[Chem. Pharm. Bull.]
36(3) 930-939 (1988)

Reactions of 3-Benzoyl-3,4-dihydro-2-methyl-4-quinazolinecarbonitrile (2-Methylquinazoline Reissert Compound) with Acid, Base, Sodium Hydride, and Electrophiles

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(Received August 17, 1987)

Acid hydrolysis of 3-benzoyl-3,4-dihydro-2-methyl-4-quinazolinecarbonitrile (**1**₁, 2-methylquinazoline Reissert compound) resulted in the formation of the oxazole (**1**₃). Alkaline hydrolysis gave 2-methylquinazoline (**1**₂) and benzoic acid (**8**). The anion (**D**¹), generated from **1**₁ and NaH in dimethylformamide (DMF), underwent decomposition to give the ketone (**1**₄) and the cyanoquinazoline (**1**₅) together with by-products **1**₂ and *O*-benzoylbenzoin (**9**). Compound **1**₁ reacted with aromatic aldehydes (**10a**—**c**) in the presence of NaH to give the benzoates (**1**_{6a}—**c**) and by-products **1**₂ and **1**₅. Alkylation (or arylation) with alkyl (or aryl) halides (**11a**, **b**) afforded the corresponding 4-substituted derivatives (**1**_{9a}, **b**) and a by-product **1**₄.

The reactivities of **1**₁ and 3-benzoyl-3,4-dihydro-4-quinazolinecarbonitrile (**2**₁, quinazoline Reissert compound) are compared.

Keywords—Reissert compound; quinazoline; hydrolysis; Reissert compound anion; rearrangement; aromatization; electronic effect; electrophilic substitution

In the preceding paper¹⁾ we reported a preparation of 3-benzoyl-3,4-dihydro-2-methyl-4-quinazolinecarbonitrile (**1**₁, 2-methylquinazoline Reissert compound). Recently we also obtained for the first time 3-benzoyl-3,4-dihydro-4-quinazolinecarbonitrile (**2**₁, quinazoline Reissert compound) through an indirect two-step procedure, as shown in Chart 1.^{2a)}

In order to elucidate the reactivity of **1**₁ with regard to the electronic effect of the methyl substituent, we examined the following reactions of **1**₁; (a) acid hydrolysis, (b) alkaline hydrolysis, (c) reaction with sodium hydride, and (d) reaction with electrophiles in the presence

Chart 1

of sodium hydride. In the present paper, we describe the results obtained from the above reactions (a) to (d) in detail, comparing the reactivity of **1**₁ with that of **2**₁ which has already been reported.²⁾

(a) Acid Hydrolysis

We reported that quinazoline Reissert compound **2**₁ was hydrolyzed in an acid medium to give the ring fission product, 2-(2-aminophenyl)-2-benzamidoacetonitrile (**2**₃) together with **2**₂ and benzoic acid (**8**) by way of the cyclic amidinium salt (**A**²).^{2a)}

On the other hand, **1**₁ reacted with acid in a different way from that of **2**₁, resulting in the formation of 4-(2-acetamidophenyl)-5-amino-2-phenyloxazole (**1**₃).

The mechanism of the formation of the oxazole **1**₃ is assumed to involve sequential quaternization, ring closure, and ring fission, as shown in Chart 2. Because electronic effects

Chart 2

of the N¹-atom and the methyl substituent of the initially formed quaternary salt (A¹) reinforce each other, we can write resonance structures A¹-1 and A¹-2, in which there is no charge separation at the N³-atom. This absence of charge separation enhances ring closure, leading to the oxazolo[3,4-*c*]quinazolinium salt (B¹). Subsequent nucleophilic attack of water at the carbon of the cyclic amidinium moiety in B¹, followed by ring fission, gives the oxazole **1**₃. The intermediate B¹ corresponds to the oxazolo[4,3-*a*]isoquinolinium salt (B³)^{3,4} observed in acid hydrolysis of 2-benzoyl-1,2-dihydro-1-isoquinolinecarbonitrile (**3**₁, isoquinoline Reissert compound).

On the other hand, in acid hydrolysis of **2**₁, the initially formed quaternary salt (A²) can not cyclize to the oxazolo[3,4-*c*]quinazolinium salt (B²), because of a positive charge at the N³-atom. Eventually, A² is hydrolyzed in acid medium, giving the ring fission product **2**₃.

(b) Alkaline Hydrolysis

It is well known that hydrolysis of **2**₁ in an alkaline medium resulted in the formation of **2**₂ and **8**.^{2a)} We also reported that in the case of **3**₁ a similar hydrolysis proceeded, and isoquinoline (**3**₂) and **8** were obtained.^{2a)}

Similarly, **1**₁ was hydrolyzed to **1**₂⁵⁾ and **8** by alkali. The reaction may well occur by the initial formation of an adduct (C¹) of the hydroxide ion at the carbonyl carbon, followed by the ready loss of a cyanide ion, leading to **1**₂ and **8**, as shown in Chart 3.

Chart 3

(c) Reaction with Sodium Hydride

Boekelheide and Weinstock reported that the anion (D³) of **3**₁ underwent rearrangement, giving 1-benzoylisoquinoline (**3**₄) with expulsion of a cyanide ion.⁶⁾ Moreover, McEwen and Cobb proposed a mechanism in which the rearrangement of the anion (D⁴) of 1-benzoyl-1,2-dihydro-2-quinolinecarbonitrile (**4**₁, quinoline Reissert compound) to 2-benzoylquinoline (**4**₄) proceeded through the aziridine intermediate (E⁴) in an intramolecular process.⁷⁾

On the other hand, recently we reported that the anion (D²) of **2**₁ underwent aromatization, which is different from the behavior of D³, resulting in the formation of 4-quinazolinecarbonitrile (**2**₅) and a benzaldehyde anion (F), together with α -phenyl-4-quinazolinylmethyl benzoate (**2**_{6a}) and *O*-benzoylbenzoin (**9**)⁸⁾ as by-products which were formed by further reaction of the resulting anion F with another molecule of **2**₁.^{2a)}

In the case of **1**₁, the anion (D¹), generated from the reaction of **1**₁ with sodium hydride, underwent both rearrangement and aromatization, resulting in the formation of 4-benzoyl-2-methylquinazoline (**1**₄)⁹⁾ and 2-methyl-4-quinazolinecarbonitrile (**1**₅)¹⁰⁾ together with **1**₂ and

Chart 4

9.

The rearrangement and aromatization may be explained as follows (Chart 5). In a resonance structure D¹⁻³, a positive charge at the N³-atom, due to the electronic effect of the N¹-atom as well as a positive charge at the neighboring carbonyl carbon decreases the stability of the N³-CO bond, favoring aromatization to **1**₅ with expulsion of the anion F rather than the formation of the aziridine intermediate E¹. On the other hand, resonance structures D¹⁻¹ and D¹⁻², in which the electron-withdrawing effect of the N¹-atom and electron-releasing effect of the methyl substituent overlap each other, do not bear a positive charge at the N³-atom, favoring ring closure to the aziridine intermediate E¹ rather than aromatization. The intermediate E¹ leads to **1**₄ with expulsion of a cyanide ion.

By-products, **9** and **1**₂, are assumed to be formed by further reactions of the resulting

anion F involving sequential formation of benzaldehyde (**10a**), benzoin condensation, and nucleophilic attack of the O-anion (G) of benzoin on the carbonyl carbon of **1₁**, as shown in Chart 5. A similar mechanism has been proposed by us¹¹⁾ for the formation of **9** and 1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**5₂**) in the reaction of 5-benzoyl-4,5-dihydro-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine-4-carbonitrile (**5₁**) with aromatic aldehydes (**10**).

On the basis of our mechanism, it can be assumed that the introduction of an electron-withdrawing group into the 4-position of **3₁** might cause the aromatization as observed in **2₁**.^{2a)} In fact, 2-benzoyl-1,2-dihydro-1,4-isoquinolinedicarbonitrile (**6_{1a}**), which was prepared by application of Ruchirawat's method¹²⁾ to 4-isoquinolinecarbonitrile (**6_{2a}**),¹³⁾ reacted with sodium hydride, giving the anticipated dicarbonitrile (**6_{3a}**).¹⁴⁾ In the case of 2-benzoyl-4-bromo-1,2-dihydro-1-isoquinolinecarbonitrile (**6_{1b}**) having an electronegative bromine atom at the 4-position, a similar aromatization occurred, resulting in the formation of 4-bromo-1-isoquinolinecarbonitrile (**6_{5b}**) and 4'-bromo-4,1'-biisoquinoline-1-carbonitrile (**6_{8b}**), which may be formed by nucleophilic substitution of the bromine atom of the resulting **6_{5b}** with the anion **D₆**, as shown in Chart 6.

Chart 6

(d) Reaction with Electrophiles

The reactions of aromatic aldehydes (**10**) and alkyl (or aryl) halides (**11**) with **2₁** were reported in the previous paper.^{2b)}

A similar reaction proceeded in the reaction of **1₁** with **10a—c** in the presence of sodium hydride, giving the benzoates (**1_{6a—c}**) and by-products **1₂** and **1₅**, as shown in Chart 7. Formation of the benzoates **1₆** may be explained by the mechanism involving sequential formation of intermediates **J¹** and **K¹**, similar to the intermediates observed in the reaction of the anions **D²** and **D⁴** with **10**,^{2b,15)} as shown in Chart 7.

Alkylation (or arylation), similar to that of **2₁**, occurred in the reaction of **1₁** with methyl iodide (**11a**) and 2,4-dinitrochlorobenzene (**11b**) in the presence of sodium hydride, yielding 4-methyl- (**1_{9a}**) and 4-(2,4-dinitrophenyl)-3-benzoyl-3,4-dihydro-2-methyl-4-quinazoline-carbonitriles (**1_{9b}**), respectively, together with **1₄** as a by-product, as shown in Chart 7.

In connection with reactions involving the formation of the anion of Reissert compounds, we examined the reaction of **6₁** with **10a** in the presence of sodium hydride. Thus, **6_{1a}** and **6_{1b}** reacted with **10a** in the same way as that of **1₁**, affording the corresponding benzoates **6_{6a}** and **6_{6b}**, respectively, together with by-products **9** and the corresponding isoquinolines (**6_{2a}** and **6_{2b}**). The benzoates **6_{6a}** and **6_{6b}** were converted into the ketone (**6_{4a}**) or the alcohol (**6_{10b}**) by alkaline hydrolysis, as shown in Chart 8.

The experimental results may be summarized as follows. i) In the reaction (a), **1₁** reacts differently from **2₁**, and the oxazole **1₃** is formed by way of the oxazolo[3,4-*c*]quinazolinium cation **B¹**. ii) In the reaction (c), **1₁** undergoes both aromatization and rearrangement (the latter did not take place in the case of **2₁**^{2b)}), resulting in the formation of the cyanoquinaz-

oline **1₅** and ketone **1₄**, respectively. iii) In the reaction (c), the isoquinoline Reissert compounds **6_{1a}** and **6_{1b}**, having an electron-withdrawing cyano group and an electronegative bromine atom at the 4-position, respectively, undergo aromatization, similar to that of **2₁**, resulting in the formation of the cyanoisoquinolines **6_{3a}** and **6_{3b}**, respectively, with elimination of the anion F. iv) The formation of the benzoates **1₆** and the alkylation products **1₉** in the reaction (d) indicates that **1₁** is potentially available as a synthetic intermediate for introduction of a functionalized carbon group at the 4-position by the use of electrophiles.

Experimental

All melting points are uncorrected. Infrared absorption (IR) spectra were recorded on a Jasco A-102 diffraction grating IR spectrometer. Proton nuclear magnetic resonance (¹H-NMR) spectra were measured at 60 MHz on a Hitachi R-24B high-resolution NMR spectrometer, and ¹³C-NMR spectra were taken at 90 MHz on a JEOL JNM-FX90Q FTNMR spectrometer. Chemical shifts are quoted in parts per million (ppm) with tetramethylsilane as an internal standard, and coupling constants (*J*) are given in hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and brs = broad singlet. Mass spectra (MS) were recorded on a JEOL JMS D-100 mass spectrometer. Samples were vaporized in a direct inlet system. Column chromatography was carried out on SiO₂, Wakogel C-200 (200 mesh).

Acid Hydrolysis of 1₁—A mixture of **1₁** (1 mmol, 275 mg) and 20% HCl (4 ml) was stirred for 10 h. On cooling, crystals separated. They were collected by suction, washed with 2 N Na₂CO₃, and extracted with CHCl₃. The extract was washed with H₂O, dried over Na₂SO₄, and concentrated to dryness. Recrystallization of the residue from benzene–MeOH gave **1₃** as colorless needles, mp 161–163 °C, in 40% yield (116 mg). *Anal.* Calcd for C₁₇H₁₅N₃O₂: C, 69.61; H, 5.15; N, 14.33. Found: C, 69.65; H, 5.17; N, 14.24. MS *m/z*: 293 (*M*⁺). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 3300, 3380 (NH), 1700 (CO). ¹H-NMR ((CD₃)₂SO): 2.07 (3H, s, CH₃), 5.10–6.12 (2H, brs, NH₂), 6.38–8.10 (9H, m, aromatic H), 10.22–10.56 (1H, brs, NH). ¹³C-NMR ((CD₃)₂SO): 23.84 (q, CH₃), 114.32 (s), 117.14 (d), 127.00 (d), 127.81 (s), 129.38 (d), 130.41 (d), 131.99 (d), 133.01 (s), 139.62 (s), 147.81 (s), 157.83 (s), 172.08 (s, CO).

Alkaline Hydrolysis of 1₁—A mixture of **1₁** (1 mmol, 275 mg) and 10% NaOH (2 ml) in MeOH (5 ml) was stirred for 1 h. The reaction mixture was neutralized with AcOH, and the solvent was removed under reduced pressure. The residue was extracted with CHCl₃. The extract was washed with H₂O, dried over Na₂SO₄, and concentrated to dryness. The residue was chromatographed on a column of SiO₂. The fraction eluted with benzene–CHCl₃ (1 : 1) gave **1₂** in 76% yield (110 mg). The fraction subsequently eluted with CHCl₃ gave **8** in 72% yield (88 mg).

Compound **1₂** was identified by comparison with an authentic specimen prepared by another route.⁵⁾

Reaction of 1₁ with NaH—NaH (60% in oil, 1 mmol, 40 mg) was added to a stirred solution of **1₁** (1 mmol, 275 mg) in *N,N*-dimethylformamide (DMF, 1 ml) under ice cooling, and the whole was stirred for a further 5 min. The reaction mixture was poured onto a large amount of ice, neutralized with AcOH, and extracted with benzene. The extract was washed with H₂O, dried over Na₂SO₄, and concentrated to dryness. The residue was chromatographed on a column of SiO₂. The fraction eluted with benzene gave **9⁸⁾** in 33% yield (35 mg). The first, second, and third fractions subsequently eluted with CHCl₃ gave **1₅**,¹⁰⁾ **1₄**,⁹⁾ and **1₂** in 20% (32 mg), 32% (80 mg), and 7% yields (10 mg), respectively.

Compounds **9**, **1₅**, and **1₄** were identified by comparison with the corresponding authentic specimens prepared by other routes.^{8–10)}

Preparation of 6₁—A solution of benzoyl chloride (22 mmol, 3.11 g) was added to a well stirred solution of **6₂** (20 mmol) and TMSCN (20 mmol, 2.23 g) in CH₂Cl₂ (30 ml), and the mixture was stirred for 5 min. AlCl₃ (2 mmol, 267 mg) was added to the mixture and the whole was stirred for 22 h at room temperature. The solution was washed with H₂O, 5% HCl, H₂O, 5% NaOH, and H₂O. The CH₂Cl₂ solution was dried over Na₂SO₄ and concentrated. The residue was recrystallized from benzene–petroleum benzin to give **6₁**.

From **6_{2a}**, 2-benzoyl-1,2-dihydro-1,4-isoquinolinedicarbonitrile (**6_{1a}**) was obtained as colorless prisms, mp 197–199 °C, in 87% yield (4.94 g). *Anal.* Calcd for C₁₈H₁₁N₃O: C, 75.78; H, 3.89; N, 14.73. Found: C, 75.52; H, 3.86; N, 14.73. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 2210 (CN), 1680 (CO). ¹H-NMR ((CD₃)₂SO): 6.71 (1H, s, C¹-H), 7.19–7.78 (10H, m, aromatic H). ¹³C-NMR ((CD₃)₂SO): 44.5 (d, C¹), 92.9 (s, C⁴), 115.3 (s, CN), 116.3 (s, CN), 123.2 (d), 123.5 (s), 125.7 (s), 127.7 (d), 128.8 (d), 129.5 (d), 129.8 (d), 130.5 (d), 130.8 (s), 132.7 (d), 138.5 (d), 168.4 (s, CO).

From **6_{2b}**, 2-benzoyl-4-bromo-1,2-dihydro-1-isoquinolinedicarbonitrile (**6_{1b}**) was obtained as colorless needles, mp 166–168 °C, in 82% yield (5.56 g). *Anal.* Calcd for C₁₇H₁₁BrN₂O: C, 60.20; H, 3.27; N, 8.26. Found: C, 60.18; H, 3.24; N, 8.26. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1660 (CO). ¹H-NMR (CDCl₃): 6.46 (1H, s, C¹-H), 6.91 (1H, s, C³-H), 7.21–7.70 (9H, m, aromatic H). ¹³C-NMR (CDCl₃): 45.2 (d, C¹), 104.9 (s, C⁴), 115.9 (s, CN), 124.6 (s), 126.0 (d), 126.5 (d), 128.8 (d), 129.2 (d), 129.7 (d), 130.5 (d), 131.5 (s), 132.4 (d), 167.7 (s, CO).

Reaction of 6₁ with NaH—NaH (3.6 mmol, 86.4 mg) was added to a well stirred solution of **6₁** (3 mmol) in DMF (10 ml) under ice cooling, then the whole was stirred for 1 h at room temperature. The reaction mixture was

poured onto a large amount of ice, neutralized with AcOH, and extracted with AcOEt. The insoluble crystalline material was collected by suction and recrystallized from benzene-petroleum benzin to give the dimer **6₈**. The extract was dried over Na₂SO₄ and concentrated to dryness. The residue was chromatographed on a column of SiO₂. The fraction eluted with benzene gave **6₅**. The fraction subsequently eluted with CHCl₃ gave **6₈**.

From **6_{1a}**, 1,4-isoquinolinedicarbonitrile (**6_{5a}**)¹⁴⁾ was obtained as slightly yellow needles from MeOH, mp 179–180.5 °C, in 71% yield (380 mg). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 2225 (CN). ¹H-NMR (CDCl₃): 7.65–8.48 (4H, m, aromatic H), 8.77 (1H, s, C³-H). Compound **6_{5a}** was identified by comparison with an authentic sample prepared from another route.¹⁴⁾

From **6_{1b}**, 4-bromo-1-isoquinolinecarbonitrile (**6_{5b}**; colorless needles from petroleum benzin, mp 124–126 °C) and 4'-bromo-4,1'-biisoquinoline-1-carbonitrile (**6_{8b}**; colorless needles from benzene-petroleum benzin, mp 233–235 °C) were obtained in 35% (211 mg) and 14% yields (146 mg), respectively.

Compound **6_{5b}** was identified by comparison with an authentic sample prepared by application of an improved Henze reaction¹⁷⁾ to 4-bromoisoquinoline 2-oxide.¹⁸⁾ *Anal.* Calcd for C₁₀H₅BrN₂: C, 51.53; H, 2.16; N, 12.02. Found: C, 51.78; H, 2.16; N, 12.25. MS *m/z*: 234 (M⁺ + 2), 232 (M⁺). ¹H-NMR (CDCl₃): 7.71–8.33 (4H, m, aromatic H), 8.71 (1H, s, C³-H).

Compound **6_{8b}**: *Anal.* Calcd for C₁₉H₁₀BrN₃: C, 63.35; H, 2.80; N, 11.67. Found: C, 63.18; H, 2.79; N, 11.61. MS *m/z*: 361 (M⁺ + 2), 359 (M⁺). ¹H-NMR (CDCl₃): 8.82 (1H, s, C³-H), 8.52 (1H, s, C^{3'}-H), 8.30–7.15 (8H, m, aromatic H).

Preparation of 6_{5b}—Compound **6_{5b}** was prepared by application of an improved Henze¹⁹⁾ reaction reported by Fife¹⁷⁾ to 4-bromoisoquinoline 2-oxide.¹⁸⁾ *N,N*-Dimethylcarbamoyl chloride (6 mmol, 645 mg) was added to a solution of 4-bromoisoquinoline 2-oxide (5 mmol, 1120 mg) and TMSCN (6 mmol, 606 mg) in dry CH₂Cl₂ (20 ml), and the whole was stirred for 24 h. The reaction mixture was washed with 10% K₂CO₃ (10 ml), dried over Na₂SO₄, and concentrated to dryness. The residue was chromatographed on a column of SiO₂. The fraction eluted with benzene gave **6_{5b}** in 62% yield (720 mg).

Reaction of 1₁ with 10 in the Presence of NaH—NaH (60% in oil, 1 mmol, 40 mg) was added to a well stirred solution of **1₁** (1 mmol, 275 mg) and **10** (1 mmol) in DMF (2 ml) under ice cooling, and the whole was stirred for 30 min. The reaction mixture was poured onto a large amount of ice, neutralized with AcOH, and extracted with benzene. The extract was dried over Na₂SO₄, concentrated, and chromatographed on a column of SiO₂. The first, second, and third fractions eluted with CHCl₃ gave **1₅**,¹⁰⁾ **1₆**, and **1₂**,⁵⁾ respectively.

From the reaction with **10a**, the benzoate **1_{6a}** (colorless prisms from benzene-petroleum benzin, mp 112 °C) in 78% yield (277 mg), **1₂** in 10% yield (15 mg), and a trace of **1₅** (2 mg) were obtained. Compound **1_{6a}**: *Anal.* Calcd for C₂₃H₁₈N₂O₂: C, 77.95; H, 5.12; N, 7.91. Found: C, 77.76; H, 5.18; N, 7.76. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1720 (CO). ¹H-NMR (CDCl₃): 2.85 (3H, s, C²-CH₃), 7.18–8.34 (15H, m, aromatic and methylidyne H).

From the reaction with **10b**, the benzoate **1_{6b}** was obtained as colorless prisms from benzene-petroleum benzin, mp 120–122 °C, in 65% yield (227 mg), together with a trace of **1₅**. Compound **1_{6b}**: *Anal.* Calcd for C₂₄H₂₀N₂O₃: C, 74.98; H, 5.24; N, 7.29. Found: C, 74.86; H, 5.24; N, 7.31. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1710 (CO). ¹H-NMR (CDCl₃): 2.84 (3H, s, C²-CH₃), 3.70 (3H, s, OCH₃), 6.70–8.30 (14H, m, aromatic and methylidyne H).

From the reaction with **10c**, the benzoate **1_{6c}** was obtained as colorless needles from benzene-petroleum benzin, mp 145 °C, in 53% yield (195 mg), together with **1₂** in 15% yield (22 mg) and **1₅** in 7% yield (12 mg). Compound **1_{6c}**: *Anal.* Calcd for C₂₄H₂₀N₂O₂: C, 78.24; H, 5.47; N, 7.60. Found: C, 78.11; H, 5.48; N, 7.54. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1720 (CO). ¹H-NMR (CDCl₃): 2.28 (3H, s, CH₃), 2.85 (3H, s, C²-CH₃), 6.98–8.33 (14H, m, aromatic and methylidyne H).

Reaction of 1₁ with 11 in the Presence of NaH—NaH (60% in oil, 1 mmol, 40 mg) was added to a well stirred solution of **1₁** (1 mmol, 275 mg) and **11** (1 mmol) in DMF (2 ml) under ice cooling, and the whole was stirred for 1 h. The reaction mixture was poured onto a large amount of ice, neutralized with AcOH, and extracted with benzene. The extract was washed with H₂O, dried over Na₂SO₄, and concentrated to dryness. The residue was chromatographed on a column of SiO₂. The first and second fractions eluted with benzene gave **1₉** and **1₄**, respectively.

From the reaction with **11a**, **1_{9a}** was obtained as a yellow oil in 51% yield (148 mg), together with **1₄** in 20% yield (50 mg). Compound **1_{9a}**: MS *m/z*: 289 (M⁺). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1680 (CO). ¹H-NMR (CDCl₃): 1.94 (6H, s, C²-CH₃ and C⁴-CH₃), 7.22–7.83 (9H, m, aromatic H).

From the reaction with **11b**, **1_{9b}** was obtained as yellow needles from benzene-petroleum benzin, mp 106–107 °C, in 57% yield (251 mg). MS *m/z*: 441 (M⁺). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1350, 1530 (NO₂), 1680 (CO). ¹H-NMR (CDCl₃): 2.00 (3H, s, C²-CH₃), 6.47–8.60 (12H, m, aromatic H).

Reaction of 6_{1a} with 10a in the Presence of NaH—NaH (1.8 mmol, 43 mg) was added to a well stirred solution of **6_{1a}** (1.5 mmol, 428 mg) and **10a** (1.8 mmol, 191 mg) in DMF (8 ml) under ice cooling, and the whole was stirred for 15 min. The reaction mixture was poured onto a large amount of ice, neutralized with AcOH, and extracted with AcOEt. The extract was washed with H₂O, dried over Na₂SO₄, concentrated, and chromatographed on a column of SiO₂. The first and second fractions eluted with benzene gave **9₈** and the benzoate **6_{6a}** in 27% (130 mg) and 48% yields (260 mg), respectively. The fraction subsequently eluted with CHCl₃ gave **6_{2a}**¹³⁾ as colorless needles from petroleum benzin, mp 103–104.5 °C, in 22% yield (50 mg).

Compound **6_{6a}** was obtained as colorless needles from benzene-petroleum benzin, mp 126–128 °C. *Anal.* Calcd for C₂₄H₁₆N₂O₂: C, 79.11; H, 4.43; N, 7.69. Found: C, 79.02; H, 4.46; N, 8.19. MS *m/z*: 364 (M⁺). IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1710

(CO), 2215 (CN). $^1\text{H-NMR}$ (CDCl_3): 7.21—8.53 (15H, m, aromatic and methylidyne H), 8.89 (1H, s, $\text{C}^3\text{-H}$).

Reaction of 6_1b with 10a in the Presence of NaH—The similar reaction of 6_1b (2 mmol, 678 mg) and 10a (2.4 mmol, 255 mg) in the presence of NaH (2.4 mmol, 58 mg) in DMF (8 ml) with stirring for 1 h gave the benzoate (6_6b) as colorless needles from benzene–petroleum benzin, mp 121—124°C, in 51% yield (263 mg) and $6_2\text{b}^{16)}$ as an oil in 17% yield (70 mg).

Compound 6_6b : *Anal.* Calcd for $\text{C}_{23}\text{H}_{16}\text{BrNO}_2$: C, 66.04; H, 3.85; N, 3.35. Found: C, 67.27; H, 4.01; N, 3.11. MS m/z : 417 (M^+), 419 ($\text{M}^+ + 2$). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1710 (CO). $^1\text{H-NMR}$ (CDCl_3): 7.20—8.27 (15H, m, aromatic and methylidyne H), 8.71 (1H, s, $\text{C}^3\text{-H}$).

Alkaline Hydrolysis of 6_6 —i) A solution of 6_6a (100 mg) in a mixture of 10% NaOH (1 ml) and MeOH (10 ml) was refluxed for 30 min. After removal of the MeOH under reduced pressure, H_2O was added to the residue, and the separated oily material was extracted with CHCl_3 . The extract was dried over Na_2SO_4 and concentrated to dryness. The extract was dried over Na_2SO_4 and concentrated to dryness. The residue was recrystallized from MeOH to give the ketone 6_4a as pale yellow needles, mp 157—159°C, in 85% yield (60 mg). *Anal.* Calcd for $\text{C}_{17}\text{H}_{10}\text{N}_2\text{O}$: C, 79.06; H, 3.90; N, 10.85. Found: C, 78.60; H, 4.19; N, 10.66. MS m/z : 258 (M^+). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 1660 (CO), 2220 (CN). $^1\text{H-NMR}$ (CDCl_3): 7.15—8.29 (9H, m, aromatic H), 8.85 (1H, s, $\text{C}^3\text{-H}$).

ii) The similar alkaline hydrolysis of 6_6b (270 mg) in a mixture of 10% NaOH (1 ml) and MeOH (10 ml) by refluxing for 20 min gave the alcohol 6_{10}b as slightly yellow prisms from MeOH, mp 136—139°C, in 34% yield (68 mg). *Anal.* Calcd for $\text{C}_{16}\text{H}_{12}\text{BrNO}$: C, 61.17; H, 3.85; N, 4.46. Found: C, 61.17; H, 3.84; N, 4.55. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3360 (OH). $^1\text{H-NMR}$ (CDCl_3): 5.79 (1H, d, $J=6\text{ Hz}$, CHOH), 6.42 (1H, d, $J=6\text{ Hz}$, CHOH), 7.15—8.30 (9H, m, aromatic H), 8.77 (1H, s, $\text{C}^3\text{-H}$).

Acknowledgement The authors are greatly indebted to the staff of the central analysis room of the University of Shizuoka for elemental analysis and mass spectral measurement.

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