) to give 1-benzyl-2-bromo-1*H*-indole-3-carbaldehyde, which was crystallized from Pr^i_2O (24%); mp 125 °C (Found: C, 61.0; H, 4.1; N, 3.2. $C_{16}H_{12}BrNO$ requires C, 61.1; H, 3.8; N, 3.5%); ν_{max} 1640 (CO); δ_H 5.5 (2H, s, CH_2), 7.11–7.33 (8H, m, ArH), 8.31–8.39 (1H, m, H-4), 10.09 (1H, s, CHO). 1-Benzyl-2-bromo-3-formylindole (4.7 g, 15 mmol) reacted with NaN_3 (1.05 g, 16 mmol) in DMSO (10 ml) by the same method of **10a** affording pure **10b** (87%); mp 96 °C (lit.,[19] 96–97).

General procedure for the preparation of triazolines 3a–e

Azides **2a**,**b** (5 mmol) and aldehydes **1a**–**d** (5 mmol) were dissolved in toluene (10 ml) and morpholine (5 mmol) was then added dropwise. The reaction mixture was stirred at room temperature for 2 h. The abundant precipitate was collected by filtration and recrystallized. Analytical and spectral data are listed in Table 1.

General procedure for the preparation of 2-alkyl-6-nitroquinazolines 4a,b,d

Triazolines **3a**,**b**,**d** (3 mmol) were mixed with $AcONH_4$ (30 mmol) and heated in an oil bath at 130 °C for 30 min. The residue was taken up with CH_2Cl_2, washed with water, dried with Na_2SO_4 and evaporated. The crude residue was purified by chromatography with ethyl acetate–cyclohexane (3:7). Analytical and spectral data are listed in Table 1.

Preparation of 2-(2-phenylethyl)-6-nitroquinazoline 4c

The triazoline **3c** (3 mmol) was dissolved in ethanol saturated with NH_3 in a sealed tube. The solution was heated in an oil bath at 150 °C for 1 h. The crude reaction mixture was evaporated at reduced pressure and purified by chromatography with ethyl acetate–cyclohexane (3:7). Analytical and spectral data are listed in Table 1.

2-[1-(Morpholin-4-yl)-butylideneamino]-5-nitrobenzaldehyde 5a

Triazoline **3d** was refluxed in toluene for 1 h. The crude reaction mixture was evaporated at reduced pressure and the residue was analyzed by ^1H NMR. The instability of the product (easy hydrolysis) made a further purification impossible. δ_H 0.83 (3H, t, CH_3, *J* 7.2), 1.38–1.63 (2H, m, CH_2), 2.27 (2H, t, CH_2, *J* 7.9), 3.51–3.89 (8H, m, morpholine), 6.77 (1H, d, H-6, *J* 8.5), 8.29 (1H, dd, H-5, *J* 2.3 and 8.5), 8.66 (1H, d, H-3, *J* 2.3).

{5-Chloro-2-[1-(morpholin-4-yl)butylideneamino]phenyl} phenyl ketone 5b

Triazoline **3e** was refluxed in *p*-xylene for 1 h. The crude reaction solution was evaporated at reduced pressure and purified by chromatography (ethyl acetate–cyclohexane, 3:7). The residue was crystallized with EtOH (62%); mp 102 °C (Found: C, 75.0; H, 6.8; N, 8.1. $C_{21}H_{23}ClN_2O_2$ requires C, 75.2; H, 6.6; N, 8.35%); δ_H 0.78 (3H, t, CH_3, *J* 7.4), 1.19–1.48 (2H, m, CH_2), 2.98–2.10 (2H, m, CH_2), 2.95–3.07 and 3.29–3.47 (4H + 4H, 2 m, morpholine), 6.67 (1H, d, H-5, *J* 8.3), 7.32–7.75 (7H, m, ArH).

General procedure for the preparation of 2,9-dialkyl-9*H*-pyrimido[4,5-*b*]indoles 11a–h

Indole azide **10a**,**b** (10 mmol) and aldehyde **1a**,**b**,**e**–**g** (5 mmol) were dissolved in toluene and morpholine (5 mmol) was added dropwise. The mixture was stirred at room temperature for 1 h until disappearance of the starting material [TLC ethyl acetate–cyclohexane (3:7)]. $AcONH_4$ (50 mmol) was added to the solution and the mixture was then refluxed for 45 min. The crude reaction mixture was extracted with Et_2O, washed with water, dried with Na_2SO_4 and concentrated under reduced pressure. The oil was purified by chromatography with ethyl acetate–cyclohexane (3:7). Analytical and spectral data are listed in Table 1.

Preparation of 1-alkyl-2-[1-(morpholin-4-yl)propylideneamino]-1*H*-indole-3-carbaldehydes 12a,b

Azides **10a**,**b** (5 mmol) and **1b** (5 mmol) were dissolved in CH_2Cl_2 and morpholine (5 mmol) was added. The solution was stirred at room temperature for 2 h until disappearance of the starting materials. The crude reaction mixture was dried with Na_2SO_4, and evaporated under reduced pressure, then crystallized with EtOH. Analytical and spectral data are listed in Table 1.

9-Benzyl-2-(2,6-dimethylheptyl)-9*H*-pyrimido[4,5-*b*]indole 11i

Product **11g** (0.4 g, 1.04 mmol) was dissolved in EtOH and 0.4 g of Pd/C 10% was added. The mixture was hydrogenated at room pressure and temperature. The reaction mixture was filtered through a Celite bed and evaporated to dryness. The residue was purified by chromatography [ethyl acetate–cyclohexane

Table 1 Analytical and spectral data for compounds **3**, **4**, **11** and **12**

Compound (Formula)	Yield (%)	Mp (*T*/°C) (solv.)	δ_H(*J*/Hz) and ν_{max} (cm^{-1}, Nujol)	Found (%) (requires)		
				C	H	N
3a ($C_{15}H_{19}N_5O_4$)	42	103 (MePh)	1.13 (3H, t, *J* 7.5, CH_3), 1.5 (2H, m, CH_2), 2.18–2.40 + 3.49–3.64 (4H + 4H, 2m, morpholine), 4.62 (1H, dt, *J* 3.0 and 7.3, H-4), 4.76 (1H, d, *J* 3.0, H-5), 7.88 (1H, d, *J* 9.15, H-5′), 8.38 (1H, dd, *J* 2.65 and 9.15, H-4′), 8.71 (1H, d, *J* 2.65, H-2′), 10.21 (1H, s, CHO); 1650 (CO)	53.8 (54.05)	5.9 (5.7)	20.9 (21.0)
3b ($C_{14}H_{17}N_5O_4$)	75	89 (MePh)	1.42 (3H, d, *J* 7.04, CH_3), 2.26–2.37 + 3.52–3.58 (4H + 4H, 2m, morpholine), 4.66–4.69 (2H, m, H-4 and H-5), 7.87 (1H, d, *J* 9.1, H-5′), 8.39 (1H, dd, *J* 2.7 and 9.1, H-4′), 8.72 (1H, d, *J* 2.7, H-2′), 10.21 (1H, s, CHO); 1680 (CO)	52.8 (52.7)	5.7 (5.3)	21.7 (21.9)
3c ($C_{20}H_{21}N_5O_4$)	97	99 (MePh)	1.99–2.06 + 3.42–3.58 (4H + 4H, 2m, morpholine), 2.72 (1H, dd, *J* 8.7 and 13.7, CHPh), 3.31 (1H, dd, *J* 5.0 and 13.7, CHPh), 4.78 (1H, d, *J* 4.2, H-5), 4.85 (1H, ddd, *J* 4.2, 5.0 and 8.7, H-4), 7.16–7.38 (5H, m, Ph), 7.78 (1H, d, *J* 9.1, H-5′), 8.34 (1H, dd, *J* 2.7 and 9.1, H-4′), 8.68 (1H, d, *J* 2.7, H-2′), 10.01 (1H, s, CHO); 1650 (CO)	60.5 (60.75)	5.7 (5.3)	17.5 (17.7)
3d ($C_{23}H_{35}N_5O_4$)	40	87 (MePh)	0.84–1.88 (21H, m, $C_{10}H_{21}$), 2.17–2.38 + 3.53–3.58 (4H + 4H, 2m, morpholine), 4.58–4.66 (1H, m, H-4), 4.75 (1H, d, *J* 2.9, H-5), 7.88 (1H, d, *J* 9.1, H-5′), 8.39 (1H, dd, *J* 2.7 and 9.1, H-4′), 8.71 (1H, d, *J* 2.7, H-2′), 10.21 (1H, s, CHO); 1620 (CO)	61.8 (62.0)	8.1 (7.9)	15.4 (15.7)
3e ($C_{20}H_{23}ClN_4O_2$)	95	142 (MePh)	0.8–0.95 (3H, m, CH_3), 1.09–1.38 (2H, m, CH_2), 2.0–2.22 + 3.22–3.43 (4H + 4H, 2m, morpholine), 4.19–4.25 (2H, m, H-5 and H-4), 7.38–7.86 (H, m, ArH); 1650 (CO)	61.9 (62.1)	5.9 (5.95)	14.2 (14.5)
4a ($C_{11}H_{11}N_3O_2$)	92	109 (Pr^i_2O)	1.05 (3H, t, *J* 7.4, CH_3), 2.01 (2H, sextet, *J* 7.4, CH_2), 3.16 (2H, t, *J* 7.4, CH_2), 8.1 (1H, d, *J* 9.5, H-8), 8.64 (1H, dd, *J* 2.5 and 9.5, H-7), 8.87 (1H, d, *J* 2.5, H-5), 9.54 (1H, s, H-4)	60.6 (60.8)	5.5 (5.1)	19.0 (19.35)
4b ($C_{10}H_9N_3O_2$)	95	143 (Pr^i_2O)	1.49 (3H, t, *J* 7.5, CH_3), 3.22 (2H, q, *J* 7.5, CH_2), 8.12 (1H, d, *J* 9.3, H-8), 8.65 (1H, d, *J* 9.3 and 2.5, H-7), 8.88 (1H, d, *J* 2.5, H-5), 9.55 (1H, s, H-4)	58.9 (59.1)	4.4 (4.4)	20.5 (20.7)
4c ($C_{16}H_{13}N_3O_2$)	38	123 (Pr^i_2O)	3.24–3.55 (4H, m, CH_2-CH_2), 7.18–7.31 (5H, m, Ph), 8.13 (1H, d, *J* 9.5, H-8), 8.66 (1H, dd, *J* 2.4 and 9.5, H-7), 8.86 (1H, d, H-5, *J* 2.4), 9.56 (1H, s, H-4)	68.6 (68.8)	4.9 (4.7)	15.1 (15.05)
4d ($C_{19}H_{27}N_3O_2$)	37	87 (Pr^i_2O)	0.83–2.05 (21H, m, $C_{10}H_{21}$), 3.17 (2H, t, *J* 7.5, CH_2), 8.12 (1H, d, *J* 9.2, H-8), 8.65 (1H, dd, *J* 2.4 and 9.2, H-7), 8.87 (1H, d, *J* 2.4, H-5), 9.54 (1H, s, H-4)	69.1 (69.3)	8.5 (8.2)	12.6 (12.8)
11a ($C_{19}H_{17}N_3$)	40	90 (Pr^i_2O)	1.47 (3H, t, *J* 7.2, CH_3), 3.13 (2H, q, *J* 7.2, CH_2), 5.65 (2H, s, CH_2Ph), 7.23–7.50 (8H, m, ArH), 8.08 (1H, d, *J* 8.2, H-5), 9.22 (1H, s, H-4)	79.5 (79.5)	6.0 (5.9)	14.6 (14.6)
11b ($C_{15}H_{15}N_3$)	39	69 (Et_2O–Pentane)	1.45 (3H, t, *J* 7.2, CH_3), 3.10 (2H, q, *J* 7.2, CH_2), 5.05–5.28 (4H, m, CH_2= and CH_2N), 5.92–6.12 (1H, m, CH), 7.25–7.58 (3H, m, ArH), 8.09 (1H, d, *J* 7.7, H-5), 9.20 (1H, s, H-4)	75.7 (75.9)	6.3 (6.3)	17.5 (17.7)
11c ($C_{20}H_{19}N_3$)	42	90 (Pr^i_2O)	1.03 (3H, t, *J* 7.2, CH_3), 1.82–2.08 (2H, m, CH_2), 3.02–3.12 (2H, m, CH_2), 5.65 (2H, CH_2Ph), 7.21–7.52 (3H, m, ArH), 8.10 (1H, d, *J* 8.3, H-5), 9.21 (1H, s, H-4)	79.7 (79.7)	6.0 (6.3)	13.7 (13.95)
11d ($C_{20}H_{19}N_3$)	39	130 (Pr^i_2O)	1.56 (6H, d, *J* 6.87, $2CH_3$), 3.88 (1H, septet, *J* 6.87, CH), 5.73 (2H, s, CH_2Ph), 7.22–7.75 (8H, m, ArH), 8.18 (1H, d, *J* 8.2, H-5), 9.38 (1H, s, H-4)	79.5 (79.7)	6.3 (6.3)	11.6 (11.55)
11e ($C_{16}H_{17}N_3$)	45	61 (Pr^i_2O)	1.03 (3H, t, *J* 7.2, CH_3), 1.82–2.05 (2H, m, CH_2), 2.95–3.12 (2H, m, CH_2), 5.00–5.25 (4H, m, CH_2N and CH_2=), 5.85–6.15 (1H, m, CH), 7.20–7.55 (3H, m, ArH), 8.07 (1H, d, *J* 7.7, H-5), 9.18 (1H, s, H-4)	76.1 (76.5)	7.1 (6.8)	16.35 (16.7)
11f ($C_{22}H_{27}N_3$)	75	Oil	0.95 (3H, d, *J* 7.2, CH_3), 1.54–2.54 (11H, m, AlkylH), 2.82–3.18 (2H, m, CH_2), 5.05–5.30 (5H, m, CH, CH_2= and CH_2N), 5.85–6.12 (1H, m, CH=), 7.22–7.55 (3H, m, ArH), 8.10 (1H, d, *J* 8.2, H-5), 10.14 (1H, s, H-4)	79.15 (79.3)	8.35 (8.1)	12.2 (12.6)
11i ($C_{26}H_{31}N_3$)	32	Oil	0.89–2.19 (17H, m, AlkylH), 2.40–2.59 (2H, m, CH_2), 5.65 (2H, s, CH_2Ph), 7.09–7.26 (8H, m, ArH), 8.08 (1H, d, *J* 8.1, H-5), 9.21 (1H, s, H-4)	80.9 (81.0)	8.2 (8.0)	10.75 (10.9)
11g ($C_{26}H_{29}N_3$)	38	Oil	0.96 (3H, d, *J* 7.2, CH_3), 1.54–2.45 (11H, m, AlkylH), 2.82–3.18 (2H, m, CH_2), 5.03–5.18 (1H, m, CH=), 5.64 (2H, s, CH_2), 7.21–7.52 (8H, m, ArH), 8.02 (1H, d, *J* 8.1, H-5), 9.21 (1H, s, H-4)	80.85 (81.25)	7.75 (7.8)	10.75 (10.9)
11h ($C_{26}H_{29}N_3$)	33	Oil[a]	0.96 (3H, d, *J* 7.2, CH_3), 1.54–2.45 (11H, m, AlkylH), 2.82–3.18 (2H, m, CH_2), 5.03–5.18 (1H, m, CH=), 5.64 (2H, s, CH_2), 7.21–7.52 (8H, m, ArH), 8.02 (1H, s, H-5), 9.21 (1H, s, H-4)	80.9 (81.25)	7.9 (7.8)	10.7 (10.9)
12a ($C_{23}H_{25}N_3O_2$)	52	180 (EtOH)	0.82 (3H, t, *J* 7.2, CH_3), 2.20–2.48 (2H, m, CH_2), 3.55–3.84 (8H, m, morpholine), 5.14 (2H, s, CH_2Ph), 7.12–7.42 (8H, m, ArH), 8.17 (1H, d, *J* 7.5, H-4), 9.67 (1H, s, CHO); 1640 (CO)	73.4 (73.6)	6.9 (6.7)	11.0 (11.2)
12b ($C_{19}H_{23}N_3O_2$)	50	104 (EtOH)	1.03 (3H, t, *J* 7.2, CH_3), 2.32–2.75 (2H, m, CH_2), 3.64–3.78 (8H, m, morpholine), 4.48–4.67 (2H, m, CH_2=), 5.02–5.22 (2H, m, CH_2N), 5.82–5.96 (1H, m, CH=), 7.15–7.26 (3H, m, ArH), 8.17 (1H, d, *J* 7.5, H-4), 9.66 (1H, s, CHO); 1640 (CO)	69.95 (70.15)	7.4 (7.1)	12.6 (12.9)

[a] $[\alpha]_D^{20}$ −11.5 (*c* 1.044 in $CHCl_3$).

(1 : 9)] affording pure **11i** (32%) (Found: C, 80.8; H, 8.2; N, 10.7. $C_{26}H_{31}N_3$ requires C, 81.0; H, 8.0; N, 10.9%); δ_H 0.89–2.19 (17H, m, alkyl), 4.40–2.59 (2H, m, CH_2), 5.65 (2H, s, CH_2Ph), 7.09–7.26 (8H, m, ArH), 8.08 (1H, d, *J* 8.1, H-5), 9.21 (1H, s, H-4).

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