# Cyclization of 1-Benzyl-1,2-dihydro-2-(substituted methylene)quinolines to Pyrrolo[1,2-*a*]quinoline Derivatives

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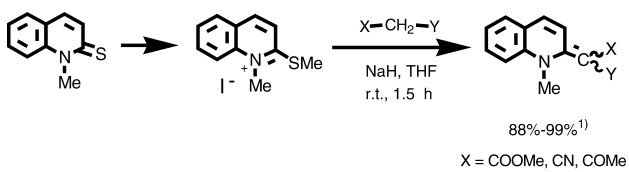
**1-Alkyl-2-alkylthioquinolinium salts were prepared from 1-alkyl-2(1*H*)-quinolones *via* 1-alkyl-2(1*H*)-thioquinolones in two steps. Under mild conditions, the reaction of 1-alkyl-2-alkylthioquinolinium iodides with active methylene compounds in the presence of sodium hydride afforded 1-alkyl-1,2-dihydro-2-(substituted methylene)quinolines in good yields. The cyclization of 1-benzylquinolines using acetic anhydride produced the corresponding pyrrolo[1,2-*a*]quinoline derivatives.**

**Key words** 1-benzyl-2(1*H*)-thioquinolone; dimethyl malonate; cyclization; pyrrolo[1,2-*a*]quinoline; 2-methylthioquinolinium iodide

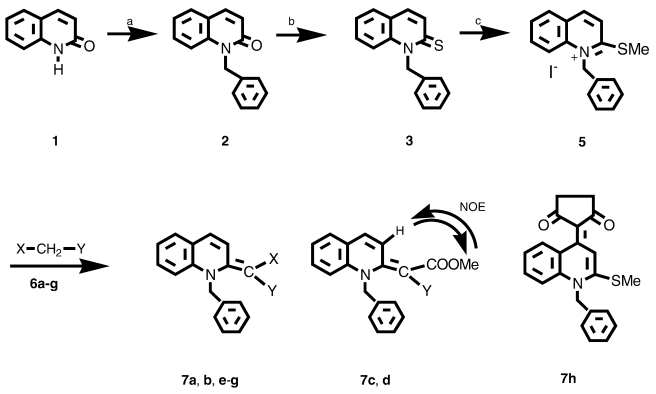
Previously we reported a new method for the formation of a carbon–carbon bond at the 2-position of a quinoline ring using the reaction of 1-methyl-2-methylthioquinolinium iodide with active methylene compounds.[1)] Excellent yields were obtained as shown in Chart 1. Various methods for the synthesis of the pyrrolo[1,2-*a*]quinoline skeleton have also been reported.[2—7)] The conventional methods for preparing the substituted pyrrolo[1,2-*a*]quinoline derivatives typically involve reactions of 2-substituted quinolines having a phenacyl group with acetic anhydride.[5,7)] Recently, Komatsu and co-workers reported synthesis of the pyrrolo[1,2-*a*]quinoline by cycloaddition of quinolinium methylide at 180 °C for 6 h in 84% yield.[8)] Further, Weaver *et al.* reported synthesis of indolizines and pyrrolo[2,1-*a*]-isoquinolines using cycloaddition of pyridinium-1- and isoquinolinium-2-yl-methylene compounds with 1,1-diiodo-2,2-dinitroethylene in 17—43% yields. But, they did not report synthesis of pyrrolo[1,2-*a*]quinolines.[9)] Therefore, 2-substituted quinolines having a benzyl group would be extremely useful as an intermediate for the synthesis of the pyrrolo-fused heterocycles. Herein, we report a new method for the synthesis of a pyrrolo[1,2-*a*]quinoline skeleton using the cyclization of 1-benzyl-1,2-dihydro-2-(substituted methylene)quinolines, which were easily prepared from the reaction of 1-benzyl-2-methylthio-quinolinium iodides with active methylene compounds, and the reaction of 1-methyl-2-alkylthioquinolinium salts with cyclic active methylene compounds.

**Reaction of 2-Alkylthioquinolinium Salts with Active Methylene Compounds** First, the reaction of 1-benzylquinolinium iodide (**5**) having a methylthio group as a leaving group at the 2-position with active methylene compounds (**6a**—**g**) was examined under mild conditions in the presence of sodium hydride (Chart 2, Table 1). 1-Benzyl-2(1*H*)-thioquinolone (**3**) was readily prepared from 2(1*H*)-quinolone (**1**) *via* 1-benzyl-2(1*H*)-quinolone (**2**) in two steps. The reaction of **3** with methyl iodide (**4a**) afforded 1-benzyl-2-methylthioquinolinium iodide (**5**) in 72% yield. The reaction of quinolinium iodide (**5**) with active methylene compounds (**6a**—**e**) in the presence of sodium hydride at room temperature for 2 h in tetrahydrofuran (THF) afforded 2-(substituted methylene)quinolines (**7a**, 91%; **7b**, 97%; **7c**, 76%; **7d**, 63%; **7e**, 62%; entries 1—5, respectively), as listed in Table 1. Furthermore, studies using cyclic active methylene compounds have shown that the reaction between **6f** and **5** at room tem-




88%-99%[1)]

Chart 1




**6a** ; **7a** : X = COOMe ; Y = COOMe
**6b** ; **7b** : X = CN ; Y = CN
**6c** ; **7c** : X = COOMe ; Y = CN
**6d** ; **7d** : X = COOMe ; Y = COMe
**6e** ; **7e** : X = COMe ; Y = COMe
**6f** ; **7f** : X = $COCH_2CH_2CH_2CO$ = Y
**6g** ; **7g** : X = $COCH_2CH_2CO$ = Y

a : $PhCH_2Cl$, KOH-EtOH, sealed tube, 100 ℃,10 h, 54%
b : $P_2S_5$ -pyridine, reflux, 5 h, 78%
c : MeI (**4a**), acetone, reflux, 6 h, 72%

Chart 2

Table 1. Reactions of **5** with **6a**—**g**

| Entry | **6** | Temp. (°C) | Time (h) | Solvent | Product **7** | Yield (%) |
|---|---|---|---|---|---|---|
| 1 | **a** | r.t. | 2 | THF | **a** | 91 |
| 2 | **b** | r.t. | 2 | THF | **b** | 97 |
| 3 | **c** | r.t. | 2 | THF | **c** | 76 |
| 4 | **d** | r.t. | 2 | THF | **d** | 63 |
| 5 | **e** | r.t. | 2 | THF | **e** | 62 |
| 6 | **f** | r.t. | 2 | THF | **f** | 22 |
| 7 | **f** | r.t. | 2 | DMF | **f** | 26 |
| 8 | **f** | 90 | 6 | DMF | **f** | 75 |
| 9 | **g** | 90 | 6 | DMF | **g** | 73 |
| 10 | **a** | 90 | 6 | DMF | **a** | 86 |

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perature for 2 h in either THF or DMF gives 2-(substituted methylene)quinoline (**7f**) in poor yields (entries 6, 7). In contrast, the reaction of **6f** with **5** at 90 °C for 6 h in DMF gave **7f** in 75% yield (entry 8). Interestingly, the reaction of **6g** with **5** at 90 °C for 6 h in DMF resulted in two products (entry 9): 2-(substituted methylene)quinoline (**7g**, 73%) and 4-(substituted methylene)quinoline (**7h**, 18%). However, the reaction of **6a** with **5** at 90 °C for 6 h afforded only one product: 2-(substituted methylene)quinoline (**7a**, entry 10).

To investigate the influence of steric or ionic effect, reactions of 1-methylquinolinium salts (**9a**—**c**) bearing methylthio, ethylthio, or isopropylthio group at the 2-position with **6a**, **f**, **g** were carried out (Chart 3, Table 2). The reaction of 1-methyl-2(1*H*)-thioquinolone (**8**)[1)] with alkyl iodides (**4a**—**c**) proceeded smoothly to produce the corresponding 1-methyl-2-alkylthioquinolinium iodides (**9a**—**c**) in high yields (Chart 3). The reactions of **9a**—**c** with **6a** at room temperature for 0.5 h gave 2-(substituted methylene)quinoline (**10a**)[1)] in 95%, 82%, and 66% yields, respectively (entries 1—3). Similar reactions of **9b**, **c** for 1.5 h afforded **10a** in 79% and 78% yields (entries 4, 5). The reactions of **9a**—**c** with **6f** in DMF gave 2-(substituted methylene)quinoline (**10f**)[1)] in 81%, 28% and 24% yields at room temperature for 2 h (entries 6—8), and 85%, 75% and 76% at 90 °C for 6 h (entries 9—11), respectively. The reaction of **9a** with **6g** gave two products: 2- and 4-(substituted methylene)quinolines (**10g**, **10h**). Reaction at room temperature (entry 12) afforded products (**10g**, 40%; **10h**, 15%), whereas reaction at 90 °C (entry 15) resulted in

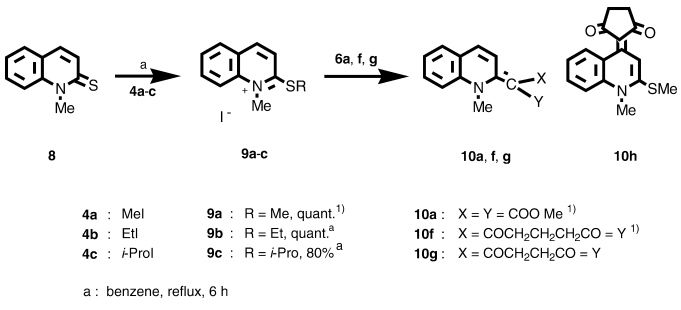


Chart 3

**10g** (82%) and **10h** (17%). However, the reactions of **9b** and **9c** with **6g** at room temperature and at 90 °C afforded only the 2-(substituted methylene)quinoline (**10g**) (entries 13, 14, 16, 17). These results indicate that at room temperature, a bulky group on the sulfur atom interfere the interaction between the carbanion arised from **6a**, **f**, **g** and the carbocation on the 2-position of the quinolines ring and tends to reduce the yields of product (Table 2, entries 6—8, 12—14). In addition, a bulky substituent on the nitrogen atom can affect the reaction of **5** with **6f** at room temperature, while at 90 °C it can not affect the reaction (Table 1, entries 6—8). Further the steric interaction between hydrogens on the 4- and 5-positions of quinoline ring is known. It can be presumed that as **6g** is smoller size than **6f**, the carbanion arising from **6g** can reacted with the carbocation on the 4-position of **5** and **9a**. On the other hand, as the carbanion arising from **6g** would be a soft base (Lewis base) than the carbanion arising from **6a**, it can be assumed that the carbanion arising from **6g** reacted with the soft acid (Lewis acid) on the 4-position.

The structures of 2-(substituted methylene)quinolines (**7a**—**g**, **10a**, **f**, **g**) and 4-substituted quinolines (**7h**, **10h**) were determined from $^1$H-NMR spectra studies as follows. For the 2-(substituted methylene)quinolines, the signals due to the alkylthio group disappeared with replacement of the alkylthio group by the active methylene compounds. In contrast, for 4-(substituted methylene)quinolines (**7h**, **10h**), a signal due to the methylthio group at 2.83 ppm and a singlet signal due to H-3 at 8.40 ppm were observed.

Spectroscopic studies of compounds (**7c**, **d**) showed nuclear Overhauser and exchange spectroscopy (NOE) correlations between the methyl of the ester (3.80, 3.69 ppm) and the proton (8.28, 8.06 ppm) at the 3-position, and therefore those configuration are suggested to be *cis*. The reaction described herein can be regarded as a promising method for carbon–carbon bond formation at the 2- and 4-positions in the quinoline ring.

**Cyclizations of 1-Benzylquinoline Compounds in Acetic Anhydride** Next, we attempted the cyclizations of 1-benzylquinoline compounds (**7a**, **d**, **e**) in acetic anhydride to provide the corresponding functionalized pyrrolo[1,2-

Table 2. Reactions of **9a**—**c** with **6a**, **f**, **g**

| Entry | 9 | 6 | Temp. (°C) | Time (h) | Solvent | Yield (%) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | 2-Position | | 4-Position | |
| 1 | **a** | **a** | r.t. | 0.5 | THF | **10a**[1)] | 95 | | — |
| 2 | **b** | **a** | r.t. | 0.5 | THF | **10a** | 82 | | — |
| 3 | **c** | **a** | r.t. | 0.5 | THF | **10a** | 66 | | — |
| 4 | **b** | **a** | r.t. | 1.5 | THF | **10a** | 79 | | — |
| 5 | **c** | **a** | r.t. | 1.5 | THF | **10a** | 78 | | — |
| 6 | **a** | **f** | r.t. | 2.0 | DMF | **10f**[1)] | 81 | | — |
| 7 | **b** | **f** | r.t. | 2.0 | DMF | **10f** | 28 | | — |
| 8 | **c** | **f** | r.t. | 2.0 | DMF | **10f** | 24 | | — |
| 9 | **a** | **f** | 90 | 6.0 | DMF | **10f** | 85 | | — |
| 10 | **b** | **f** | 90 | 6.0 | DMF | **10f** | 75 | | — |
| 11 | **c** | **f** | 90 | 6.0 | DMF | **10f** | 76 | | — |
| 12 | **a** | **g** | r.t. | 2.0 | DMF | **10g** | 40 | **10h** | 15 |
| 13 | **b** | **g** | r.t. | 2.0 | DMF | **10g** | 25 | | — |
| 14 | **c** | **g** | r.t. | 2.0 | DMF | **10g** | 20 | | — |
| 15 | **a** | **g** | 90 | 6.0 | DMF | **10g** | 82 | **10h** | 17 |
| 16 | **b** | **g** | 90 | 6.0 | DMF | **10g** | 69 | | — |
| 17 | **c** | **g** | 90 | 6.0 | DMF | **10g** | 67 | | — |

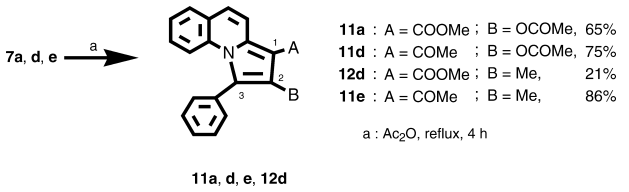


Chart 4

*a*]quinoline derivatives (Chart 4). Refluxing of **7a**, **e** in acetic anhydride for 4 h afforded the corresponding pyrrolo[1,2-*a*]quinolines (**11a**, 65% and **11e**, 86%, respectively). The cyclization of **7d**, which has an ester and acetyl groups, proceeded smoothly to afford **11d** (75%) and **12d** (21%). Unfortunately, the cyclization of **7b** and **7c** was unsuccessful with the recovery of the starting materials. The structures of **11a**, **d**, **e** and **12d** were determined from the $^1$H-NMR spectra for **11a**, **d**, **e** and **12d**, which showed that the signals (5.50—5.92 ppm) due to the methylene proton of benzyl groups in **11a**, **d**, **e** and **12d** disappeared by dehydration and condensation.

In conclusion, we have developed a methodology for the pyrrolo-fused heterocycles. Thus, the reactions between active methylene compounds and quinolinium salts having an alkylthio group as a leaving group at the 2-position to give 1-alkyl-2- or 4-(substituted methylene)quinolines under mild conditions in high yields were described. The cyclizations in the acetic anhydride of 1-benzylquinolines having an ester or acetyl group produced pyrrolo[1,2-*a*]quinolines in good yields.

**Experimental**

**General** The following instruments were used to obtain physical data: Melting points, Yanaco micromelting point apparatus (values are uncorrected); IR spectra, Perkin Elmer FT-IR1725X spectrophotometer; MS spectra, JEOL JMN-DX 303/JMA-DA 5000 spectrometer; NMR spectra, JNM-GSX 400 ($^1$H-NMR, 400 MHz; $^{13}$C-NMR, 100 MHz), JNM-EX270 ($^1$H-NMR, 270 Hz; $^{13}$C-NMR, 67.8 MHz), JEOL JNM-PMX 60SI spectrometers with tetramethylsilane (TMS) as an internal standard, and elemental analyses, Perkin Elmer 2400 CHN Elemental Analyzer. The following experimental conditions were used for chromatography: column chromatography, Merck Kieselgel silica gel 60 (230—400 mesh); TLC, precoated TLC plates with $60F_{254}$ (2 mm, Merck).

**Synthesis of 2** An ethanol solution (10 ml) of KOH (0.59 g, 10.5 mmol), quinolone (**1**: 1.45 g, 10 mmol), and benzyl chloride (1.35 g, 10.5 mmol) was heated at 100 °C for 10 h in a sealed tube and then removed the solvent by evaporation *in vacuo*. The residue was washed with hexane and recrystallized from isopropyl ether to give **2** as colorless needles (1.27 g, 54%): mp 70 °C. IR (KBr) cm$^{-1}$: 1651, 1591, 831, 765, 734. $^1$H-NMR ($CDCl_3$) $\delta$: 5.56 (2H, s, $CH_2$), 6.80 (1H, d, $J$=9.4 Hz, H-3), 7.17 (7H, m, H-aromatic), 7.41 (1H, dd, $J$=1.5, 8.1 Hz, H-aromatic), 7.75 (1H, dd, $J$=1.5, 7.7 Hz, H-aromatic), 7.73 (1H, d, $J$=9.4 Hz, H-4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 45.89, 115.01, 120.92, 121.67, 122.15, 126.56 (C2), 127.22, 128.75 (C2), 128.79, 130.57, 136.33, 139.49, 139.51, 162.45. MS *m*/*z*: 235 ($M^+$), 129, 91. HR-MS Calcd for $C_{16}H_{13}NO$, 235.0997. Found: 235.1045.

**Synthesis of 3** A pyridine solution (8 ml) of **2** (1.18 g, 5 mmol) and phosphorus pentasulfide (1.6 g, 1 mmol) was heated at 150 °C for 5 h. The reaction mixture was diluted with water (10 ml), then extracted with $CHCl_3$. The $CHCl_3$ layer was dried over $MgSO_4$ and evaporated. The residue was recrystallized from acetone to give **3** as yellow needles (0.98 g, 78%): mp 109—110 °C. IR (KBr) cm$^{-1}$: 1649, 1614, 1136, 766, 712. $^1$H-NMR ($CDCl_3$) $\delta$: 6.31 (2H, s, $CH_2$), 7.17—7.37 (6H, m, H-aromatic), 7.41—7.53 (3H, m, H-aromatic), 7.57—7.65 (1H, m, H-aromatic), 7.74 (1H, d, $J$=9.0 Hz, H-4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 53.49, 116.56, 124.11, 124.53, 126.36 (C2), 127.32, 128.84, 128.87 (C2), 131.22, 132.12, 133.46, 134.99, 140.55, 185.43. MS *m*/*z*: 251 ($M^+$), 218, 91. HR-MS Calcd for $C_{16}H_{13}NS$, 251.0769. Found: 251.0750.

**General Procedure for the Syntheses of 1-Alkyl-2-alkylthioquinolinium Iodides (5, 9b, c)** A benzene solution (7 ml) of **3** (0.5 g, 2 mmol) and **4a** (1.42 g, 10 mmol) was gently refluxed for 6 h. The resulting yellow precipitate was collected by filtration then recrystallized from methanol to give 1-benzyl-2-methylthioquinolinium iodide (**5**, 0.57 g, 72%). Reactions of **8** with **4b**, **c** were carried out under similar conditions to give 2-ethylthio-1-methylquinolinium iodide (**9b**, 100%) and 1-methyl-2-isopropylthioquinolinium iodide (**9c**, 80%), respectively.

**5**: Yellow crystalline powder (methanol), mp 109—110 °C. IR ($CHCl_3$) cm$^{-1}$: 1597, 770, 753. $^1$H-NMR (DMSO-$d_6$) $\delta$: 3.03 (3H, s, SMe), 6.28 (2H, s, $CH_2$), 7.23 (2H, m, H-Ph), 7.36—7.42 (3H, m, H-Ph), 7.92 (1H, ddd, $J$=0.6, 7.8, 8.4 Hz, H-aromatic), 8.11 (1H, ddd, $J$=1.5, 7.8, 9.1 Hz, H-aromatic), 8.20 (1H, d, $J$=9.0 Hz, H-3), 8.30 (1H, dd, $J$=0.6, 9.1 Hz, H-aromatic), 8.42 (1H, dd, $J$=1.5, 8.4 Hz, H-aromatic), 9.10 (1H, d, $J$=9.0 Hz, H-4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 15.88, 54.55, 117.68, 120.10, 125.70 (C2), 127.67, 128.05, 128.57 (C2), 130.21, 131.65, 134.98, 139.45 (C2), 143.25, 167.08. *Anal.* Calcd for $C_{17}H_{16}NIS$: C, 51.91; H, 4.10; N, 3.56. Found: C, 51.76; H, 3.83; N, 3.59.

**9b**: Yellow needles (methanol), mp 104 °C. IR (KBr) cm$^{-1}$: 1594, 1319, 1142, 769, 743. $^1$H-NMR (DMSO-$d_6$) $\delta$: 1.47 (3H, t, $J$=7.5 Hz, CMe), 3.63 (2H, q, $J$=7.5 Hz, $SCH_2$), 4.40 (3H, s, NMe), 7.92 (1H, dd, $J$=0.7, 8.0 Hz, H-aromatic), 8.13—8.20 (2H, m, H-aromatic), 8.37 (1H, dd, $J$=0.7, 8.0 Hz, H-aromatic), 8.47 (1H, d, $J$=9.3 Hz, H-3), 8.96 (1H, d, $J$=9.3 Hz, H-4). $^{13}$C-NMR (DMSO-$d_6$) $\delta$: 13.18, 27.53, 40.36, 118.23, 120.12, 125.78, 128.31, 130.28, 134.87, 140.26, 142.85, 165.39. *Anal.* Calcd for $C_{12}H_{14}NIS$: C, 43.52; H, 4.26; N, 4.23. Found: C, 43.03; H, 4.03; N, 4.20.

**9c**: Yellow needles (methanol), mp 139—140 °C. IR (KBr) cm$^{-1}$: 1614, 1597, 1321, 1144, 819, 766. $^1$H-NMR (DMSO-$d_6$) $\delta$: 1.53 (6H, d, $J$=6.6 Hz, CMe×2), 4.36 (1H, m, $J$=6.6 Hz, SCH), 4.39 (3H, s, NMe), 7.92 (1H, ddd, $J$=0.6, 7.6, 8.4 Hz, H-aromatic), 8.14 (1H, dd, $J$=1.7, 7.6 Hz, H-aromatic), 8.19 (1H, ddd, $J$=1.7, 7.1, 8.4 Hz, H-aromatic), 8.37 (1H, dd, $J$=0.6, 7.1 Hz, H-aromatic), 8.46 (1H, d, $J$=9.3 Hz, H-3), 8.97 (1H, d, $J$=9.3 Hz, H-4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 22.18 (C2), 39.24, 39.98, 118.37, 120.82, 125.87, 128.40, 130.26, 134.89, 140.36, 143.00, 164.68. *Anal.* Calcd for $C_{13}H_{16}NIS$: C, 45.23; H, 4.67; N, 4.06. Found: C, 45.05; H, 4.37; N, 3.99.

**General Procedure for the Reactions of Quinolinium Salts (5, 9a—c) with Active Methylene Compounds (6a—g)** To a suspension of NaH (15 mg, 0.6 mmol) in THF (5 ml) was added dimethyl malonate (**6a**, 79 mg, 0.6 mmol) at 0 °C under $N_2$. The mixture was stirred for 10 min at rt, followed by the addition of **5** (197 mg, 0.5 mmol). The reaction mixture was stirred for 2 h at rt, quenched with $H_2O$ (5 ml), and treated with saturated $Na_2S_2O_3$ solution (3 ml). The reaction mixture was extracted with $CHCl_3$. The $CHCl_3$ layer was dried over $MgSO_4$, and concentrated *in vacuo* to give 1-benzyl-1,2-dihydro-2-[bis-(methoxycarbonyl)methylene]quinoline (**7a**, 159 mg, 91%). Reactions of **5** with **6b**—**g** and **9a**—**c** with **6a**, **f**, **g** were carried out by similar procedures (specific conditions are listed in Tables 1 and 2 to give 1-benzyl-2-[bis(cyano)methylene]-1,2-dihydroquinoline (**7b**), 1-benzyl-2-[cyano(methoxycarbonyl)methylene]-1,2-dihydroquinoline (**7c**), 2-[acetyl(methoxycarbonyl)methylene]-1-benzyl-1,2-dihydroquinoline (**7d**), 2-[bis(acetyl)methylene]-1-benzyl-1,2-di-hydroquinoline (**6e**), 1-benzyl-1,2-dihydro-2-(2,6-dioxocyclohexylidene)quinoline (**7f**), 1-benzyl-1,2-dihydro-2-(2,5-dioxocyclopentylidene)quinoline (**7g**), 1-benzyl-1,4-dihydro-2-methylthio-4-(2,5-dioxocyclopentylidene)quinoline (**7h**), 1-methyl-1,2-dihydro-2-[bis(methoxycarbonyl)methylene]quinoline (**10a**),[1)] 1,2-dihydro-1-methyl-2-(2,6-dioxocyclohexylidene)quinoline (**10f**),[1)] 1,2-dihydro-1-methyl-2-(2,5-dioxocyclopentylidene)quinoline (**10g**), and 1,4-dihydro-1-methyl-2-methylthio-4-(2,5-dioxocyclopentylidene)quinoline (**10h**). The yields are listed in Tables 1 and 2.

**7a**: Yellow plates (methanol), mp 182—183 °C. IR (KBr) cm$^{-1}$: 1709, 1671, 1604, 827, 756, 713. $^1$H-NMR ($CDCl_3$) $\delta$: 3.75 (6H, s, OMe×2), 5.50 (2H, s, $CH_2$), 6.95 (2H, d, $J$=7.0 Hz, H-aromatic), 7.15—7.20 (3H, m, H-aromatic), 7.23—7.31 (1H, m, H-aromatic), 7.40 (1H, ddd, $J$=1.5, 7.0, 8.5 Hz, H-aromatic), 7.49 (1H, d, $J$=8.8 Hz, H-aromatic), 7.59 (1H, d, $J$=8.5 Hz, H-aromatic), 7.82 (1H, d, $J$=9.5 Hz, H-3 or 4), 7.93 (1H, d, $J$=9.5 Hz, H-3 or 4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 51.10 (C2), 58.22, 119.44, 125.00, 125.65, 126.45 (C2), 127.61, 127.03, 128.34, 128.76 (C2), 130.64, 135.04, 135.96 (C2), 138.92, 163.02, 168.04 (C2). MS *m*/*z*: 349 ($M^+$), 230, 91. HR-MS Calcd for $C_{21}H_{19}NO_4$, 349.1314. Found: 349.1327.

**7b**: Red needles (methanol), mp 232—234 °C. IR (KBr) cm$^{-1}$: 2198, 2179, 1628, 1568, 812, 765, 720. $^1$H-NMR ($CDCl_3$) $\delta$: 5.84 (2H, s, $CH_2$), 7.12 (2H, d, $J$=6.9 Hz, H-aromatic), 7.31—7.40 (4H, m, H-aromatic), 7.49—7.55 (2H, m, H-aromatic), 7.55—7.65 (2H, m, H-aromatic), 7.72 (1H, d, $J$=9.5 Hz, H-3 or 4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 54.32, 116.10, 117.00, 118.00, 121.07, 123.62 (C2), 125.31, 125.55 (C2), 128.16, 129.12, 129.28 (C2), 132.33, 134.33, 137.06, 139.83, 159.91. MS *m*/*z*: 283 ($M^+$), 91. HR-MS Calcd for $C_{19}H_{13}N_3$, 283.1109. Found: 283.1136.

**7c**: Yellow plates (methanol), mp 171—172 °C. IR (KBr) $cm^{-1}$: 2187, 1681, 1624, 824, 750, 736. $^1$H-NMR ($CDCl_3$) $\delta$: 3.80 (3H, s, OMe), 5.70 (2H, s, $CH_2$), 6.94 (2H, d, $J$=6.6 Hz, H-aromatic), 7.19—7.32 (4H, m, H-aromatic), 7.41—7.42 (2H, m, H-aromatic), 7.60 (1H, d, $J$=7.7 Hz, H-aromatic), 7.74 (1H, d, $J$=9.5 Hz, H-4), 8.28 (1H, d, $J$=9.5 Hz, H-3). $^{13}$C-NMR ($CDCl_3$) $\delta$: 51.69, 58.27, 118.69, 120.79, 123.53, 124.92, 124.95, 126.23, 127.78, 128.52, 128.84 (C2), 131.14, 135.73 (C2), 136.02, 139.51, 160.68 (C2), 166.72. MS *m/z*: 316 ($M^+$), 257, 91. HR-MS Calcd for $C_{20}H_{16}N_2O_2$, 316.1212. Found: 316.1222.

**7d**: Yellow plates (methanol), mp 105—106 °C. IR (KBr) $cm^{-1}$: 1655, 1608, 1581, 825, 751, 716. $^1$H-NMR ($CDCl_3$) $\delta$: 2.54 (3H, s, COMe), 3.69 (3H, s, OMe), 5.80 (2H, s, $CH_2$), 6.98—7.00 (2H, m, H-Ph), 7.14—7.27 (3H, m, H-Ph), 7.46 (1H, ddd, $J$=1.0, 7.3, 7.3 Hz, H-aromatic), 7.56 (1H, ddd, $J$=1.5, 7.3, 8.8 Hz, H-aromatic), 7.76—7.82 (2H, m, H-aromatic), 7.89 (1H, d, $J$=9.1 Hz, H-4), 8.06 (1H, d, $J$=9.1 Hz, H-3). $^{13}$C-NMR ($CDCl_3$) $\delta$: 29.80, 50.28, 57.79, 98.75, 120.08, 126.37 (C2), 126.57 (C2), 126.94, 127.77, 128.90, 128.95, 129.80, 131.53, 135.88, 138.02, 138.31, 165.38, 168.38, 190.91. MS *m/z*: 333 ($M^+$), 230, 91. HR-MS Calcd for $C_{21}H_{19}NO_3$, 333.1365. Found: 333.1377.

**7e**: Yellow plates (methanol), mp 166—167 °C. IR (KBr) $cm^{-1}$: 1681, 1615, 1608, 832, 760, 750. $^1$H-NMR ($CDCl_3$) $\delta$: 2.43 (6H, s, COMe×2), 5.92 (2H, s, $CH_2$), 7.05 (2H, dd, $J$=1.6, 8.1 Hz, H-Ph), 7.16—7.28 (3H, m, H-Ph), 7.56 (1H, ddd, $J$=1.0, 8.0, 9.0 Hz, H-aromatic), 7.64 (1H, ddd, $J$=1.6, 7.1, 8.7 Hz, H-aromatic), 7.83—7.87 (2H, m, H-aromatic), 7.90 (1H, d, $J$=8.8 Hz, H-4), 8.25 (1H, d, $J$=8.8 Hz, H-3). $^{13}$C-NMR ($CDCl_3$) $\delta$: 25.48 (C2), 51.23, 119.65, 124.90, 125.68, 126.99 (C2), 127.51, 127.66, 128.76, 128.66 (C2), 130.34, 135.45, 135.76 (C2), 138.73, 163.52, 168.51 (C2). MS *m/z*: 317 ($M^+$), 274, 232, 91. HR-MS Calcd for $C_{21}H_{19}NO_2$, 317.1416. Found: 317.1422.

**7f**: Yellow needles (acetone), mp 270—275 °C. IR (KBr) $cm^{-1}$: 1620, 1566, 757, 751, 718. $^1$H-NMR ($CDCl_3$) $\delta$: 1.97—2.16 (2H, m, $CH_2$), 2.48—2.57 (4H, m, $COCH_2$×2), 5.89 (2H, s, $NCH_2$), 7.00 (2H, dd, $J$=1.6, 8.3 Hz, H-Ph), 7.08—7.27 (3H, m, H-Ph), 7.50 (1H, ddd, $J$=1.0, 7.1, 8.6 Hz, H-aromatic), 7.60 (1H, ddd, $J$=1.6, 7.1, 8.6 Hz, H-aromatic), 7.83 (1H, dd, $J$=1.6, 8.6 Hz, H-aromatic), 7.91 (1H, dd, $J$=1.0, 8.6 Hz, H-aromatic), 8.07 (1H, d, $J$=8.9 Hz, H-4), 8.25 (1H, d, $J$=8.9 Hz, H-3). $^{13}$C-NMR ($CDCl_3$) $\delta$: 21.40, 34.59 (C2), 56.89, 108.59, 119.55, 124.60, 125.44 (C2), 126.10, 126.58, 127.44, 128.32 (C2), 129.00, 132.06, 134.99, 136.89, 140.40, 158.58, 201.00 (C2). MS *m/z*: 329 ($M^+$), 321, 91. HR-MS Calcd for $C_{22}H_{19}NO_2$, 329.1416. Found: 329.1394.

**7g**: Yellow needles (acetone), mp 239—240 °C. IR (KBr) $cm^{-1}$: 1657, 1605, 836, 755, 718. $^1$H-NMR ($CDCl_3$) $\delta$: 2.60 (4H, s, $CH_2$×2), 5.99 (2H, s, $NCH_2$), 6.86 (2H, dd, $J$=1.5, 6.9 Hz, H-Ph), 7.13—7.23 (3H, m, H-Ph), 7.51 (1H, ddd, $J$=1.0, 7.0, 7.0 Hz, H-6 or 7), 7.62 (1H, ddd, $J$=1.5, 7.0, 8.5 Hz, H-6 or 7), 7.82—7.87 (2H, m, H-5,8), 8.32 (1H, d, $J$=9.1 Hz, H-3 or 4), 8.40 (1H, d, $J$=9.1 Hz, H-3 or 4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 33.95 (C2), 57.89, 109.58, 119.64, 125.49, 125.99 (C2), 126.70, 126.88, 127.87, 128.98 (C2), 129.19, 132.06, 135.57, 138.79, 140.30, 157.68, 200.47 (C2). MS *m/z*: 315 ($M^+$), 230, 181, 91. HR-MS Calcd for $C_{21}H_{17}NO_2$, 315.1259. Found: 315.1278.

**7h**: Yellow needles (acetone), mp 220 °C. IR (KBr) $cm^{-1}$: 1681, 1651, 1547, 1174, 820, 752, 711. $^1$H-NMR ($CDCl_3$) $\delta$: 2.64 (4H, s, $CH_2CH_2$), 2.82 (3H, s, SMe), 5.83 (2H, s, $NCH_2$), 7.05 (2H, dd, $J$=2.6, 7.8 Hz, H-Ph), 7.31—7.40 (3H, m, H-Ph), 7.49—7.56 (2H, m, H-7, 8), 7.68 (1H, ddd, $J$=1.5, 6.8, 8.3 Hz, H-6), 8.47 (1H, s, H-3), 8.58 (1H, dd, $J$=1.5, 8.3 Hz, H-5). $^{13}$C-NMR ($CDCl_3$) $\delta$: 16.42, 33.82 (C2), 53.48, 110.81, 114.51, 115.71, 123.64, 124.98, 125.70 (C2), 128.52, 129.40 (C2), 132.46, 132.69, 133.87, 140.59, 152.98, 159.26, 201.73 (C2). MS *m/z*: 361 ($M^+$), 270, 91. HR-MS Calcd for $C_{22}H_{19}NO_2S$, 361.1137. Found: 361.1157.

**10g**: Pale yellow columns (methanol), mp 236—238 °C. IR (KBr) $cm^{-1}$: 1660, 830, 750. $^1$H-NMR ($CDCl_3$) $\delta$: 2.63 (4H, s, $CH_2$×2), 4.15 (3H, s, NMe), 7.61 (1H, ddd, $J$=1.5, 7.4, 8.9 Hz, H-aromatic), 7.80—7.90 (2H, m, H-aromatic), 7.96 (1H, dd, $J$=0.8, 9.4 Hz, H-5 or 8), 8.19 (1H, d, $J$=9.0 Hz, H-4), 8.33 (1H, d, $J$=9.0 Hz, H-3). $^{13}$C-NMR ($CDCl_3$) $\delta$: 34.08 (C2), 42.70, 108.99, 117.96, 125.18, 126.03, 126.80, 129.05, 132.47, 139.22, 139.85, 156.56, 200.57 (C2). MS *m/z*: 239 ($M^+$). HR-MS Calcd for $C_{15}H_{13}NO_2$, 239.0946. Found: 239.0949.

**10h**: Pale yellow columns (methanol), mp >300 °C. IR (KBr) $cm^{-1}$: 1600, 840, 750. $^1$H-NMR ($CDCl_3$) $\delta$: 2.61 (4H, s, $CH_2$×2), 2.83 (3H, s, SMe), 4.13 (3H, s, NMe), 7.55 (1H, ddd, $J$=1.5, 6.9, 8.4 Hz, H-6 or 7), 7.69 (1H, dd, $J$=1.5, 8.4 Hz, H-8), 7.80 (1H, ddd, $J$=1.5, 6.9, 8.4 Hz, H-6 or 7), 8.40 (1H, s, H-3), 8.54 (1H, dd, $J$=1.5, 8.4 Hz, H-5). $^{13}$C-NMR ($CDCl_3$) $\delta$: 16.43, 33.80 (C2), 37.17, 110.50, 114.35, 114.86, 123.46, 124.91, 132.76, 133.68, 140.69, 152.59, 159.01, 201.61 (C2). MS *m/z*: 285 ($M^+$). HR-MS Calcd for $C_{16}H_{15}NO_2S$, 285.0823. Found: 285.0805.

**General Procedure for the Cyclization Reactions of 7a, d, e with Acetic Anhydride** A mixture of **7a** (0.349 g, 1.0 mmol) and acetic anhydride (4 ml) was refluxed for 4 h and then concentrated *in vacuo*. The residure was purified by silica gel column chromatography, in which the first fraction eluted with hexane–ether (1 : 1) gave methyl 2-acetoxy-3-phenylpyrrolo[1,2-*a*]quinolinyl-1-carboxylate (**11a**, 0.232 g, 65%). Reaction of **7d** with acetic anhydride was carried out similarly to give methyl 2-methyl-3-phenylpyrrolo[1,2-*a*]quinolinyl-1-carboxylate (**11d**, 75%) and 2-acetoxy-1-acetyl-3-phenylpyrrolo[1,2-*a*]quinoline (**12d**, 21%); reaction of **7e** with acetic anhydride afforded 1-acetyl-2-methyl-3-phenylpyrrolo[1,2-*a*]quinoline (**11e**, 86%).

**11a**: Yellow plates (acetone), mp 165—166 °C. IR (KBr) $cm^{-1}$: 1761, 1694, 1605, 791, 773, 761. $^1$H-NMR ($CDCl_3$) $\delta$: 2.25 (3H, s, COMe), 3.95 (3H, s, OMe), 6.93 (1H, d, $J$=7.3 Hz, H-3), 7.45—7.63 (8H, m, H-aromatic), 7.83 (1H, d, $J$=7.3 Hz, H-4), 9.39 (1H, ddd, $J$=0.7, 1.4, 8.3 Hz, H-aromatic). $^{13}$C-NMR ($CDCl_3$) $\delta$: 20.64, 51.60, 101.44, 113.70, 119.17, 121.31, 125.38, 126.61, 126.91, 127.61, 127.65, 127.83, 128.82, 129.02, 129.13 (C2), 129.80, 130.06 (C2), 137.30, 164.77, 170.01. MS *m/z*: 359 ($M^+$), 285. HR-MS Calcd for $C_{22}H_{17}NO_4$, 359.1158. Found: 359.1172.

**11d**: The second fraction: Yellow needles (acetone), mp 185—186 °C. IR (KBr) $cm^{-1}$: 1764, 1718, 1655, 1604. $^1$H-NMR ($CDCl_3$) $\delta$: 2.15 (3H, s, COMe), 2.51 (3H, s, OCOMe), 7.14 (1H, dd, $J$=1.6, 7.1 Hz, H-5 or 8), 7.16—7.36 (2H, m, H-6, 7), 7.40—7.54 (6H, m, H-Ph, 3), 7.71 (1H, dd, $J$=1.5, 8.1 Hz, H-5 or 8), 8.50 (1H, d, $J$=9.4 Hz, H-4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 20.69, 30.00, 108.22, 117.76, 118.92, 121.10, 124.46, 125.49, 125.55, 127.76, 128.95, 129.01 (C2), 129.07, 130.5 (C2), 131.26, 132.75, 133.31, 138.47, 169.60, 192.12. MS *m/z*: 343 ($M^+$), 301, 286. HR-MS Calcd for $C_{22}H_{17}NO_3$, 343.1208. Found: 343.1222.

**12d**: The first fraction: Yellow plates (acetone), mp 123 °C. IR ($CHCl_3$) $cm^{-1}$: 1718, 1700, 1605. $^1$H-NMR ($CDCl_3$) $\delta$: 2.66 (3H, s, CMe), 3.56 (3H, s, OMe), 7.14 (1H, ddd, $J$=1.6, 7.1, 8.7 Hz, H-aromatic), 7.21—7.39 (2H, m, H-aromatic), 7.44 (1H, d, $J$=9.4 Hz, H-3), 7.53 (5H, s, H-Ph), 7.69 (1H, dd, $J$=1.5, 7.7 Hz, H-aromatic), 8.51 (1H, d, $J$=9.4 Hz, H-4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 20.64, 31.60, 101.44, 113.70, 119.17, 121.31, 125.38, 126.61, 126.91, 127.61, 127.65, 127.83, 128.82, 129.02, 129.13 (C2), 129.80, 130.06 (C2), 137.30, 170.01. MS *m/z*: 315 ($M^+$), 300, 284. HR-MS Calcd for $C_{21}H_{17}NO_2$, 315.1259. Found: 315.1227.

**11e**: Yellow needles (acetone), mp 110—111 °C. IR (KBr) $cm^{-1}$: 1693, 1642, 1601, 821, 805, 748. $^1$H-NMR ($CDCl_3$) $\delta$: 2.30 (3H, s, COMe), 2.65 (3H, s, CMe), 7.09 (1H, ddd, $J$=1.6, 6.9, 8.5 Hz, H-aromatic), 7.15—7.29 (2H, m, H-aromatic), 7.35—7.40 (3H, m, H-3, aromatic), 7.42—7.60 (3H, m, H-aromatic), 7.67 (1H, dd, $J$=1.5, 7.9 Hz, H-aromatic), 8.42 (1H, d, $J$=9.4 Hz, H-4). $^{13}$C-NMR ($CDCl_3$) $\delta$: 13.05, 31.68, 100.51, 115.92, 117.77, 118.91, 123.89, 123.95, 124.59, 125.45, 127.39, 128.51, 128.60, 128.63, 129.08 (C2), 131.24, 133.43, 134.41, 134.71, 195.04. MS *m/z*: 299 ($M^+$), 284. HR-MS Calcd for $C_{21}H_{17}NO$, 299.1310. Found: 299.1321.

## References


1) Tomisawa H., Tanbara T., Kato H., Hongo H., Fujita R., *Heterocycles*, **15**, 277—280 (1981).
2) Tominaga Y., Matsuda Y., *J. Syn. Org. Chem. Jpn.*, **43**, 669—679 (1985). References cited therein.
3) Roberts E. M., Gates M., Boekelheide V., *J. Org. Chem.*, **20**, 1443—1447 (1955).
4) Hurst J., Melton T., Wibberley D. G., *J. Chem. Soc.*, **1965**, 2948—2955 (1965).
5) Melton T., Taylor J., Wibberley D. G., *J. Chem. Soc. Chem. Commun.*, **1965**, 151—152 (1965).
6) Henrick C. A., Ritchie E., Taylor W. C., *Aust. J. Chem.*, **20**, 2467—2477 (1967).
7) Irwin W. J., Wibberley D. G., *J. Chem. Soc.*, *Perkin Trans 1*, **1974**, 250—252 (1974).
8) Komatsu M., Kasano Y., Yamaoka S., Minakata S., *Synthesis*, **2003**, 1398—1402 (2003).
9) Boultadakis E., Chung B., Elsegood M. R. J., Weaver G. W., *Synlett*, **2002**, 1547—1549 (2002).