# Sterically Hindered *N*-Aryl-2(1*H*)-Quinolones and *N*-Aryl-6(5*H*)-Phenanthridinones: Separation of Enantiomers and Barriers to Racemization

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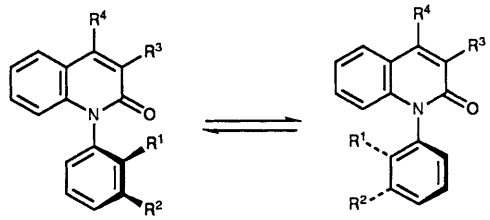
The novel *N*-aryl-4-chloro-3-methyl-2(1*H*)-quinolones (**1**)–(**4**) have been synthesized by condensation of the appropriate diphenylamine with diethyl methylmalonate and subsequent chlorination of the resulting *N*-aryl-4-hydroxy-3-methyl-2(1*H*)-quinolones (**7**)–(**10**). 5-(1-Naphthyl)-6(5*H*)-phenanthridinone (**5**) has been synthesized by the Chapman rearrangement of the 6-(1-naphthoxy)phenanthridine (**11**). Separation of the enantiomers (*M*) and (*P*) of the quinolones (**1**)–(**4**) and phenanthridinones (**5**), (**6**) was achieved by liquid chromatography on triacetylcellulose. The barriers to partial rotation about the C–N bond in (**1**)–(**6**) were determined by thermal racemization of enantiomers and are compared with those of structurally related molecules.

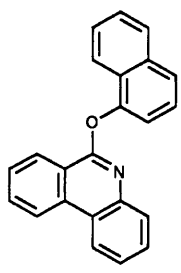
Compared with the numerous classical studies on the separation of enantiomers of biphenyl derivatives and their rate of racemization,[1] relatively few similar studies have been published on heterocyclic analogues of biphenyl.[2] Bock and Adams[3] showed in 1931 that *N*-(2-carboxyphenyl)-2,5-dimethylpyrrole-3-carboxylic acid is chiral due to restricted rotation about the C–N bond between the aryl and pyrrole rings. Kashima and Katch[4] succeeded in resolving the rotational isomers of *ortho*- substituted 1-aryl-4,6-dimethylpyrimidin-2(1*H*)-ones and the corresponding thiones. In both cases the separation of enantiomers was achieved *via* formation of diastereoisomeric salts. A prerequisite for the application of this method is the presence of special functional groups (*e.g.* $CO_2H$) in the molecule. However, it has been shown that liquid chromatography on triacetylcellulose (TAC) is a versatile alternative method for the separation of enantiomers[5] as it does not depend on the presence of a special functional group on the molecule. Liquid chromatography has been successfully applied to the separation of the enantiomers of *N*-aryl-Δ-4-thiazoline-2-thiones[6] and compounds of pharmaceutical interest, *e.g.* the anaesthetic ketamine,[5] the tranquilizer etaqualone[5] and the anthelmintic praziquantel.[5] The present study has precedent in the work of Shinkai *et al.*[7] on resolution of atropisomeric flavins with restricted rotation about the C–N bond by liquid chromatography on a chiral stationary phase. In connection with our previous studies on some *N*-aryl-4-pyridones,[8] *N*-arylpyrroles,[9] and methaqualone[10] an anticonvulsive and hypnotic agent, we have studied sterically hindered *N*-aryl-2(1*H*)-quinolones (**1**)–(**4**) and *N*-arylphenanthridin-6(5*H*)-ones (**5**), (**6**) (Scheme).

Because of restricted rotation about the C–N bond the ground state of compounds (**1**)–(**6**) is non-planar, which gives rise to chirality. The principal aim of this study was to separate enantiomers (*M*) and (*P*) of (**1**)–(**6**) by liquid chromatography on TAC in order to study substituent effects upon the barriers to racemization.




| | $R^1$ | $R^2$ | $R^3$ | $R^4$ |
|---|---|---|---|---|
| (**1**) | F | H | Me | Cl |
| (**2**) | Cl | H | Me | Cl |
| (**3**) | Me | H | Me | Cl |
| (**4**) | OMe | H | Me | Cl |
| (**5**) | Benzo | | Benzo | |
| (**6**) | Me | H | Benzo | |

**Scheme.**




(**11**)

## Results

*Synthetic Work.*—The desired novel *N*-aryl-4-chloro-3-methyl-2(1*H*)-quinolones (**1**)–(**4**) were obtained by the condensation of a suitable diphenylamine containing an *ortho*-substituent in one phenyl group with diethyl methylmalonate by a general procedure described by Kappe[11] and subsequent chlorination[12] of the resulting *N*-aryl-4-hydroxy-3-methyl-2(1*H*)-quinolones (**7**)–(**10**) (Table 1). The yields varied from 14–24%.[13] 5-(1-Naphthyl)phenanthridin-6(5*H*)-one (**5**) was prepared by use of the Chapman rearrangement[14] at 335–350 °C of the 6-(1-naphthoxy)phenanthridine (**11**). This intermediate was obtained from the 6-chlorophenanthridine[15] which in turn was prepared by treatment of the starting fluorenone with sodium azide in concentrated sulphuric acid (a reaction which has been described by Schmidt[16]) and subsequent chlorination[15] of the

**Table 1.** Analytical and spectroscopic data.

| Compd. | Formula | M.p./°C | Found(%) Required C | H | N | $\nu_{C=O}$/cm$^{-1}$ [c] | $\lambda_{max}$/nm [d](log ε) |
|---|---|---|---|---|---|---|---|
| (1) | $C_{16}H_{11}ClFNO$ | 218–220 [a] | 66.53 | 3.73 | 4.97 | 1 645s | 343sh (3.52) 328 (3.73) 317sh (3.64) |
| | | | 66.79 | 3.85 | 4.87 | | 282sh (3.78) 273 (3.85) |
| (2) | $C_{16}H_{11}Cl_2NO$ | 154–155 [a] | 62.65 | 4.53 | 4.67 | 1 645s | 342sh (3.57) 328 (3.77) 315sh (3.70) |
| | | | 62.56 | 4.59 | 4.56 | | 282sh (3.82) 273 (3.89) |
| (3) | $C_{17}H_{14}ClNO$ | 142–144 [a] | 72.21 | 4.72 | 5.18 | 1 650s | 341sh (3.61) 328 (3.78) 315sh (3.67) |
| | | | 71.96 | 4.97 | 4.94 | | 280sh (3.81) 272 (3.88) |
| (4) | $C_{17}H_{14}ClNO_2$ | 174–176 [a] | 68.22 | 4.77 | 4.65 | 1 643s | 345sh (3.56) 330 (3.74) 320sh (3.67) |
| | | | 68.11 | 4.71 | 4.67 | | 280sh (3.90) 276 (3.89) |
| (7) | $C_{16}H_{12}FNO_2$ | 293–295 [b] | 71.43 | 4.55 | 5.00 | 1 630sh | 327sh (3.73) 315 (3.84) 305sh (3.74) |
| | | | 71.37 | 4.49 | 5.20 | | 286 (3.89) 276 (3.89) |
| (8) | $C_{16}H_{12}ClNO_2$ | 262–264 [b] | 67.21 | 4.48 | 4.77 | 1 625sh | 327sh (3.79) 315 (3.91) 305sh (3.74) |
| | | | 67.26 | 4.23 | 4.90 | | 285 (3.95) 273 (3.94) |
| (9) | $C_{17}H_{15}NO_2$ | 220–222 [b] | 76.72 | 5.85 | 5.37 | 1 630m | 327sh (3.71) 315 (3.83) 305sh (3.71) |
| | | | 76.96 | 5.70 | 5.28 | | 284 (3.91) 274 (3.89) |
| (10) | $C_{17}H_{15}NO_3$ | 231–233 [b] | 72.45 | 5.42 | 4.88 | 1 630s | 327sh (3.76) 315 (3.84) 303sh (3.70) |
| | | | 72.58 | 5.38 | 4.98 | | 278sh (4.00) 273 (4.02) |

[a] From EtOH–ethyl acetate (1:1). [b] From EtOH–$H_2O$ (96:4). [c] In KBr. [d] In absolute EtOH.

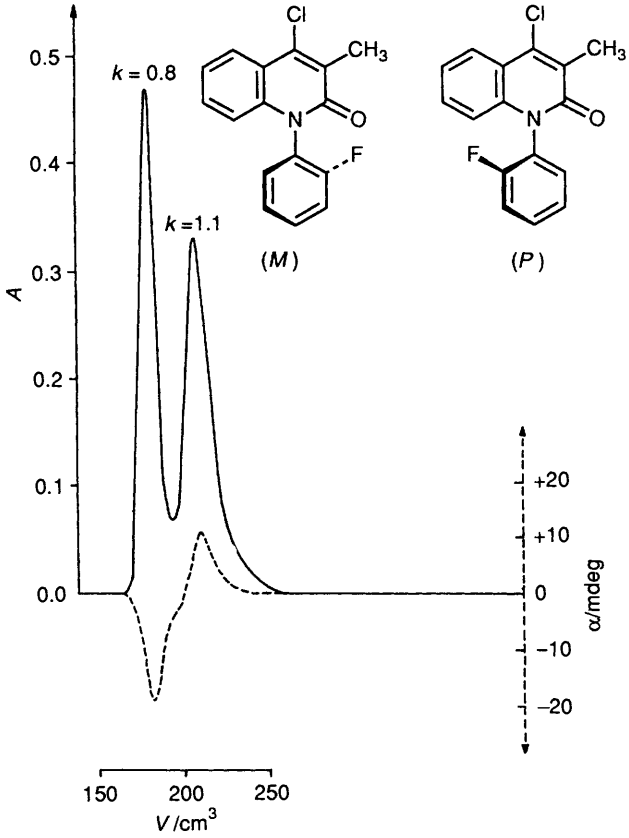
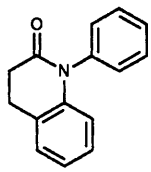



**Figure.** Chromatogram of (*MP*)-(**1**) in EtOH:$H_2O$ (96:4) after chromatography through a column of triacetylcellulose (particle size 0.02–0.03 mm). (----) Rotation angle (α) at 365 nm; (————) Absorbance (*A*) at 278 nm; V, volume of eluate; *k*, capacity factor.[5]

resulting phenanthridin-6(5*H*)-one.[16] Although the total yield of this four-step route was low (4%), the last rearrangement step proceeded surprisingly smoothly. (±)-5-(2-Methylphenyl)-phenanthridin-6(5*H*)-one, [(±)-(**6**)],[17,18] required for this study was obtained from Prof. R. M. Acheson, Oxford, UK.

$^1$H *NMR Studies.*—In order to prove structures of the quinolones (**1**)–(**4**) and (**7**)–(**10**), and phenanthridinones (**5**)–(**6**) their $^1$H NMR spectra were examined in detail. The spectral assignments are given in Table 2. The spectra of the quinolones (**1**)–(**4**) and (**7**)–(**10**) showed the close similarity of all comparable signals through the series. The diagnostic quinoline signal[19] $H^c$ appears in all spectra at high field (δ 6.4–6.7) owing to shielding by the *N*-aryl substituent. The $H^b$ signal occurs at a lower field (δ 8.0–8.1) than $H^c$ due to the proximity of $H^b$ to the chlorine atom and hydroxy group in compounds (**1**)–(**4**) and (**7**)–(**10**), respectively. These assignments are in good agreement with structurally related molecules such as 3-substituted 1-phenyl-2-quinolones,[19] 4-hydroxy-1-methyl-3-phenyl-1,2-dihydroquinolin-2-one,[11] and 1-hydroxy-2-phenyl-6,7-dihydro-5*H*-benzo[*i,j*]quinolizin-3-one.[11] In the spectra of phenanthridinones (**5**) and (**6**) (Table 2) the high field position of the proton $H^c$ [δ 6.5 and 6.6 in (**5**) and (**6**), respectively] may be again, as in the case of quinolones (**1**)–(**4**) and (**7**)–(**10**), rationally explained by the anisotropic effect of the adjacent aryl group. Comparison with the $^1$H NMR spectrum of 1-phenyl-3,4-dihydroquinolin-2(1*H*)-one[20] (**12**) in which aromatic protons appear at δ 6.2–7.3 is consistent with this assignment.

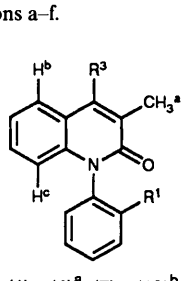



(**12**)

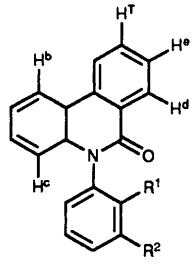
The fact that no aromatic protons have been observed in the region below δ 7.35 in the *N*-alkyl substituted phenanthridinone[21] where the aryl group has been replaced by an alkyl group, is also in accord with our assignment. Proton $H^d$ (δ 8.6 in (**5**) and (**6**) appears at a lower field than protons $H^e$ (δ 7.6 in (**6**) and $H^f$ [δ 7.9 and 7.8 in (**5**) and (**6**), respectively] due to the deshielding effect of the adjacent carbonyl oxygen.

*Separation and Racemization of Enantiomers.*—The enantiomers of (**1**)–(**6**) were separated analytically by liquid chromatography on TAC. An almost complete separation of enantiomers was achieved for (*MP*)-(**1**) as can be seen from the analytical chromatogram (Figure) showing only a small overlap of the enantiomer peaks. Capacity factors,[5,22] which correspond to stabilities of diastereoisomeric sorbates, and relative reten-

**Table 2.** Values of $\delta_H$ (ppm) and $J$/Hz for protons a–f.




(1)—(4)[a], (7)—(10)[b]




(5), (6)[a]

| | R[1] | R[2] | R[3] | a | b | c | d | e | f | Aromatic |
|---|---|---|---|---|---|---|---|---|---|---|
| (1) | F | H | Cl | 2.4 (s) | 8.0–8.1 (m) | 6.7–6.8 (m) | — | — | — | 7.3–7.6 (m) |
| (2) | Cl | H | Cl | 2.4 (s) | 8.0–8.1 (m) | 6.5–6.6 (m) | — | — | — | 7.2–7.7 (m) |
| (3) | Me 2.0 (s) | H | Cl | 2.4 (s) | 8.0–8.1 (m) | 6.5–6.6 (m) | — | — | — | 7.1–7.5 (m) |
| (4) | OMe 3.7 (s) | H | Cl | 2.4 (s) | 8.0–8.1 (m) | 6.6–6.7 (m) | — | — | — | 7.1–7.6 (m) |
| (5) | Benzo 8.0; 8.1 (2d) $^3J$ = 8.2 and 8.3 Naphthyl 2H | | | — | — | 6.5 (dd) $^3J$ = 7.9 $^4J$ = 1.3 | 8.6 (ddd)[c] $^3J$ = 8.0 $^4J$ = 1.5 $^5J$ = 0.5 | — | 7.9 (ddd)[c] $^3J$ = 8.3 and 7.1 $^4J$ = 1.5 | 7.2–7.6 and 7.6–7.7 (m) 8H; 8.3–8.4 (m) 2H |
| (6) | Me 2.1 (s) | H | | — | — | 6.6 (m) | 8.6 (ddd)[c] $^3J$ = 8.0 $^4J$ = 1.5 $^5J$ = 0.5 | 7.6 (ddd)[c] $^3J$ = 7.1 and 8.0 $^4J$ = 1.1 | 7.8 (ddd)[c] $^3J$ = 7.1 and 8.3 $^4J$ = 1.5 | 7.2–7.5 (m) 6H 8.3–8.4 (m) 2H |
| (7) | F | H | OH 10.7 (br s) | 2.1 (s) | 8.1 (dd) $^3J$ = 7.7 $^4J$ = 1.8 | 6.3 (dd) $^3J$ = 7.0 $^4J$ = 1.0 | — | — | — | 7.1–7.6 (m) |
| (8) | Cl | H | OH 10.3 (br s) | 2.1 (s) | 8.1 (dd) $^3J$ = 7.5 $^4J$ = 1.8 | 6.3 (dd) $^3J$ = 7.7 $^4J$ = 1.4 | — | — | — | 7.1–7.7 (m) |
| (9) | Me 1.9 (s) | H | OH 10.3 (br s) | 2.1 (s) | 8.1 (dd) $^3J$ = 7.4 $^4J$ = 1.8 | 6.4 (dd) $^3J$ = 8.1 $^4J$ = 1.4 | — | — | — | 7.1–7.5 (m) |
| (10) | OMe 3.0 (s) | H | OH 10.3 (br s) | 2.1 (s) | 8.0 (dd) $^3J$ = 7.3 $^4J$ = 2.1 | 6.4 (dd) $^3J$ = 7.9 $^4J$ = 1.5 | — | — | — | 7.1–7.6 (m) |

[a] Taken in $CDCl_3$. [b] Taken in DMSO. [c] Probable assignment.

**Table 3.** Chromatographic parameters for separation of enantiomers by liquid chromatography on TAC.[a]

| | R[1] | R[2] | $k'_1$ (Y)[c] | $k'_2$[b] | $\alpha$[d] |
|---|---|---|---|---|---|
| (*MP*)-(1) | F | H | 0.8 (−) | 1.1 | 1.4 |
| (*MP*)-(2) | Cl | H | 0.8 (−) | 1.3 | 1.6 |
| (*MP*)-(3) | $CH_3$ | H | 0.6 (−) | 1.0 | 1.5 |
| (*MP*)-(4) | $OCH_3$ | H | 0.5 (−) | 0.5 | 1.2 |
| (*MP*)-(5) | Benzo | | 1.3 (+) | 1.4 | 1.1 |
| (*MP*)-(6) | $CH_3$ | H | 0.7 (+) | 0.8 | 1.2 |

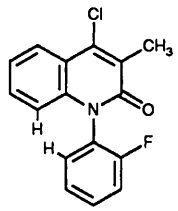
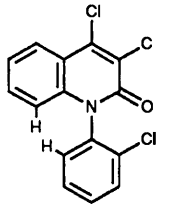
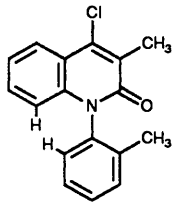
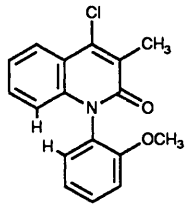
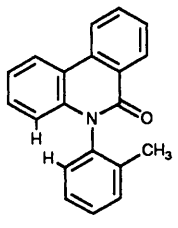
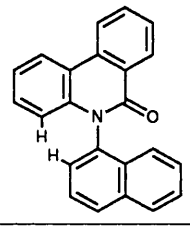
[a] EtOH:$H_2O$ (96:4 v/v) was used in all cases as the eluant, other experimental conditions are given in the experimental part. [b] Capacity factors of enantiomers.[5,22] [c] Sign of rotation at 365 nm of the first-eluted enantiomer. [d] Relative retention of enantiomers.[5,22]

tions[5,22] of both enantiomers are given in Table 3. The barriers to partial rotation about the C–N bond in (**1**)–(**6**) (see Table 4) were determined by thermal racemization of preparatively enriched enantiomers. First-order kinetics were followed by polarimetry for the duration of two half-lives.

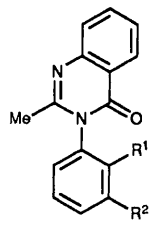
## Discussion

It has been observed that a methyl group exerts a greater steric effect than a chlorine atom in restricting internal rotation in hindered biphenyls[23] and in 1-arylhydantoins.[24] This is consistent with the relative size of these groups as determined by X-ray crystallographic measurements of their van der Waals radii.[25] In contrast with these observations, we have found that the free enthalpy of activation, $\Delta G^{\ddagger}$, for restricted rotation about the C–N bond is even slightly higher, *i.e.* 0.2 kJ mol$^{-1}$ for the *o*-chloro derivative (**2**) than for the *o*-methyl derivative (**3**) (see Table 4). This slight and reverse difference in the relative influences of the *o*-chloro- and *o*-methyl- substituents may be attributed to a dipolar interaction in the transition state for enantiomerization of quinolone (**2**) (see below). Biaryls possess in their ground states sufficient flexibility to minimize steric interactions between the two rings by adopting conformations in which the aryl rings are not coplanar with the hetero rings. Therefore, it is probable, as stated by Coolebrook and co-workers,[24] for 3-arylhydantoins and thiohydantoins 'that most of the influence on the values of $\Delta G^{\ddagger}$ arises from interactions in the transition states.' $\Delta G^{\ddagger}$ values refer therefore, in the first approximation, to the partial rotation about the C–N bond *via* the energetically more favourable transition state. There are two possible transition states for this rotation: the *ortho*-aryl substituent passing either the carbonyl group or the benzo ring (*cf.* Scheme). The preferred pathway, corresponding to less steric hindrance and, accordingly, to lower free enthalpy, seems, from a study of Dreiding models, to be one in which the bulky *ortho*-substituent passes the carbonyl rather than the benzo ring (*cf.* formulae in Table 4). It is plausible that the increase in $\Delta G^{\ddagger}$ of the chloro relative to the methylquinolone results from an

**Table 4.** Barriers to partial rotation about the C–N bond.

| Compound | TS[a] | $T$/°C | $\Delta G^{\ddagger}$[b]/kJ mol$^{-1}$ |
|---|---|---|---|
| (*MP*)-(**1**) |  | 53.0 | 105.1 ± 0.2 |
| (*MP*)-(**2**) |  | 129.0 | 127.4 ± 0.3 |
| (*MP*)-(**3**) |  | 129.0 | 127.2 ± 0.3 |
| (*MP*)-(**4**) |  | 85.7 | 118.8 ± 0.2 |
| (*MP*)-(**6**) |  | 80.5 | 119.3 ± 0.2 |
| (*MP*)-(**5**) |  | 109.6 | 126.5 ± 0.2 |

[a] Probable transition states for enantiomerizations (*P*) ⇌ (*M*). *cf.* Scheme. [b] Free enthalpies of activation obtained by thermal racemization of enriched enantiomers.



| | $R^1$ | $R^2$ |
|---|---|---|
| (**14**) | Me | H |
| (**13**) | Benzo | |

electrostatic repulsion between the electronegative chlorine and oxygen atoms. The $\Delta G^{\ddagger}$ value for (**5**) is approximately 7 kJ mol$^{-1}$ higher than the corresponding one for (**6**) (see Table 4). This difference may be attributed to more severe steric interactions in the transition state for the enantiomeric inversion of phenanthridinone (**5**), than in (**6**). Analogously, the barrier to partial rotation of 2-methyl-3-(1-naphthyl)quinazolin-4(3*H*)-one (**13**)[26] in diglyme was found to be 137.7 ± 0.1 kJ mol$^{-1}$ at 129.2 °C, which is approximately 6 kJ mol$^{-1}$ higher than that corresponding of 2-methyl-3-(*o*-tolyl)quinazolin-4(3*H*)-one (**14**)[26] ($\Delta G^{\ddagger}$ = 131.9 ± 0.5 kJ mol$^{-1}$ at 130 °C). It follows that in both cases a substitution of an *ortho*-tolyl group by the 1-naphthyl results in an increase of the rotational barrier. This is also in qualitative agreement with the result that the barrier to racemization in 2,2′-dimethylbiphenyl[27] is lower by 21 kJ mol$^{-1}$ than the corresponding one for 1,1′-binaphthyl.[28] Surprisingly, phenanthridinones (**5**) and (**6**) show barriers which are lower by approximately 12 kJ mol$^{-1}$ than the corresponding values for the quinazolinones (**13**) and (**14**), respectively. A possible explanation for this finding might be that in the transition state the phenanthridinone ring is twisted in a way similar to a helical phenanthrene ring.[29] A non-planar phenanthridinone fragment would exert less steric hindrance to rotation than a planar one.

## Experimental

M.p.s were determined on Kofler Mikroheiztisch (Reichert, Wien) and Büchi SMP 20 instruments and are not corrected. IR spectra were recorded on a Perkin-Elmer 297 Infracord and UV spectra on a Hitachi Perkin-Elmer 124 spectrometer. The $^1$H NMR spectra of (**1**)–(**4**) and (**7**)–(**10**) were recorded on JEOL JNM FX (PFT mode, 8K data points, 90 MHz). The $^1$H NMR spectra of (**5**)–(**6**) were taken on a Bruker WH 250 (PFT mode, 32K data points, 250 MHz) spectrometer. The EIMS (electron impact mass spectra) of (**1**) and (**7**) were recorded on a Varian MAT CH7 instrument operating at 70 eV. The EIMS of (**2**), (**4**), and (**5**) were recorded on a Varian MAT 711 double focusing mass spectrometer with ionizing energy 80 eV and emission current 0.8 mA. The exact measurements of (**2**)–(**4**) were performed by using the same instrument at resolution 12 500 (10% relative value definition). The EIMS of (**8**) and (**9**) were recorded on a Varian MAT 112 S mass spectrometer with ionizing energy 80 eV. Low- and high-resolution mass spectra of (**5**) were taken on Varian CH 5 and Varian MAT 311 A spectrometers respectively, both with ionizing energy 70 eV. Specific rotations were measured by means of a Perkin-Elmer 241 electronic polarimeter. Elemental analyses were performed by the Central Analytical Service, Institut 'Ruder Bošković,' Zagreb. Analytical data are presented in Table 1.

*Chromatography.*—Low-pressure liquid chromatography (column 300–325 mm) at flow rate 3.2–4.0 cm$^3$ min$^{-1}$, $\Delta p$ = 1.7–

2.0 bar * on triacetylcellulose as a stationary phase with particle diameter of 0.02–0.03 mm, and ethanol:water 96:4 (v/v) as the eluant at 22–25 °C was used for separations of enantiomers. Injected quantities of racemates were 1–20 mg in 1 $cm^3$ of ethanol. Sample injection and detector systems along with other details of the chromatographic equipment have been described previously.[5]

N-*Arylacetamides* (**19**)–(**22**).—These were prepared by acetylation of the corresponding *ortho*-substituted anilines by analogy to the procedure in the literature,[31] the yields varying in the range 80–83%. The following compounds were obtained in this way.

N-(2-*Fluorophenyl*)*acetamide* (**19**). Acetic anhydride (11.85 g, 0.116 mol) was added slowly, over approximately 20 min, to stirred 2-fluoroaniline (10.9 g, 0.097 mol) under cooling to maintain the reaction temperature at 60–70 °C. At the end of this period the temperature was allowed to rise to approximately 80 °C. After this, the reaction mixture was poured out in a porcelain dish and a solidified product was obtained. This was crushed, filtered, and washed with water and light petroleum (b.p. 40–70 °C) to give the pure compound (**19**). M.p. 73–74 °C (Found: C, 62.65; H, 5.3. Calc. for $C_6H_8FNO$: C, 62.74; H, 5.27%).

N-(2-*Chlorophenyl*)*acetamide* (**20**).—M.p. 85 °C (Found: C, 56.45; H, 4.6. Calc. for $C_8H_8ClNO$: C, 56.67; H, 4.72%); $\delta_H$($CDCl_3$; 22 °C) 2.2 (3 H, s, Me), 6.9–8.3 (4 H, m, Ph), and 7.1 (1 H, br s, N–H).

N-(2-*Methylphenyl*)*acetamide* (**21**).[31]—M.p. 105–107 °C (lit.,[31] 110 °C), $\delta_H$($CDCl_3$; 22 °C) 2.17 (3 H, s, *Me*$C_6H_4$), 2.24 (3 H, s, *Me*CO), and 7.1–7.7 (4 H, m, Ph).

N-(2-*Methoxyphenyl*)*acetamide* (**22**).—M.p. 89–90 °C (Found: C, 65.35; H, 6.6. Calc. for $C_9H_{11}NO_2$: C, 65.44; H, 6.71%); $\delta_H$($CDCl_3$; 22 °C) 2.1 (3 H, s, Me), 3.8 (3 H, s, OMe), 6.8–8.3 (4 H, m, Ph), and 7.3 (1 H, br s, N–H).

*Diphenylamines* (**15**)–(**18**).—Diphenylamines containing *ortho*-substituents in one phenyl group were obtained by condensation of bromobenzene with the corresponding *N*-arylacetamides (**19**)–(**22**) and subsequent hydrolysis of the *N*-acetyldiarylamines by a procedure analogous to that in the literature.[32] The following compounds were obtained in this way.

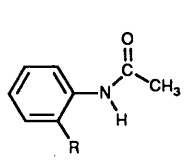
2-*Fluorodiphenylamine* (**15**).—*N*-(2-Fluorophenyl)acetamide (**19**) (6.4 g, 0.04 mol) and bromobenzene (10 $cm^3$, 0.1 mol) were refluxed together with stirring for 17 h in the presence of $K_2CO_3$ (5.4 g, 0.04 mol) and CuI (0.8 g, 0.004 mol). The $K_2CO_3$ used was first dried in an oven for 24 h at 200 °C. The CuI was dried for 3 h at 140 °C before use. Freshly distilled bromobenzene was dried over molecular sieves type 4A for 24 h before use. The resulting mixture was cooled and then extracted with 70 $cm^3$ of benzene. The benzene was evaporated off and excess bromobenzene was removed by distillation (b.p. 46–48 °C/12 Torr). The oil which remained was refluxed for 2 h with KOH (4.7 g, 0.08 mol) in 45 $cm^3$ of absolute EtOH. The EtOH was evaporated off, and the oily residue was shaken with 80 $cm^3$ of benzene and 70 $cm^3$ of saturated aqueous NaCl. The benzene solution was dried ($MgSO_4$), and evaporated to dryness. The oily residue was purified by distillation, b.p. 107 °C/0.03 Torr. Yield 63% (Found: C, 76.81; H, 5.43. Calc. for $C_{12}H_{10}FN$: C, 76.98; H, 5.39%).

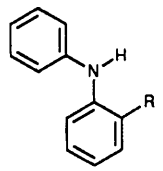
* 1 bar = $10^5$ Pa.

2-*Chlorodiphenylamine* (**16**).—B.p. 112 °C/0.02 Torr (lit.,[33] 152–153 °C/4 Torr.)

2-*Methyldiphenylamine* (**17**).—B.p. 99 °C/0.15 Torr (lit.,[32] 112–115 °C/8 Torr; lit.,[33] 143–146 °C/4–5 Torr).

2-*Methoxydiphenylamine* (**18**).—B.p. 112 °C/0.4 Torr (lit.,[33] 156–158 °C/2.5–3 Torr).





| R | R |
|---|---|
| (**19**) F | (**15**) F |
| (**20**) Cl | (**16**) Cl |
| (**21**) Me | (**17**) Me |
| (**22**) OMe | (**18**) OMe |

N-(2-*Fluorophenyl*)-4-*hydroxy*-3-*methyl*-2(1*H*)-*quinolone* (**7**).—A stirred mixture of 2-fluorodiphenylamine (**15**) (4.5 g, 0.024 mol) and diethyl methylmalonate (3.4 g, 0.024 mol) was slowly heated to 250–270 °C, under ethanol vapour formed during the reaction, for appoximately 1 h. The solidified product was obtained after the reaction mixture had been cooled to room temperature and trituration with methanol. After filtration, the crude precipitate was dissolved in 0.5 mol $dm^{-3}$ aqueous sodium hydroxide and filtered off from the insoluble material. The alkaline solution was extracted twice with 50 $cm^3$ of benzene and the aqueous alkaline layer was then precipitated in concentrated hydrochloric acid. The crude residue was recrystallized from an appropriate solvent to give the pure compound (**7**) (see Table 1). *m/z* 269 ($M^{+\bullet}$, 100%), 250 (77), 240 (8), 213 (48), and 185 (16); [direct inlet temperature ($T_{di}$), 100 °C]. The other novel quinolones (**8**)–(**10**) (see Table 1) were prepared by procedures analogous to that described for the quinolone (**7**).

N-(2-*Chlorophenyl*)-4-*hydroxy*-3-*methyl*-2(1*H*)-*quinolone* (**8**).—*m/z* 287 (4%) 285 ($M^{+\bullet}$, 6), 251 (22), 250 (100), 195 (6), and 194 (4) ($T_{di}$, 180 °C).

N-(o-*Tolyl*)-4-*hydroxy*-3-*methyl*-2(1H)-*quinolone* (**9**). *m/z* 266 (16%), 265 ($M^{+\bullet}$, 74), 264 (21), 250 (37), 249 (21), 248 (100), 180 (21), and 132 (21) ($T_{di}$, 100 °C).

N-(2-*Methoxyphenyl*)-4-*hydroxy*-3-*methyl*-2(1*H*)-*quinolone* (**10**). *m/z* 282 (6%), 281 ($M^{+\bullet}$, 41) 280 (4), 251 (21), 250 (100), 196 (6), and 175 (12) ($T_{di}$ 180 °C).

N-(2-*Fluorophenyl*)-4-*chloro*-3-*methyl*-2(1*H*)-*quinolone* (**1**).—A mixture of *N*-(2-fluorophenyl)-4-hydroxy-3-methyl-2(1*H*)-quinolone (**7**) (1.2 g, 0.004 mol) and phosphorus oxychloride (8 $cm^3$) was heated under reflux for 2 h. A reaction mixture was cooled to room temperature and poured out onto crushed ice. The residue was treated with 2 mol $dm^{-3}$ aqueous sodium hydroxide to give a pH of 4–5. The crude precipitate was filtered off and recrystallized from an appropriate solvent to give the pure compound (**1**) (see Table 1). *m/z* 289 (29%), 287 ($M^{+\bullet}$, 86), 270 (34), 268 (100), 222 (20), and 140 (11) ($T_{di}$, 100 °C). The other novel quinolones (**2**)–(**4**) (see Table 1) were prepared by a procedure analogous to that described for the quinolone (**1**).

N-(2-*Chlorophenyl*)-4-*chloro*-3-*methyl*-2(1*H*)-*quinolone* (**2**). *m/z* 305 (6%), 303 ($M^{+\bullet}$, 9), 271 (6), 270 (34), 269 (19), 268 (100), 204 (7), and 102 (8) ($T_{di}$, 100 °C) (Found: $M^{+\bullet}$, 303.02121. Calc. for $C_{16}H_{11}Cl_2NO$: $M^{+\bullet}$ 303.02177).

N-(o-*Tolyl*)-4-*chloro*-3-*methyl*-2(1*H*)-quinolone (**3**). *m/z* 285 (19%), 284 (16), 283 ($M^{+\bullet}$, 55), 282 (19), 270 (13), 269 (13), 268 (70), 267 (21), 266 (100), and 204 (13) ($T_{di}$ 100 °C) (Found: $M^{+\bullet}$, 283.076898. Calc. for $C_{17}H_{14}ClNO$; *M* 283.07639).

N-(2-*Methoxyphenyl*)-4-*chloro*-3-*methyl*-2(1*H*)-*quinolone* (**4**). *m/z* 301 (9%), 299 ($M^{+\bullet}$, 25) 270 (34), 269 (18), 268 (100), and 193 (10) (Found: $M^{+\bullet}$, 299.07154. Calc. for $C_{17}H_{14}ClNO_2$; *M* 299.07131).

5-(1-*Naphthyl*)*phenanthridin*-6(5H)-*one* (**5**).—6-(1-Naphthyloxy)phenanthridinone (**11**) (250 mg, 7.8 mmol) was heated on a sand bath at 335–350 °C for 2 h. After being cooled, the product was dissolved in chloroform (2 $cm^3$) and purified by double column chromatography on silica gel using light petroleum (b.p. 40–70 °C)–ethyl acetate (3:1) as the solvent. Recrystallization from acetone gave yellowish crystals of (**5**) (yield 32%) m.p. 225–226 °C. $\lambda_{max}$[EtOH–$H_2O$ (95:5)] 260 (log ε 4.32), 270 (4.22), 292 (3.99), 324 (3.92), and 337 (3.83); *m/z* 321 ($M^{+\bullet}$, 100%), 304 (31) (Found: $M^{+\bullet}$, 321.1148. Calc. for $C_{23}H_{15}NO$: *M*, 321.1154).

(±)-5-(o-*Tolyl*)*phenanthridin*-6(5H)-*one* (**6**).[17,18]

(+)-5-(2′-*Methylphenyl*)*phenanthridin*-6(5H)-*one* (**6**). M.p. 110–114 °C, $[\alpha]_{365}^{22}$ = +695 ± 26° $cm^3$ $g^{-1}$ $dm^{-1}$ (2.3 g $dm^{-3}$ in EtOH–$H_2O$, 95:5); *P* = 0.81 ± 0.06.* $[\alpha]_{365}^{22}$† = ±858 ± 88° $cm^3$ $g^{-1}$ $dm^{-1}$.

(−)-5-(2-o-*Tolyl*)*phenanthridin*-6(5H)-*one* (**6**). M.p. 108–111 °C. $[\alpha]_{365}^{22}$ = −227 ± 9° $cm^3$ $g^{-1}$ $dm^{-1}$ (2.6 g $l^{-1}$ in EtOH–$H_2O$, 95:5); *P* = 0.28 ± 0.04*. $[\alpha]_{365}^{22}$† = ±810 ± 140° $cm^3$ $g^{-1}$ $dm^{-1}$.

6-(1-*Naphthyloxy*)*phenanthridine* (**11**).—6-Chlorophenanthridine[15] (1 g, 4.7 mmol) was heated with 1-naphthol (10 g, 6.94 mmol) at 150–160 °C by a procedure analogous to that described in the literature.[14] After cooling, aqueous sodium hydroxide solution (60 $cm^3$, 5% w/v) was added to the reaction mixture, the undissolved material was filtered off, and the residue was extracted with ether. Drying and removal of the ether gave a yellow precipitate which crystallized from ethyl acetate to give slightly yellow crystals of (**11**) (yield 17%), m.p. 176–177.5 °C.

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* Enantiomeric purity determined by liquid chromatography according to the lit.[30]

† Calculated specific rotations for the pure enantiomers.

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