A New Reaction of Tris(alkylthio)cyclopropenium Salt with *m*-Substituted Anilines Affording Quinoline Derivatives

Shigeo YONEDA* and Hideo KOJIMA
Department of Applied Chemistry, University of Osaka Prefecture,
Sakai, Osaka 591
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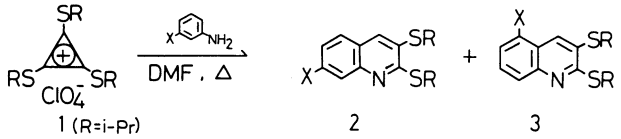
Synopsis. The reaction of tris(alkylthio)cyclopropenium salt with *m*-substituted anilines gave quinoline derivatives.

Owing to its high strain and aromatic character, the tris(alkylthio)cyclopropenium ion (**1**) undergoes a wide range of reactions including substitution,[1] ring opening,[1] and one-electron oxidation reactions.[2] We have recently reported that the reaction of tris(*t*-butylthio)cyclopropenium salt with dialkylamines ($R^1NHCH_2R^2$) resulted in the formation of the corresponding bis(*t*-butylthio)pyrroles.[3] This finding led us to explore a new "one-pot" synthesis of heterocyclic compounds using tris(alkylthio)cyclopropenium salt as a building block.

We now report the successful synthesis of quinolines from **1** and *m*-substituted anilines under mild reaction conditions.

The reactions were carried out in *N*,*N*-dimethylformamide (DMF) at 85 °C for 5—100 h to give 7- and 5-substituted quinolines **2a—d** and **3a—d** in good yields. The results are summarized in Table 1.



1 (R=i-Pr) 2 3

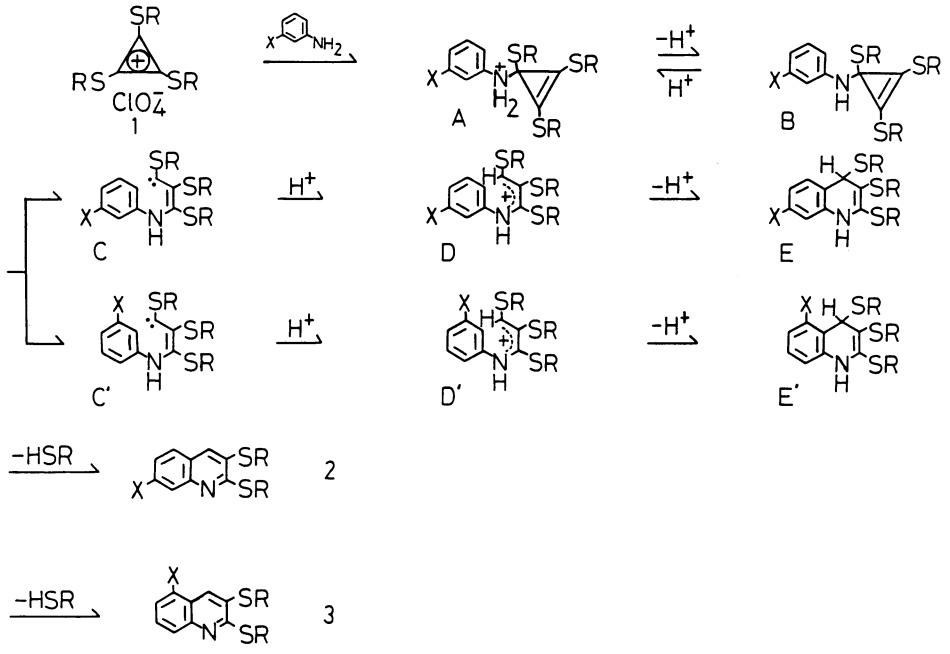
a, X = OMe
b, X = NH_2
c, X = OH
d, X = Me

Table 1. Reaction of **1** with *m*-Substituted Anilines

	X	Time/h	Yield/%[a]	
			2	**3**
a	OMe	50	68	7
b	NH_2	5	9	25
c	OH	5	85	<1
d	Me	93	52	9

a) Isolated yield except for **2d** and **3d**. The yields of **2d** and **3d** were determined by ^1H NMR.

Scheme 1 outlines a possible pathway for the formation of **2** and **3**. Reversible generation of B from the initially formed ammonium salt A leads to a facile ring opening to C and C′. Protonation of C and C′ would afford D and D′, respectively. Subsequent intramolecular electrophilic aromatic substitution would give the six-membered intermediates E and E′ and result in the formation of **2** and **3** by thiol elimination.



Scheme 1.

Experimental

^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-GX 270 FT NMR spectrometer using chloroform-*d* as a solvent and tetramethylsilane as an internal standard; the chemical shifts are reported in δ values. Mass spectra were recorded on a Shimadzu LKB-9000 spectrometer(70eV). Infrared spectra were recorded on a Hitachi 215 spectrometer. Column chromatography was performed on silica gel (Wakogel C-300). Melting points were determined with a Yanaco MP-S3 melting point apparatus and were uncorrected.

General Synthetic Method of Quinoline Derivatives, 2a—d and 3a—d. All quinoline derivatives were prepared by the reaction of **1** with *m*-substituted anilines in dry DMF. The general procedure will be illustrated below by using the syntheses of **2a** and **3a**.

To a solution of *m*-anisidine (0.5 mmol) in dry DMF (15 ml) was added dropwise a solution of tris(isopropylthio)-cyclopropenium perchlorate (**1**) (0.5 mmol) in dry DMF (15 ml) at 85 °C under nitrogen. The reaction mixture was stirred at 85 °C for 50 h, then poured into water (200 ml), and extracted with ether (200 ml). The organic layer was washed with water (200 ml) and dried (Na_2SO_4). The solvent was evaporated off under reduced pressure, the residual oil was chromatographed on silica gel [hexane–chloroform (3:1) as eluent], and final purification by recrystallization from methanol gave both 7- and 5-methoxyquinolines (**2a** and **3a**) as colorless needles in 68% and 7% yields, respectively.

2a: mp 65.0—65.5 °C; IR (KBr) 1620, 1580, 1495, 1445, 1335, 1225, 1125, 1030, 850, and 825 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.94 (1H, s, 4-H), 7.55 (1H, d, *J*=9.0 Hz, 5-H), 7.24 (1H, d, *J*=2.6 Hz, 8-H), 7.06 (1H, dd, *J*=9.0 and 2.6 Hz, 6-H), 4.21 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 3.94 (3H, s, OMe), 3.47 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 1.48 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr), 1.30 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr); ^{13}C NMR ($CDCl_3$)δ=163.3, 161.2, 149.0, 140.0, 128.2, 124.8, 120.9, 118.0, 106.6, 55.5, 38.4, 35.4, 23.0$_4$ (2C), and 23.0$_0$ (2C); MS (70 eV) *m/z* 307 (M^+).

3a: mp 66.0—68.0 °C; IR (KBr) 1620, 1575, 1560, 1465, 1335, 1270, 1210, 1130, 1010, and 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.38 (1H, s, 4-H), 7.51—7.49 (2H, m, benzene ring), 6.75 (1H, dd, *J*=5.8 and 2.8 Hz, benzene ring), 4.21 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 3.97 (3H, s, OMe), 3.55 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 1.47 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr), and 1.34 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr); ^{13}C NMR ($CDCl_3$) δ=162.6, 154.9, 147.8, 133.6, 129.4, 127.2, 120.1, 118.0, 103.5, 55.7, 38.2, 35.5, 23.0(2C), and 22.9(2C); MS (70 eV) *m/z* 307 (M^+).

Similar reactions of **1** with several *m*-substituted anilines were carried out. The reaction of **1** with *m*-phenylenediamine afforded **2b** as reddish brown solid and **3b** as yellow oil.

2b: mp 89—91 °C; IR (KBr) 3450, 3360, 3225, 1620, 1575, 1495, 1335, 1230, 1120, 1050, 990, 850, and 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.87 (1H, s, 4-H), 7.46 (1H, d, *J*=8.6 Hz, 5-H), 7.05 (1H, d, *J*=2.4 Hz, 8-H), 6.83 (1H, dd, *J*=8.6 and 2.4 Hz, 6-H), 4.16 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 4.03 (2H, broad s, NH_2), 3.43 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 1.46 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr), 1.28 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr); ^{13}C NMR ($CDCl_3$) δ=163.5, 149.1, 148.2, 140.9, 128.5, 122.9, 119.7, 116.8, 108.5, 38.6, 35.2, 23.1 (2C), and 23.0 (2C); MS (70 eV) *m/z* 292 (M^+).

3b: IR (neat) 3475, 3375, 3240, 1620, 1580, 1550, 1465, 1370, 1340, 1245, 1150, 1080, 1055, 955, and 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.04 (1H, s, 4-H), 7.45—7.35 (2H, m, benzene ring), 6.69 (1H, dd, *J*=7.0 and 1.5 Hz, benzene ring), 4.20 (1H, sep, *J*=6.9 Hz, CH of *i*-Pr), 4.12 (2H, broad s, NH_2), 3.51 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 1.47 (6H, d, *J*=6.9 Hz, CH_3 of *i*-Pr), 1.31 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr); ^{13}C NMR ($CDCl_3$) δ=162.8, 148.2, 142.1, 134.4, 130.4, 125.8, 118.7, 116.0, 109.4, 38.6, 35.4, 23.1 (2C), and 23.0 (2C); MS (70 eV) *m/z* 292 (M^+).

The reaction of **1** with *m*-aminophenol afforded **2c** and **3c** as yellow oil.

2c: IR (neat) 3375, 1620, 1580, 1560, 1495 , 1450, 1335, 1200, 1130, 1050, 995, 860, and 810 cm^{-1}; ^1H NMR ($CDCl_3$) δ=7.93 (1H, s, 4-H), 7.56 (1H, d, *J*=8.6 Hz, 5-H), 7.25 (1H, d, *J*=2.7 Hz, 8-H), 7.03 (1H, dd, *J*=8.6 and 2.7 Hz, 6-H), 5.69 (1H, broad s, OH), 4.17 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 3.47 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 1.45 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr), 1.30 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr); ^{13}C NMR ($CDCl_3$) δ=163.5, 157.4, 148.4, 140.2, 128.8, 125.0, 120.9, 117.2, 110.0, 38.5, 35.6, 23.0 (2C), and 22.9 (2C); MS (70 eV) *m/z* 293 (M^+).

3c: IR (neat) 3400, 1620, 1580, 1555, 1465, 1335, 1275, 1200, 1130, 1080, 1050, and 805 cm^{-1}; ^1H NMR ($CDCl_3$) δ=8.34 (1H, s, 4-H), 7.51—7.39 (2H, m, benzene ring), 6.73 (1H, dd, 7.3 and 1.2 Hz, benzene ring), 5.44 (1H, broad s, OH), 4.21 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 3.56 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 1.48 (6 H, d, *J*=6.7 Hz, CH_3 of *i*-Pr), 1.35 (6H, d,*J*=6.7 Hz, CH_3 of *i*-Pr); MS (70 eV) *m/z* 293 (M^+).

The reaction of **1** with *m*-toluidine afforded a mixture of **2d** and **3d** as colorless solid.

2d: ^1H NMR ($CDCl_3$) δ=7.93 (1H, s, 4-H), 7.69 (1H, s, 8-H), 7.54 (1H, d, *J*=8.4 Hz, 5-H), 7.22 (1H, dd, *J*=8.4 and 1.1 Hz, 6-H), 4.21 (1H, sep, *J*=7.0 Hz, CH of *i*-Pr), 3.50 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 2.51 (3H, s, Me), 1.48 (6H, d, *J*=7.0 Hz, CH_3 of *i*-Pr), 1.31 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr); MS (70 eV) *m/z* 291 (M^+).

3d: ^1H NMR ($CDCl_3$) δ=8.15 (1H, s, 4-H), 7.76 (1H, d, *J*=8.6 Hz, benzene ring), 7.51—7.46 (2H, m, benzene ring), 4.20 (1H, sep, *J*=7.0 Hz, CH of *i*-Pr), 3.54 (1H, sep, *J*=6.7 Hz, CH of *i*-Pr), 2.61 (3H, s, Me), 1.48 (6H, d, *J*=7.0 Hz, CH_3 of *i*-Pr), 1.33 (6H, d, *J*=6.7 Hz, CH_3 of *i*-Pr); MS (70 eV) *m/z* 291 (M^+).

References

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