

## Photochemistry of Ethyl 2-Cyano-1,2-dihydroquinoline-1-carboxylates (Reissert Compounds): Synthesis of 2-Cyanomethylindole-1-carboxylates

By Masazumi Ikeda,\* Saeko Matsugashita, and Yasumitsu Tamura, Faculty of Pharmaceutical Sciences, Osaka University, 133-1, Yamada-kami, Suita, Osaka, Japan

Irradiation of ethyl 2-cyano-1,2-dihydroquinoline-1-carboxylates (Reissert compounds) gives ethyl *N*-[*o*-(3-cyanoallenyl)phenyl]carbamates, which are readily converted into ethyl 2-cyanomethylindole-1-carboxylates by treatment with alumina.

In recent years the photochemistry of 1,2-dihydronaphthalenes<sup>1</sup> and their heterocyclic analogues<sup>2</sup> has been investigated extensively. As noted previously,<sup>2g</sup> irradiation of ethyl 2-cyano-1,2-dihydroquinoline-1-carboxylates (Reissert compounds) (1) gives allenic compounds (2) which can be transformed into ethyl 2-cyanomethylindole-1-carboxylates (3). Because the esters (3) are considered to be potential synthetic precursors of 2-substituted indole derivatives otherwise available only by multi-step processes,<sup>3</sup> we have investigated this photochemical reaction in some detail. We describe here the synthesis of several ethyl 2-cyanomethylindole-1-carboxylates (3) as well as a procedure for their large-scale synthesis.

The starting Reissert compounds (1) were synthesised from the corresponding quinolines essentially as described by Popp and his co-workers.<sup>4</sup>

For preparative purposes, irradiation of an ethereal solution of the cyano-ester (1a) with a 350 W high-pressure mercury lamp through a glass filter at 0–5 °C gave the most satisfactory results. The reaction was conveniently followed by n.m.r. spectroscopy. The photochromic behaviour of the starting material (1a) can also be used as indicator of the progress of the reaction. Thus, a dark brown colour was present until all the starting material had been consumed, and at the end of the reaction a yellow solution was obtained. As described later, the initial photoproduct is the allenic compound (2a). However, since it was difficult to isolate this material (2a) in pure state,<sup>†</sup> the product was converted directly into ethyl 2-cyanomethylindole-1-carboxylate (3a), either by treatment of the photolysate with alumina (in large-scale runs) or by preparative t.l.c. on alumina or silica gel (in small-scale runs). In a typical experiment, indole-1-carboxylate (3a) was isolated in 83% overall yield from 2.0 g of (1a). Although the reaction can also be satisfactorily performed by irradiation in a Pyrex tube in 100 mg-scale runs, prolonged irradiation or large-scale experiments led to an

increase in the amount of polymeric material, presumably owing to decomposition of the allenic compound formed, and a resulting decrease in the yield of (3a). That ether is the solvent to be preferred was indicated by the observation that the reaction of (1a) in cyclohexane, benzene, methylene chloride, or acetone in either glass or Pyrex was slower than that in ether and gave a complex mixture from which (3a) was isolated in lower yields. Temperature is a critical factor. For example, when a solution of (1a) in ether was irradiated in a glass tube at 20 °C for 15 h, most of the starting material was recovered, with small amounts of impurities, in spite of the fact that the colour change was observed.

That the initial photoproduct from irradiation of (1a) in ether is the allene (2a) was suggested from the spectral data of the crude material obtained after evaporation of the solvent. The i.r. spectrum (CHCl<sub>3</sub>) showed intense absorption at 3 420 (NH), 2 220 (C≡N),<sup>‡</sup> 1 950 (C=C=C), and 1 720 cm<sup>-1</sup> (C=O), and the n.m.r. spectrum exhibits two doublets (*J* 6.6 Hz) at δ 6.85 (1 H) and 5.62 (1 H) attributable to two allenic protons. Treatment of the crude (2a) with alumina or silica gel gave (3a) in good yields.

The structure of (3a) was apparent from spectral comparisons (see Experimental section) with ethyl indole-1-carboxylate<sup>6</sup> and from some interconversions described later. The formation of (3a) from (2a) is considered to proceed by base- or acid-catalysed intramolecular cyclisation.<sup>7</sup>

<sup>2</sup> (a) B. Singh, *J. Amer. Chem. Soc.*, 1968, **90**, 3893; 1969, **91**, 3670; (b) K. R. Huffman, M. Burger, W. A. Henderson, jun., M. Joy, and E. F. Ullman, *J. Org. Chem.*, 1969, **34**, 2407; (c) A. Padwa and G. A. Lee, *J.C.S. Chem. Comm.*, 1972, 795; *J. Org. Chem.*, 1975, **40**, 1142; (d) P. T. Izzo and A. S. Kende, *Tetrahedron Letters*, 1966, 5731; (e) J. Kolc and R. S. Becker, *J. Amer. Chem. Soc.*, 1969, **91**, 6513; *J. Chem. Soc. (B)*, 1972, 17; (f) B. S. Lukjanow, M. I. Knjazschanski, J. W. Rewinski, L. E. Niworozschkin, and W. I. Minikin, *Tetrahedron Letters*, 1973, 2007; (g) M. Ikeda, S. Matsugashita, and Y. Tamura, *J.C.S. Chem. Comm.*, 1973, 922; (h) M. Ikeda, S. Matsugashita, F. Tabusa, H. Ishibashi, and Y. Tamura, *J.C.S. Chem. Comm.*, 1974, 433; 1975, 575; (i) M. Ikeda, S. Matsugashita, and Y. Tamura, *Chem. and Pharm. Bull. (Japan)*, 1976, **24**, 1400.

<sup>3</sup> For example, see W. Schindler, *Helv. Chim. Acta*, 1957, **40**, 2156.

<sup>4</sup> F. D. Popp, L. E. Katz, C. W. Klinowski, and J. M. Wefer, *J. Org. Chem.*, 1968, **33**, 4447.

<sup>5</sup> F. P. Popp, *Adv. Heterocyclic Chem.*, 1965, **9**, 1.

<sup>6</sup> S. Kasparek and R. A. Heacock, *Canad. J. Chem.*, 1966, **44**, 2805.

<sup>7</sup> M. C. Caserio, 'Selective Organic Transformations,' ed. B. S. Thygarayan, Wiley, London, 1970, vol. 1, p. 272.

<sup>†</sup> Compound (2a) was partially transformed into (3a) during work-up.

<sup>‡</sup> Quinoline Reissert compounds show no i.r. cyano-absorption.<sup>5</sup>

<sup>1</sup> (a) R. C. Cookson, S. M. de B. Costa, and J. Hudec, *Chem. Comm.*, 1969, 1272; (b) H. Kleinhuis, R. L. C. Wijting, and E. Havinga, *Tetrahedron Letters*, 1971, 255; (c) K. Salisbury, *ibid.*, p. 737; (d) H. Heimgarter, H.-J. Hansen, and H. Schmid, *Helv. Chim. Acta*, 1972, **55**, 3005; (e) D. A. Seeley, *J. Amer. Chem. Soc.*, 1972, **94**, 4378.



tions (in either ether or ethanol) we employed. On the basis of this observation and documented examples of the photolytic behaviour of 1,2-dihydronaphthalenes,<sup>1</sup> we previously suggested that the photoisomerisation [(1) → (2)] involves (8) as intermediate.<sup>2g</sup> However, our preliminary mechanistic study has shown that this reaction is mechanistically different from that of the carbocyclic system and the aza-polyene (8) is not a precursor of the allene (3). The details will be reported later.

## EXPERIMENTAL

N.m.r. spectra were determined with a Hitachi R-22 spectrometer (90 MHz; tetramethylsilane as internal standard). I.r. spectra were recorded with a Hitachi EPI-G2 spectrophotometer, u.v. spectra with a Hitachi 124 spectrophotometer, and mass spectra with a Hitachi RMU-6D instrument at 70 eV. Irradiations were carried out with an Eikosha 350 W high-pressure mercury lamp. Merck PF<sub>254</sub> alumina was used for preparative layer chromatography (p.l.c.).

**Reissert Compounds (1a–f).**—Reissert compounds (1) were prepared from the corresponding quinolines according to the method of Popp and his co-workers.<sup>4</sup> Ethyl 2-cyano-1,2-dihydroquinoline-1-carboxylate (1a) (27%) had m.p. 68–69° (from ethanol) (lit.,<sup>4</sup> 70–72°); the 6-methyl derivative (1b) (49%) had m.p. 120–121° (from ethanol) (Found: C, 69.3; H, 5.9; N, 11.5. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub> requires C, 69.4; H, 5.8; N, 11.6%); the 7-methyl derivative (1c) (35%) had m.p. 79–80° (from ethanol) (Found: C, 69.3; H, 5.8; N, 11.5%); the 6-methoxy-derivative (1d) (46%) had m.p. 87–88° (from ethanol) (Found: C, 65.0; H, 5.2; N, 10.85. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub> requires C, 65.1; H, 5.5; N, 10.85%); the 4-methyl derivative (1e) (59%) had m.p. 80–81° (from ethanol) (Found: C, 69.4; H, 5.8; N, 11.6%); the 3-methyl derivative (1f) (32%) had m.p. 81–82° [from light petroleum (b.p. 60–80 °C)] (Found: C, 69.3; H, 5.8; N, 11.75%).

**Irradiation of the Cyano-ester (1a).**—(A) *Isolation of the allene (2a) and its conversion into the indole-1-carboxylate (3a).* A solution of (1a) (150 mg) in ether (20 ml) was irradiated in a Pyrex tube at 2 °C until the starting material had disappeared (10 h; checked by n.m.r. spectroscopy). The ether was removed *in vacuo* to give an oil consisting essentially of the allene (2a);  $\nu_{\max}$  (CHCl<sub>3</sub>) 3 420, 2 220, 1 950, and 1 720 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 7.0–7.65 (4 H, m, aromatic), 6.85 (1 H, d, *J* 6.6 Hz, allenic), 5.62 (1 H, d, *J* 6.6 Hz, allenic), 4.18 (2 H, q, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>), and 1.22 (3H, t, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>). The crude (2a) (103 mg) was subjected to p.l.c. (benzene) to give ethyl 2-cyanomethylindole-1-carboxylate (3a) (67%), m.p. 121° [from light petroleum (b.p. 60–80 °C)] (Found: C, 68.2; H, 5.4; N, 12.3. C<sub>13</sub>H<sub>13</sub>N<sub>2</sub>O<sub>2</sub> requires C, 68.4; H, 5.3; N, 12.3%);  $\nu_{\max}$  (KCl) 2 250 and 1 725 cm<sup>-1</sup>;  $\lambda_{\max}$  (EtOH) 225, 253, 261, 281, and 291 nm (log  $\epsilon$  4.31, 4.09, 4.07, 3.50, and 3.54);  $\delta$  (CDCl<sub>3</sub>) 8.1 (m, 1 H, H-7), 7.1–7.6 (3 H, m, aromatic), 6.75br (1 H, s, H-3), 4.56 (2 H, q, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>), 4.16br (2 H, s, CH<sub>2</sub>·CN), and 1.51 (3 H, t, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>); *m/e* 228 (M<sup>+</sup>). Use of silica gel (Merck GF<sub>254</sub>) and benzene as solvent gave the similar result.

(B) *Preparative procedure.* A solution of (1a) (2 g) in ether (300 ml) in an immersion apparatus (glass filter) was

irradiated at 2 °C until the starting material had disappeared (18 h). To the photolysate was added alumina (Woelm neutral) (2 g) and the mixture was stirred for 5 h at room temperature. The alumina was filtered off and concentration of the filtrate afforded (3a) (1.67 g, 83%).

(C) *Irradiation in ethanol.* A solution of (1a) (100 mg) in ethanol (14 ml) was irradiated in a glass tube at 2 °C until the starting material had disappeared (15 h; checked by t.l.c.). The ethanol was evaporated off and the residue was submitted to p.l.c. (benzene) to afford ethyl o-(3-cyano-1-ethoxyallyl)phenylcarbamate (7) (55 mg, 46%), m.p. 73–74° [from light petroleum (b.p. 60–80 °C)] (Found: C, 65.5; H, 6.7; N, 10.0. C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>3</sub> requires C, 65.7; H, 6.6; N, 10.2%);  $\nu_{\max}$  (CCl<sub>4</sub>) 3 360, 2 210, and 1 740 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 8.28br (1 H, s, NH), 8.03 (1 H, d, *J* 8 Hz, aromatic), 6.9–7.5 (3 H, m, aromatic), 6.71 (1 H, dd, *J*<sub>bc</sub> 12.0, *J*<sub>ab</sub> 8.0 Hz, H<sub>b</sub>), 5.45 (1 H, d, *J*<sub>bc</sub> 12.0 Hz, H<sub>c</sub>), 5.30 (1 H, d, *J*<sub>ab</sub> 8.0 Hz, H<sub>a</sub>), 4.22 (2 H, q, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>), 3.60 (2 H, q, *J* 7 Hz, O·CH<sub>2</sub>·CH<sub>3</sub>), 1.17 (3 H, t, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>), and 1.14 (3 H, t, O·CH<sub>2</sub>·CH<sub>3</sub>);  $\lambda_{\max}$  (EtOH) 223 and 284 nm (log  $\epsilon$  4.22 and 3.07); *m/e* 274 (M<sup>+</sup>). Irradiation of the same solution of (1a) at 20 °C also gave the adduct (7) (44%).

**Irradiation of the Cyano-ester (1b).**—(A) A solution of (1b) (300 mg) in ether (40 ml) was irradiated in a Pyrex tube at 2 °C for 10 h. The ether was evaporated off and the residue was subjected to p.l.c. (benzene) to give the indole (3b) (20 mg, 14%), m.p. 108–109° [from light petroleum (b.p. 60–80 °C)] (Found: C, 69.3; H, 5.9; N, 11.3. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub> requires C, 69.4; H, 5.8; N, 11.6%);  $\nu_{\max}$  (KCl) 2 250 and 1 730 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 7.93 (1 H, d, *J* 9 Hz, H-7), 7.29br (1 H, s, H-4), 7.12 (1 H, dd, *J* 9 and 2 Hz, H-6), 6.64 (1 H, s, H-3), 4.52 (2 H, q, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>), 4.12br (2 H, s, CH<sub>2</sub>·CN), 2.41 (3 H, s, CH<sub>3</sub>), and 1.50 (3 H, t, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>);  $\lambda_{\max}$  (EtOH) 232, 256, 263sh, 286, 290, and 297 nm (log  $\epsilon$  4.39, 4.14, 4.11, 3.53, 3.56, and 3.56); *m/e* 242 (M<sup>+</sup>). The remaining product consisted mainly of the starting material and polymeric material. Prolonged irradiation resulted in an increase in the amount of polymeric material.

(B) A solution of (1b) (150 mg) in ether (20 ml) was irradiated in a glass tube at 2 °C. Samples were removed every 5 h and analysed by n.m.r. spectroscopy. The starting material was 50% consumed after 15 h. Separation of the mixture by p.l.c. (benzene) gave (3b) in poor yield.

**Irradiation of the Cyano-ester (1c).**—(A) A solution of (1c) (300 mg) in ether (40 ml) was irradiated in a Pyrex tube at 2 °C for 10 h and concentrated. The indole (3c) was isolated by p.l.c. (benzene) in 17% yield (25 mg); m.p. 98–99° [from light petroleum (b.p. 60–80 °C)] (Found: C, 69.4; H, 5.8; N, 11.5. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>2</sub> requires C, 69.4; H, 5.8; N, 11.6%);  $\nu_{\max}$  (KCl) 2 250 and 1 740 cm<sup>-1</sup>;  $\delta$  (CDCl<sub>3</sub>) 7.92br (1 H, s, H-7), 7.38 (1 H, d, *J* 8 Hz, H-4), 7.06br (1 H, d, *J* 8 Hz, H-5), 6.65 (1 H, s, H-3), 4.53 (2 H, q, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>), 4.11br (2 H, s, CH<sub>2</sub>·CN), 2.49 (3 H, s, CH<sub>3</sub>), and 1.50 (3 H, t, *J* 7 Hz, CO<sub>2</sub>·CH<sub>2</sub>·CH<sub>3</sub>);  $\lambda_{\max}$  (EtOH) 227, 259, 263sh, 283sh, 288sh, and 294 nm (log  $\epsilon$  4.15, 3.95, 3.94, 3.20, 3.08, and 3.08); *m/e* 242 (M<sup>+</sup>).

(B) Irradiation of the same solution of (1c) in a glass tube at 2 °C for 15 h gave a mixture of (1c) (major) and several photoproducts including the allene (2c).

**Irradiation of the Cyano-ester (1d).**—(A) A solution of (1d) (150 mg) in ether (20 ml) was irradiated in a Pyrex tube at 2 °C for 10 h. The indole (3d) was isolated by p.l.c. (benzene) in 10% yield (15 mg); m.p. 114–115° [from light petroleum (b.p. 60–80 °C)] (Found: C, 64.9; H, 5.5; N, 10.8. C<sub>14</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub> requires C, 65.1; H, 5.5; N, 10.85%);  $\nu_{\max}$  (KCl)

2 250 and 1 720  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 7.95br (1 H, d,  $J$  10 Hz, H-7), 6.96 (1 H, s, H-4), 6.90br (1 H, d,  $J$  10 Hz, H-6), 6.68br (1 H, s, H-3), 4.53 (2 H, q,  $J$  7 Hz,  $\text{CO}_2\cdot\text{CH}_2\cdot\text{CH}_3$ ), 4.15br (2 H, s,  $\text{CH}_2\cdot\text{CN}$ ), 3.86 (3 H, s,  $\text{OCH}_3$ ), and 1.51 (3 H, t,  $J$  7 Hz,  $\text{CO}_2\cdot\text{CH}_2\cdot\text{CH}_3$ );  $\lambda_{\text{max}}$  (EtOH) 240, 261, 297, and 307 nm ( $\log \epsilon$  4.48, 4.23, 3.71, and 3.69);  $m/e$  258 ( $M^+$ ).

(B) Irradiation of the same solution of (1d) in a glass tube at 2 °C for 15 h and work-up gave (3d) in poor yield.

*Irradiation of the Cyano-ester (1e).*—(A) A solution of (1e) (300 mg) in ether (40 ml) was irradiated in a Pyrex tube at 2 °C for 8 h and concentrated. The residue was submitted to p.l.c. (benzene) to give compounds (3e) and (4) in 32 and 10% yields, respectively. The *indole* (3e) had m.p. 88–89° [from light petroleum (b.p. 30–60 °C)] (Found: C, 69.4; H, 5.9; N, 11.3.  $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_2$  requires C, 69.4; H, 5.8; N, 11.6%);  $\nu_{\text{max}}$  (KCl) 2 250 and 1 715  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 8.1 (1 H, m, H-7), 7.1–7.5 (3 H, m, H-4, -5, and -6), 4.55 (2 H, q,  $J$  7 Hz,  $\text{CO}_2\cdot\text{CH}_2\cdot\text{CH}_3$ ), 4.10 (2 H, s,  $\text{CH}_2\cdot\text{CN}$ ), 2.26 (3 H, s,  $\text{CH}_3$ ), and 1.51 (3 H, t,  $J$  7 Hz,  $\text{CO}_2\cdot\text{CH}_2\cdot\text{CH}_3$ );  $\lambda_{\text{max}}$  (EtOH) 229, 263, 286, and 294 ( $\log \epsilon$  4.32, 4.06, 3.37, and 3.37);  $m/e$  242 ( $M^+$ ). The physical and spectral data of (4) will be detailed in a subsequent paper.

(B) Irradiation of the same solution of (1e) in a glass tube at 2 °C for 15 h and work-up as above gave (3e) and (4) in 34 and 16% yields, respectively.

*2-Methylindole (5).*—A mixture of the indole (3a) (350

mg) in ethanol (10 ml) and 10% potassium hydroxide (10 ml) was refluxed for 3 h and the solvent was evaporated off *in vacuo*. The residue was acidified (dil. HCl) and extracted with chloroform. The dried extract was concentrated and the residual solid was recrystallized from light petroleum (b.p. 60–80 °C) to give (5) in quantitative yield; m.p. 58–59° (lit.,<sup>10</sup> 59°).

*Indole-2-acetonitrile (6a).*—A suspension of the indole (3a) (190 mg) and potassium carbonate (190 mg) in methanol (15 ml) was stirred at room temperature for 1 h. The potassium carbonate was filtered off, the filtrate was concentrated, and the residual solid was recrystallized from light petroleum (b.p. 80–100 °C) to give the nitrile (6a) (127 mg, 98%), m.p. 103–104° (lit.,<sup>3</sup> 96–98°).

*3-Methylindole-2-acetonitrile (6b).*—By using the same procedure as above, the *nitrile* (6b) was obtained from (3a) (100 mg) in 79% yield; m.p. 90–91° [from light petroleum (b.p. 60–80 °C)] (Found: C, 77.6; H, 5.9; N, 16.5.  $\text{C}_{11}\text{H}_{10}\text{N}_2$  requires C, 77.6; H, 5.9; N, 16.5%);  $\nu_{\text{max}}$  (KCl) 3 350 and 2 250  $\text{cm}^{-1}$ ;  $\delta$  ( $\text{CDCl}_3$ ) 7.9–8.2br (1 H, s, NH), 7.0–7.6 (4 H, m, aromatic), 3.77 (2 H, s,  $\text{CH}_2\cdot\text{CN}$ ), and 2.23 (3 H, s,  $\text{CH}_3$ ).

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<sup>10</sup> W. Madelung, *Ber.*, 1912, **45**, 1128.