Reinvestigation of the Synthesis of 3-Dimethylallyl-4-hydroxy-2-quinolones. A Novel Route to Tetracyclic Heteroaromatic Compounds [1]

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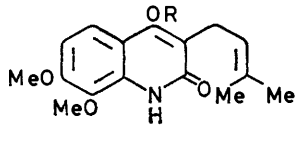
The reaction of diethyl 2-(3-methylbut-2-enyl)malonate with a variety of anilines has been used in the past as a method of alkaloid synthesis. It has now been found that this reaction yields, in addition to the expected 3-dimethylallyl-4-hydroxy-2-quinolones, 3,3'-methylenebis-4-hydroxy-2-quinolones, and dibenzo[*b,h*][1,6]naphthyridin-6(5*H*)-ones. A mechanism is suggested to explain this unusual reaction.

THE reaction of diethyl 2-(3-methylbut-2-enyl)malonate with anilines has been used as a general method of synthesis of 3-dimethylallyl-4-hydroxy-2-quinolones.[2,3] These compounds were then converted into naturally occurring alkaloids.[2,3] When we isolated the alkaloid preskimmianine (1; R = Me)[4] from the root of *Dictamnus albus* L, therefore, it seemed that the most straightforward method of confirming the structure would be to synthesise the alkaloid by this method. The synthesis indeed proved to be successful [4] but a second product was found in the reaction of 2,3-dimethoxyaniline with diethyl 2-(3-methylbut-2-enyl)malonate in refluxing diphenyl ether in addition to the expected quinolone (1; R = H). This compound crystallised from acetic acid as needles, m.p. 247—249 °C, $C_{29}H_{18}N_2O_5$. It had a characteristic u.v. spectrum and the i.r. spectrum exhibited amide carbonyl absorption at 1 665 cm^{-1}. The n.m.r. spectrum showed the presence of four methoxy-groups and four *ortho*-coupled aromatic protons, one of which lay to unusually low field at τ 1.30. There was a further aromatic singlet at τ 0.88.

Several structures are consistent with the quoted data. The structure (2a) seemed the most attractive of these to us and we were able to obtain † samples of (2b) [5] and (2c) [6] to compare with our compound. Compound (2b) [5] had an n.m.r. spectrum which showed an *ortho*-coupled aromatic doublet at τ 0.88 and a singlet at τ 0.66, while compound (2c) [6] showed an *ortho*-coupled doublet at τ 1.33 and a singlet at τ 1.04. The u.v. spectra of the two model compounds had similarities to that of the new compound and all three spectra showed a bathochromic shift on addition of acid.



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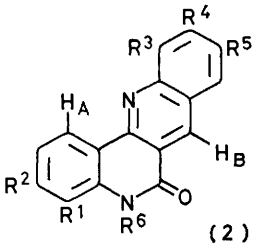
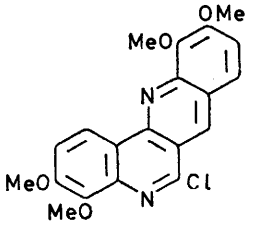


(2)

	R^1	R^2	R^3	R^4	R^5	R^6
a;	OMe	OMe	OMe	OMe	H	H
b;	H	H	H	H	H	Me
c;	H	NMe_2	H	H	OMe	Me
d;	OMe	OMe	OMe	OMe	H	Me
e;	H	H	H	H	H	H
f;	OMe	H	OMe	H	H	H
g;	OMe	OMe	OMe	H	OMe	H



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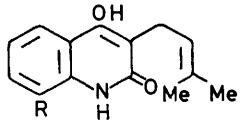
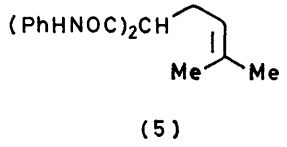


(4) a; R = H
b; R = OMe



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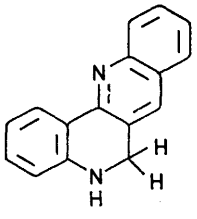

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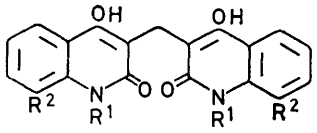


(7)

† We thank Dr. F. G. Mann, F.R.S., Cambridge, and Dr. H. Harnisch, Bayer A.G., for gifts of samples.

[1] Preliminary communication, R. Oels, R. Storer, and D. W. Young, *Chem. and Ind.*, 1974, 499.

[2] E. A. Clarke and M. F. Grundon, *J. Chem. Soc.*, 1964, 438.

[3] R. M. Bowman and M. F. Grundon, *J. Chem. Soc.* (*C*), 1966, 1084.

[4] R. Storer and D. W. Young, *Tetrahedron Letters*, 1972, 2199; *Tetrahedron*, 1973, **29**, 1217.

[5] J. T. Braunholtz and F. G. Mann, *J. Chem. Soc.*, 1955, 381.

[6] H. Harnisch and A. Brack, *Annalen*, 1970, **740**, 164.

The new compound, $C_{20}H_{18}N_2O_5$, could be *N*-methylated using methyl iodide and sodium hydride to yield a derivative, $C_{21}H_{20}N_2O_5$, which presumably had the structure (2d). It could also be converted into an unstable chloride (3) on reaction with $POCl_3$.

It was now necessary to confirm the structure suggested for our new compound and to see whether similar interesting products might be formed in synthesis of other 3-dimethylallyl-4-hydroxy-2-quinolones. We therefore reinvestigated the reaction of aniline with diethyl 2-(3-methylbut-2-enyl)malonate in refluxing diphenyl ether. This reaction had been reported [3] to yield the quinolone (4a). We obtained this product in addition to 2-(3-methylbut-2-enyl)malondianilide (5) and a compound $C_{16}H_{10}N_2O$ which had spectral similarities to the putative compound (2a). The compound was therefore considered to have the structure (2e) being easily methylated with methyl iodide and sodium hydride to yield compound (2b).

An authentic specimen of the *N*-methyl derivative (2b) was prepared from the known compound (6).[7] Initial attempts to oxidise this compound led not unnaturally to dibenzo[*b*,*h*][1,6]naphthyridine, but when compound (6) was methylated using methyl iodide and sodium hydride under an atmosphere of nitrogen, the desired compound (2b) was obtained. Oxidation to the amide had presumably occurred during the work-up procedure for the *N*-methyl-5,6-dihydro-derivative. The authentic specimen of (2b) thus obtained was identical in all respects to the sample obtained *via* the 3-dimethylallyl-4-hydroxy-2-quinolone synthesis.

The unusual products from the synthesis of 3-dimethylallyl-4-hydroxy-2-quinolones had been obtained in two separate reactions. In a further example of the synthesis of 3-dimethylallyl-4-hydroxy-2-quinolones, *ortho*-anisidine had been used to prepare the quinolone (4b).[2] We found that the yield of the corresponding product (2f) was not high enough in this reaction to permit characterisation. When, however, the quinolone (4b) was allowed to react with *ortho*-anisidine in refluxing diphenyl ether, the desired compound (2f) was obtained.

Having shown that the reaction of diethyl 2-(3-methylbut-2-enyl)malonate with anilines produced not only the ' normal ' products but also gave the unusual products of general structure (2), it was necessary to investigate the reaction conditions to see if the yield of the tetracyclic compounds could be optimised. The reaction of diethyl 2-(3-methylbut-2-enyl)malonate with aniline was, therefore, monitored by u.v. spectroscopy and t.l.c. It was found that formation of the tetracyclic product (2) was encouraged by prolonged heating. An initial product in some reactions was the dianilide (5), a compound which yielded mixtures of the quinolone (4a) and the tetracyclic compound (2e) when heated in the absence of a solvent.

In many of the reactions in which we had obtained compounds of type (2) additional by-products were found. These proved to be the appropriate substituted 3,3'-methylenebis-4-hydroxy-2-quinolones (7), identical with authentic samples prepared from the substituted 4-hydroxy-2-quinolones by reaction with formaldehyde.

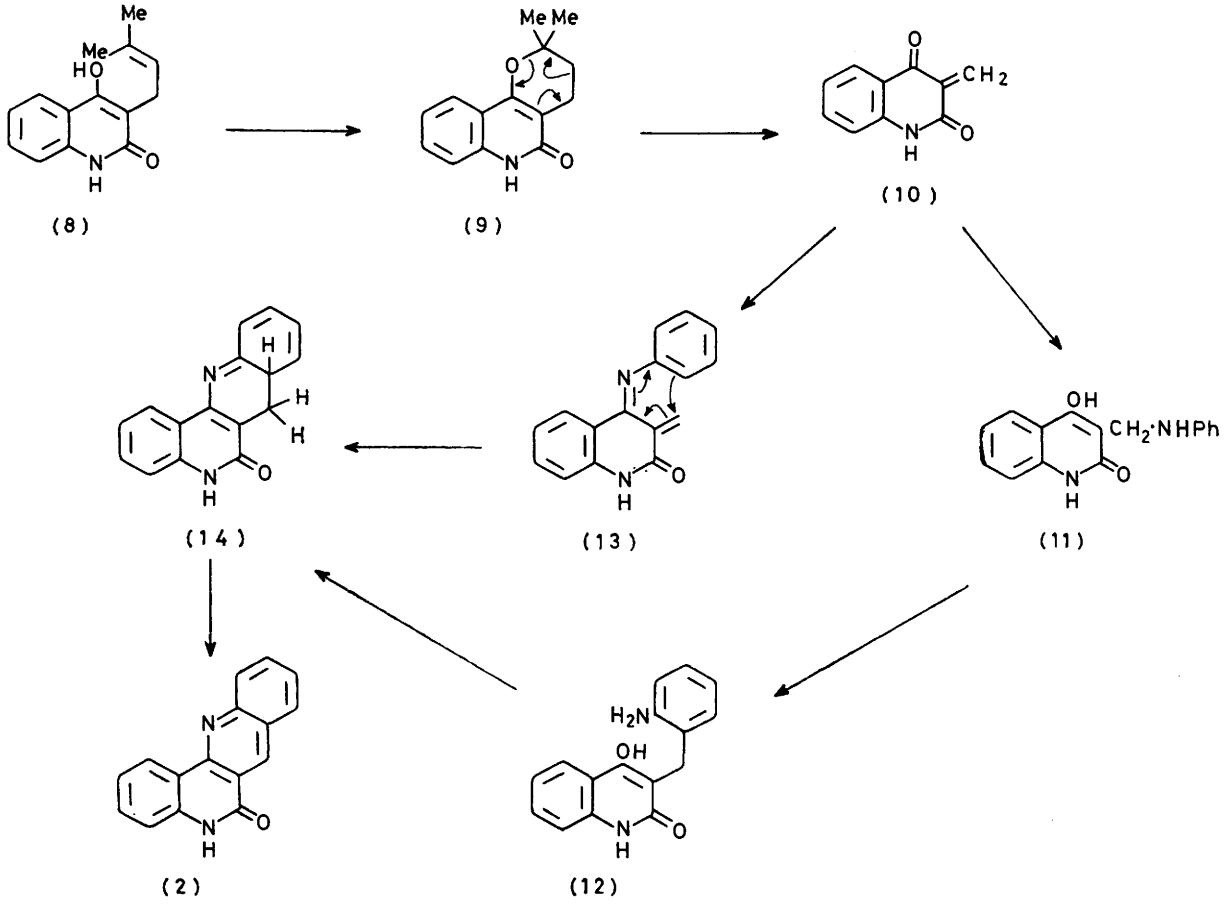
Since in the reaction of diethyl 2-(3-methylbut-2-enyl)malonate with anilines the yields of compounds of type (2) were raised by an increase in the reflux time and further, since reaction of the quinolone (4a) with *ortho*-anisidine gave the tetracyclic compound (2f), it seemed reasonable to assume that the quinolones (4) were intermediates in the reaction. This was supported by the fact that when the compound (1; R = H) was treated with 2,4-dimethoxyaniline in refluxing diphenyl ether the ' mixed ' tetracyclic compound (2g) was obtained.

A possible explanation for the formation of compound (2) in this reaction is suggested in the Scheme. The quinolone (8) might cyclise *via* internal Markownikoff addition of the 4-hydroxy-group to the side-chain olefinic bond to yield the tricyclic derivative (9). This compound might then undergo retro-Diels–Alder reaction at the high temperature of the reaction to yield the ' quinone methide ' type of compound (10). Addition of aniline to this compound should by precedent,[8] yield the Mannich base (11) which might rearrange [9] to the intermediate (12). Alternatively, aniline might add directly to the quinone methide (10) to yield the intermediate (13). The intermediates (12) and (13) would both be capable of cyclisation to the tetracyclic compound (14) which might oxidise readily to (2).

The formation of the 3,3'-methylenebis-4-hydroxy-2-quinolones (7) might also be explained by this Scheme. A retro-Mannich reaction would allow the Mannich base (11) to yield the parent 4-hydroxy-2-quinolone. This might then condense with the ' quinone methide ' (10) to yield the bisquinolone (7).

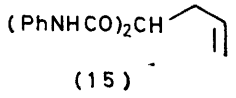
The feasibility of the cyclisation of the quinolone (8) to the tricyclic compound (9) in this Scheme was tested by allowing aniline to react with diethyl 2-(prop-2-enyl)malonate in refluxing diphenyl ether. This reaction had been reported [10] to yield no characterisable products, but we were able to isolate the diphenylmalonamate (15) and a compound with an n.m.r. spectrum completely in accord with the tricyclic structure (16). The absence of a shift to shorter wavelengths in the u.v. spectrum in hexane compared to that in methanol [11,12] and the absence in the n.m.r. spectrum of the low-field C_5 proton [13] which would be expected in the alternative linear 4-quinolone supported this structure. Thus Markownikoff cyclisation had occurred under the reaction conditions. In this case, the direction of cyclisation yielded a five-membered ring and so the

[7] G. R. Clemo and W. H. Perkin, *J. Chem. Soc.*, 1924, **125**, 1608.
[8] A. B. Turner, *Quart Rev.*, 1964, **18**, 347.
[9] See M. J. S. Dewar in ' Molecular Rearrangements,' ed. P. de Mayo, Interscience, New York, 1963, vol. 1, p. 295.
[10] R. H. Baker, G. R. Lappin, and B. Riegel, *J. Amer. Chem. Soc.*, 1946, **68**, 1284.
[11] H. Rapoport and K. G. Holden, *J. Amer. Chem. Soc.*, 1960, **82**, 4395.
[12] J. A. Bosson, M. Rasmussen, E. Ritchie, A. V. Robertson, and W. C. Taylor, *Austral. J. Chem.*, 1963, **16**, 480.
[13] A. V. Robertson, *Austral. J. Chem.*, 1963, **16**, 451.



SCHEME

retro-Diels–Alder reaction and the subsequent reactions in the Scheme were precluded.



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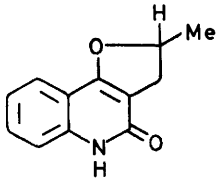

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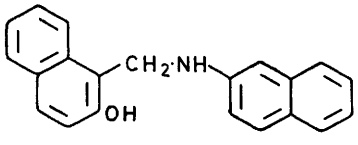

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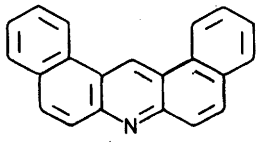

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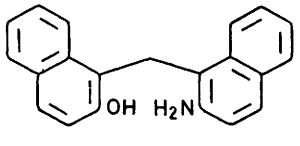

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The sequence of steps in the Scheme from the Mannich base (11) through the intermediate compounds (12) and (14) to (2) has an analogy in the known reaction [14,15] of the Mannich base (17) which yields the dibenzacridine (18) *via* the intermediate compound (19). An attempt was made to stop the reaction sequence at the oxidation level of compound (14) by using *N*-methylaniline in the reaction. The only tetracyclic compound to be isolated from this reaction was the compound (2b). Thermal *N*-demethylation had, therefore, occurred in the reaction. The bisquinolone (7; $R^1 = Me$, $R^2 = H$), was also obtained in this reaction.

We are currently examining the possibility of exploiting this interesting but low-yielding reaction by developing it into a useful and general synthesis of polycyclic heteroaromatic compounds.

EXPERIMENTAL

M.p.s were determined on the Kofler block and are uncorrected. I.r. spectra were recorded on a Perkin-Elmer 237 machine and u.v. spectra on a Unicam SP 800 spectrophotometer. N.m.r. spectra were recorded on Varian T60 and HA100 instruments and mass spectra on Hitachi RMU-6 (low-resolution spectra) and A.E.I. MS9 machines

[14] R. S. Corley and E. R. Blout, *J. Amer. Chem. Soc.*, 1947, **69**, 761.

[15] E. R. Blout and R. S. Corley, *J. Amer. Chem. Soc.*, 1947, **69**, 763.

(high-resolution spectra). We thank Mr. and Mrs. A. G. Olney for microanalyses and Mr. P. Dew and Mr. A. Greenway for n.m.r. and mass spectra respectively.

Reaction of 2,3-*Dimethoxyaniline with Diethyl* 2-(3-*Methylbut-2-enyl*)*malonate*.—Diethyl 2-(3-methylbut-2-enyl)malonate (8.1 g, 35.3 mmol) and 2,3-dimethoxyaniline (5.45 g, 35.6 mmol) were dissolved in redistilled diphenyl ether (70 ml) and heated at reflux under nitrogen for 2.5 h. The reaction mixture was cooled and 4-*hydroxy*-7,8-*dimethoxy*-3-*dimethylallyl*-2-*quinolone* (3.11 g, 31%) separated out of solution. The solution was filtered and hexane was added to the filtrate when a yellow powder (526 mg, 4%) separated out. This was filtered off, washed with water, and recrystallised from glacial acetic acid as yellow needles (374 mg), m.p. 248—249 °C (Found: C, 65.55; H, 5.1; N, 7.6. $C_{20}H_{18}N_2O_5$ requires C, 65.55; H, 4.95; N, 7.65%), *m/e* 366 (M^+); $\nu_{max.}$ (Nujol) 3 180 (NH), 1 710, and 1 640 cm^{-1}; $\nu_{max.}$ ($CHCl_3$) 3 380 (NH) and 1 665 cm^{-1} (amide); $\lambda_{max.}$ (MeOH) 216, 232sh, 252, 262sh, 295sh, 301, and 358 nm (log ε 4.49, 4.34, 4.45, 4.29, 4.59 4.60, and 3.78); $\lambda_{max.}$ (H^+–MeOH) 219, 235sh, 250, 277, 306, 316, and 424 nm (log ε 4.58, 4.47, 4.29, 4.42, 4.35, 4.37, and 4.26); τ ($CDCl_3$) 0.88 [1 H, s, H_B in (2)], 1.40 [1 H, d, *J* 9.5 Hz, H_A in (2)], 2.31, 2.68, and 3.13 (all 1 H, d, *J* = 9.5 Hz, *ortho*-coupled ArH), 5.80 (3 H, s, OMe), 6.00 (3 H, s, OMe), and 6.08 (6 H, s, OMe). An NH proton absorption at τ 1.16 was exchangeable with D_2O. The compound was concluded to be 3,4,10,11-*tetramethoxydibenzo*[b,h][1,6]*naphthyridin*-6(5H)-*one* (2a).

Methylation of 3,4,10,11-*Tetramethoxydibenzo*[b,h][1,6]-*naphthyridin*-6(5H)-*one* (2a).—The tetracyclic product from the above reaction (60 mg, 0.164 mmol) was suspended in dry benzene (18 ml) with sodium hydride (15 mg) in an atmosphere of dry nitrogen. The mixture was heated to reflux with stirring for 3 h and dry methyl iodide (3 ml) in dimethylformamide (5 ml) was added. The mixture was heated for a further 5 h at reflux under nitrogen and then cooled and poured into a mixture of ice–water. The mixture was extracted thoroughly with chloroform. The extracts were dried (Na_2SO_4) and the solvent was removed *in vacuo* to yield a yellow solid (56 mg, 90%) which was crystallised from 95% ethanol as yellow needles, m.p. 169—170 °C (Found: C, 66.0; H, 5.4; N, 7.05. $C_{21}H_{20}N_2O_5$ requires C, 66.3; H, 5.3; N, 7.35%), *m/e* 380 (M^+); $\nu_{max.}$ (Nujol) 1 655 cm^{-1} (amide); $\lambda_{max.}$ (MeOH) 225, 236sh, 257, 303, 363, and 374 nm (log ε 4.27, 4.17 4.26, 4.44, 3.65, and 3.65); $\lambda_{max.}$ (H^+–MeOH) 223, 240sh, 279, 307, 321sh, and 429 nm (log ε 4.35, 4.27, 4.22, 4.22, 4.16, and 3.93); τ ($CDCl_3$) 0.90 [1 H, s, H_B in (2)], 1.13, 2.26, 2.65, and 3.01 (each 1 H, d, *J* = 9 Hz, *ortho*-coupled ArH), 5.76, 5.93, and 6.18 (each 3 H, s, OMe or NMe), and 6.01 (6 H, s, OMe or NMe).

Treatment of 3,4,10,11-*Tetramethoxydibenzo*[b,h][1,6]-*naphthyridin*-6(5H)-*one* (2a) *with* $POCl_3$.—Compound (2a) (20 mg, 0.055 mmol) and $POCl_3$ (2 ml) were heated together for 2 h during which time the temperature of the oil-bath was raised to 125 °C. Heating was continued at this temperature for a further 30 min and then excess of $POCl_3$ was removed *in vacuo*. The resultant red glass was dissolved in chloroform and added to a mixture of ice (15 g) and 5% aqueous ammonia solution (25 ml). The mixture was stirred well and the colour of the chloroform layer changed from red to yellow. The chloroform layer was separated off and the remaining aqueous layer was extracted well with chloroform. The combined chloroform layers were dried (Na_2SO_4) and the solvent was removed *in vacuo* to yield an orange semi-solid, which appeared as one spot on t.l.c., $\nu_{max.}$ ($CHCl_3$) 1618 and 1598 cm^{-1} (Ar); $\lambda_{max.}$ (MeOH) 243, 251, 270, 294, 310sh, and 392 nm; λ(H^+–MeOH) 242, 250sh, 300sh, and 410 nm. The mass spectrum had parent ions at *m/e* 383 and 385 of intensity ratio 3 : 1 as expected for compound (3); τ ($CDCl_3$) 0.93 (1 H, s, ArH), 1.03, 2.16, 2.54, and 2.61 (each 1 H, d, *J* = 9 Hz, *ortho*-coupled ArH), and 5.69, 5.84, 5.90, and 5.95 (each 3 H, s, OMe).

Reaction of Aniline and Diethyl 2-(3-*Methylbut-2-enyl*)-*malonate*.—Diethyl 2-(3-methylbut-2-enyl)malonate (2.9 g, 12.7 mmol) and aniline (redistilled; 7 g, 75.3 mmol) were heated in diphenyl ether (30 ml) at reflux for 15 h. The diphenyl ether was removed by distillation *in vacuo* and the residue was treated with dichloromethane. The insoluble material was a high-melting solid, m.p. >350 °C, with an i.r. spectrum identical to that of a sample of 3,3′-*methylenebis*-4-*hydroxy*-2-*quinolone* (7; $R^1 = R^2 = H$) prepared by the method of Menzer *et al.*[16] The dichloromethane solution was evaporated to dryness and the resultant material was dissolved in glacial acetic acid. With time crystals of *dibenzo*[b,h][1,6]*naphthyridin*-6(5H)-*one* (2e) separated out. This compound was purified by sublimation *in vacuo* (46 mg, 1.5%), m.p. 329—330 °C (Found: C, 78.2; H, 4.5; N, 11.55. $C_{16}H_{10}N_2O$ requires C, 78.05; H, 4.1; N, 11.4%); $\nu_{max.}$ (Nujol) 1 670 cm^{-1}; $\lambda_{max.}$ (MeOH) 265sh, 273 and 287 nm (log ε 4.30, 4.50, and 4.09); $\lambda_{max.}$ (H^+) 260sh, 273, 288, 299, and 358 nm (log ε 4.0, 4.13, 4.05, 4.0, and 2.99; τ [$(CD_3)_2SO$] 0.7 (1 H, s, ArH), 1.21 (1 H, d, *J* = 7 Hz, ArH) and 1.65—2.80 (m, ArH).

In one such experiment, refluxing the above mixture for 18 h gave a good yield [4.01 g from 2.9 g of diethyl 2-(3-methylbut-2-enyl)malonate] of a compound which crystallised from methanol, m.p. 184—186 °C (Found: C, 75.0; H, 7.0; N, 8.4. $C_{20}H_{22}N_2O_2$ requires C, 74.5; H, 6.9; N, 8.7%); $\nu_{max.}$ 1 670 cm^{-1}; τ ($CDCl_3$) 0.78 (2 H, s, NH), 2.36—2.96 (10 H, m, ArH), 4.82 (1 H, t, *J* = 7.5 Hz, olefinic), 6.58 (1 H, t, *J* = 7.5 Hz, COCHCO), 7.23 (2 H, t, *J* = 7.5 Hz, allylic CH_2), 8.36 and 8.40 (6 H, 2 × s, Me). This was evidently 2-(3-*methylbut*-2-*enyl*)*malondianilide* (5).

Methylation of Dibenzo[b,h][1,6]*naphthyridin*-6(5H)-*one*.—Dibenzo[*b*,*h*][1,6]naphthyridin-6(5*H*)-*one* (60 mg, 0.24 mmol) was suspended in dry benzene (18 ml) and heated with a 60% dispersion of sodium hydride in mineral oil (10 mg) in an atmosphere of nitrogen for 3 h at reflux. Dry dimethylformamide (5 ml) and dry methyl iodide (6 ml) were added and heating was continued for a further 5 h at reflux. The cooled mixture was poured into ice–water and extracted with chloroform. The extracts were dried (Na_2SO_4) and the solvent was removed *in vacuo* to yield a solid which recrystallised from aqueous ethanol (46 mg), m.p. 224—225 °C (lit.,[2] m.p. 218 °C), $\nu_{max.}$ (Nujol) 1 650 cm^{-1} (amide); $\lambda_{max.}$ (MeOH) 230, 266sh, 275, 290, and 301sh nm (log ε 4.58, 4.64, 4.76, 4.34, and 4.19); $\lambda_{max.}$ (H^+) 230, 257, 275, 285, 300, and 360 nm (log ε 4.58, 4.37, 4.43, 4.33, 4.24, and 3.79); τ ($CDCl_3$) 0.66 [1 H, s, H_B in (2)], 0.90 [1 H, dd, *J* 8 and 2 Hz, H_A in (2)], 1.72 [1 H, d, *J* = 8 Hz, Ar], 1.94 (1 H, d, *J* = 8 Hz, Ar), 2.0—2.7 (5 H, ArH), and 6.15 (3 H, s, NMe).

Permangamate Oxidation of 5,6-*Dihydrodibenzo*[b,h][1,6]-*naphthyridine* (6).—5,6-Dihydrodibenzo[*b*,*h*][1,6]naphthyridine[7] (400 mg, 1.72 mmol) was dissolved in acetone

[16] C. Menzer, P. Meunier, J. LeCocq, and D. Billet, *Bull. Soc. chim. France*, 1945, **12**, 430.

(minimum) and a small excess of a saturated solution of potassium permanganate was added dropwise to the solution. This mixture was shaken for 1 h and then filtered; the residue was then further extracted with boiling acetone. The acetone solutions were combined and the solvent was removed *in vacuo* to yield a solid which crystallised from acetone as cream needles (373 mg, 93%). This compound had all the characteristics of *dibenzo*[b,h][1,6]*naphthyridine*, with m.p. 186—187 °C (reported [7] m.p. 186—187 °C), $\nu_{max.}$ (Nujol) 1 600 cm^{-1} (Ar), *m/e* 230 (M^+), τ ($CDCl_3$) 0.71 (1 H, s, Ar), 1.28 (1 H, s, Ar), and 1,6—1.8 (8 H, Ar).

Oxidative Methylation of 5,6-*Dihydrodibenzo*[b,h][1,6]-*naphthyridine* (6).—5,6-Dihydrodibenzo[*b,h*][1,6]naphthyridine [7] (60 mg, 0.26 mmol) was suspended in dry benzene (18 ml). A 60% dispersion of sodium hydride in mineral oil (10 mg) was added to the suspension which was then heated to reflux in an atmosphere of nitrogen for 3 h. Dry dimethylformamide (5 ml) and dry methyl iodide (5 ml) were added. Reflux was continued for a further 5 h. The mixture was cooled, poured into ice–water, and extracted with chloroform. The extracts were dried (Na_2SO_4) and the solvent was removed *in vacuo* to yield a solid which was recrystallised from aqueous ethanol (20 mg, 30%), m.p. 224—225 °C. The spectra of this compound were identical to those of the product from methylation of dibenzo[*b,h*]-[1,6]naphthyridin-6(5*H*)-one. When the reaction was attempted in the absence of a nitrogen atmosphere, intractible gums were obtained.

Reaction of ortho-*Anisidine with Diethyl* 2-(3-*Methylbut*-2-*enyl*)*malonate*.—*ortho*-Anisidine (2.94 g, 23.9 mmol) and diethyl 2-(3-methylbut-2-enyl)malonate (5.55 g, 24.3 mmol) were dissolved in diphenyl ether and the mixture was heated at reflux for 3 h in an atmosphere of nitrogen. 4-*Hydroxy*-8-*methoxy*-3-*dimethylallyl*-2-*quinolone* (670 mg, 11%) precipitated from the solution on cooling. This was recrystallised from ethanol, m.p. 224—228 °C (lit.,[2] m.p. 228—230 °C), $\lambda_{max.}$ (MeOH) 244, 250, 279, 287, and 320 nm (lit.,[2] $\lambda_{max.}$ 243, 250, 280, 288, and 320 nm). The diphenyl ether-soluble material was refluxed for a further 3 h when further material (3.4 g) was obtained by precipitation. Recrystallisation from ethanol gave ethanol-insoluble material (64 mg), *m/e* 394, with an i.r. spectrum identical to that of a sample of 3,3′-*methylenebis*-4-*hydroxy*-8-*methoxy*-2-*quinolone* (7; R^1 = H, R^2 = OMe) obtained by independent synthesis. The ethanol-soluble material yielded a further sample of the quinoline (4b) (3.12 g).

Reaction of 4-*Hydroxy*-8-*methoxy*-3-*dimethylallyl*-2-*quinolone with* ortho-*Anisidine*.—The 2-quinolone (4b) (500 mg, 1.93 mmol) and *ortho*-anisidine (240 mg, 1.95 mmol) were refluxed in dry diphenyl ether (5 ml) in an atmosphere of nitrogen for 7 h. On cooling, the bisquinolone (7; R^1 = H, R^2 = OMe) (104 mg) separated out. This insoluble solid, m.p. > 350 °C (*m/e* 394) (Found: C, 63.75; H, 5.0; N, 7.0. $C_{21}H_{18}N_2O_6$ requires C, 63.95; H, 4.6; N, 70%), had an i.r. spectrum identical with a sample prepared by independent synthesis. The diphenyl ether was removed *in vacuo* from the filtrate and the resultant mixture was dissolved in chloroform. The solution was washed well with 2N-aqueous sodium hydroxide and water and dried (Na_2SO_4). The solvent was removed *in vacuo* to yield a solid which was subjected to preparative t.l.c. and sublimed to yield the tetracyclic compound (2f), m.p. 271—273 °C (Found: C, 70.35; H, 4.9; N, 8.8. $C_{18}H_{14}N_2O_3$ requires C, 70.6; H, 4.6; N, 9.15%), $\nu_{max.}$ (Nujol) 1 665 cm^{-1} (amide); $\lambda_{max.}$ (MeOH) 226, 244, 252, 293, and 356 nm (log ε 4.47, 4.48, 4.47, 4.61, and 3.76); $\lambda_{max.}$ H^+–MeOH) 226, 240, 255, 293, 312, and 376 nm (log ε 4.43, 4.41, 4.41, 4.47, 4.07, and 3.86); τ [$(CD_3)_2SO$] 0.78 (1 H, s, H_B), 2—3 (6 H, Ar), 5.91 (3 H, s, OMe), and 6.05 (3 H, s, OMe).

Synthesis of 3,3′-*Methylenebis*-4-*hydroxy*-8-*methoxy*-2-*quinolone* (7; R^1 = H, R^2 = OMe).—4-Hydroxy-8-methoxy-2-quinolone (1 g, 2.55 mmol) was dissolved in boiling water (70 ml) and 40% aqueous formaldehyde solution (5 ml) was added to it. The mixture was heated at reflux for 2 min. The product precipitated on cooling and was washed well with ethanol and dried. The resultant solid (450 mg), m.p. >350 °C, $\nu_{max.}$ (Nujol) 1 650 cm^{-1}, was extremely insoluble in most solvents.

Pyrolysis of 2-(3-*Methylbut*-2-*enyl*)*malondianilide* (5).—2-(3-Methylbut-2-enyl)malondianilide (5) (1 g, 3.1 mmol) was heated in an atmosphere of nitrogen at 260 °C without solvent for 4.5 h. The resultant product was dissolved in ethanol to leave the insoluble dibenzo[*b,h*][1,6]naphthyridin-6(5*H*)-one (2e) (80 mg, 10.5%). The ethanol-soluble portion of the product proved to be a mixture of unchanged dianilide and 3-dimethylallyl-4-hydroxy-2-quinolone (4a).

Reaction of 4-*Hydroxy*-7,8-*dimethoxy*-3-(3-*methylbut*-2-*enyl*)-2-*quinolone* (1; R = H) *with* 2,4-*Dimethoxyaniline*.—4-Hydroxy-7,8-dimethoxy-3-(3-methylbut-2-enyl)-2-quinolone (110 mg, 0.397 mmol) and 2,4-dimethoxyaniline (55 mg, 0.359 mmol) were dissolved in diphenyl ether (5 ml) and heated at reflux for 7 h in an atmosphere of dry nitrogen. The reaction mixture was cooled and hexane (5 ml) was added to precipitate a solid which was washed with hexane and recrystallised from glacial acetic acid. This solid was dissolved in chloroform and the solution washed with 2N-sodium hydroxide and water and then dried (Na_2SO_4). The solvent was removed *in vacuo* to yield compound (2g), a yellow solid (5 mg) which separated from 95% ethanol as yellow plates, m.p. 275—277 °C (Found: *m/e* 366.119 28. $C_{20}H_{18}N_2O_5$ requires *M*, 366.121 56), $\nu_{max.}$ ($CHCl_3$) 3 370 (NH) and 1 665 cm^{-1} (amide); $\lambda_{max.}$ (MeOH) 235sh, 253, 263, 300, 345s, and 410 nm; $\lambda_{max.}$ (H^+–MeOH) 234sh, 251, 280, 308, 332, 388, and 466 nm; τ($CDCl_3$) 0.94 (1 H, s, H_B in 2), 1.08 (1 H, exchangeable with D_2O, NH), 1.43 (1 H, d, *J* 9 Hz, Ar), 2.48 (1 H, Ar), 3.06 (1 H, d, *J* 8 Hz, Ar), 3.16 (1 H, Ar), 5.92, 6.03, 6.05, and 6.09 (all 3 H, s, OMe).

Reaction of Diethyl 2-(*Prop*-2-*enyl*)*malonate with Aniline*.—Diethyl 2-(prop-2-enyl)malonate (5 g, 25 mmol) and aniline (2.32 g, 25 mmol) were dissolved in diphenyl ether (50 ml) and refluxed for 12 h in an atmosphere of nitrogen. At this point a solid precipitated out on cooling and this proved to be 2-(*prop*-2-*enyl*)*malondianilide*, (15), m.p. 199—201 °C (Found: C, 73.15; H, 6.35; N, 9.4. $C_{18}H_{18}N_2O_2$ requires C, 73.45; H, 6.15; N, 9.5%). Reflux was therefore continued for a further day. Light petroleum (b.p. 60—80 °C) was added to the solution when the *tricyclic compound* (16) * was precipitated as a solid (1.25 g, 25%). This product was triturated with diethyl ether and recrystallised from acetone, m.p. 232 °C (Found: C, 71.25; H, 5.9; N, 6.2. $C_{12}H_{11}NO_2$ requires C, 71.6; H, 5.5; N, 6.9%), *m/e* 201, $\lambda_{max.}$ (MeOH) 279, 290, 315, and 326 nm, $\lambda_{max.}$ (cyclohexane) 280, 292, 319, and 333 nm; τ ($CDCl_3$) −1.92 (1 H, s,

* This compound (m.p. 233 °C) has been prepared by an independent method.[17] We thank Professor Kappe for bringing this work to our attention.

[17] T. Kappe, P. F. Fritz, and E. Ziegler, *Chem. Ber.*, 1973, **116**, 1927.

NH, exchangeable with D_2O), 2.25—2.9 (4 H, m, Ar), 4.75 (1 H, m, C*H*), 6.57 and 7.12 (2 H, AB, J_{AB} 15 Hz, J_{AX} 10 Hz, J_{BX} 7 Hz, CH_2), and 8.43 (3 H, d, J 6 Hz, Me).

Reaction between N-*Methylaniline and Diethyl* 2-(3-*methylbut*-2-*enyl*)*malonate*.—*N*-Methylaniline (1 g, 9.34 mmol) and diethyl 2-(3-methylbut-2-enyl)malonate (1 g, 4.4 mmol) were dissolved in dry diphenyl ether (6 ml) and refluxed for 14 h in an atmosphere of nitrogen. The solvent was removed *in vacuo*. The resulting material was triturated with light petroleum and digested in boiling ethanol. The ethanol-insoluble material, m.p. 300—302 °C (270 mg), had an i.r. spectrum identical to that of *NN'-dimethyl*-3,3'-*methylenebis*-4-*hydroxy*-2-*quinolone* (7; R^1 = Me, R^2 = H) prepared by an independent method. The ethanol-soluble material was recrystallised from ethanol and proved to be 5-*methyldibenzo*[b,h][1,6]*naphthyridin*6(5H)-*one* (2b) identical with an authentic specimen (*vide infra*) in all respects.

NN-*Dimethyl*-3,3'-*methylenebis*-4-*hydroxy*-2-*quinolone* (7; R^1 = Me, R^2 = H).— 4-Hydroxy-*N*-methyl-2-quinolone (200 mg) was added to water (50 ml) and boiled for 5 min with 40% aqueous formaldehyde solution (excess). The solution was cooled and the resultant precipitate was washed well with ethanol to yield a white solid (120 mg), m.p. 300—302 °C [Found: C, 69.1; H, 5.4; N, 7.75. $C_{21}H_{18}N_2O_4$ requires C, 69.6; H, 5.0; N, 7.75%), *m/e* 362, $\nu_{max.}$ (Nujol) 1 645 cm^{-1} (amide).

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