Intramolecular Ring Closure of 1-Aroylindoles by Palladium Acetate

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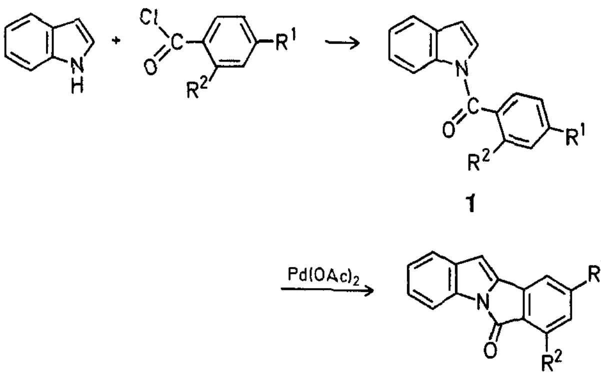
In recent years synthetic methods for polycyclic compounds containing the indole ring, which are of interest in connection with existence of biologically active substances, have been extensively investigated. Carruthers and Evans[1] reported the formation of 6-oxo-6*H*-isoindolo[2,1-*a*]indole (**2a**) by photolysis of 1-*o*-iodobenzoylindole, however, no intramolecular ring closure of 1-benzoylindole (**1a**) was observed[1]. We previously reported the intramolecular ring closure of 3-benzoyl-1-methylindoles[2] and now wish to report a synthesis of 6-oxo-6*H*-isoindolo[2,1-*a*]indoles (**2**) by an intramolecular dehydrogenation of 1-aroylindoles (**1**) with palladium(II) acetate.

Heating of an acetic acid solution containing **1a** and 0.5 equiv. of palladium acetate under nitrogen afforded **2a** in 47% yield, based on the indole **1a** consumed (conversion 87%). Under similar conditions 1-aroylindoles (aroyl = *p*-methyl-, *o*-methyl-, *p*-chloro-, and *o*-chlorobenzoyl; **1b–1e**) reacted with palladium acetate to give the corresponding polycyclic indoles **2**, although a steric hindrance due to the *ortho*-substitution led to decreased yields of the ring-closed products. The results are summarized in Table 2.



2a $R^1 = H, R^2 = H$
b $R^1 = CH_3, R^2 = H$
c $R^1 = H, R^2 = CH_3$
d $R^1 = Cl, R^2 = H$
e $R^1 = H, R^2 = Cl$

1-Aroylindoles (1a–1e):

To a stirred solution of indole (50 mmol) and sodium hydride (50 mmol) in dimethylformamide (150 ml), aroyl chloride (50 mmol) in dimethylformamide (50 ml) is added under nitrogen atmosphere. The solution is heated at 70° for 20 h. The reaction mixture is poured into an excess of ice-cooled water and extracted with benzene. The benzene extract is dried with sodium sulfate and

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Table 1. 1-Aroylindoles **1a–e**

Product	Yield [%]	m.p. (Lit. m.p.)	Molecular formula[a]	I.R. (nujol)[b] $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$)[c] δ [ppm]
1a	64	65–66° (67–68°)[3]	$C_{15}H_{11}NO$ (221.3)	1680	6.63 (d, 1H, J=4Hz); 7.26–7.94 (m, 9H); 8.46–8.65 (m, 1H)
1b	68	84–85°	$C_{16}H_{13}NO$ (235.3)	1680	2.46 (s, 3H); 6.65 (d, 1H, J=4Hz); 7.30–7.83 (m, 8H); 8.40–8.60 (m, 1H)
1c	61	58–59°	$C_{16}H_{13}NO$ (235.3)	1680	2.33 (s, 3H); 6.66 (d, 1H, J=4Hz); 7.16 (d, 1H, J=4Hz); 7.23–7.84 (m, 7H); 8.50–8.74 (m, 1H)
1d	43	114.5–115.5° (111–112°)[4]	$C_{15}H_{10}ClNO$ (255.7)	1680	6.84 (d, 1H, J=4Hz); 7.47–8.10 (m, 8H); 8.60–8.80 (m, 1H)
1e	50	63–64° (68–70°)[5]	$C_{15}H_{10}ClNO$ (255.7)	1680	6.82 (d, 1H, J=4Hz); 7.23 (d, 1H, J=4Hz); 7.50–8.00 (m, 7H); 8.70–8.90 (m, 1H)

[a] All products gave satisfactory microanalyses (C ±0.29, H ±0.23).

[b] Recorded on a Jasco IRA-1 spectrometer.

[c] Measured at 60 MHz on a Jeol MH-60 spectrometer.

Table 2. 6-Oxo-6*H*-isoindolo[2,1-*a*]indoles **2a–2e**

Product	Yield [%] (Conversion [%])	m.p. (Lit. m.p.)	Molecular formula[a]	I.R. (nujol)[b] $\nu_{C=O}$ [cm^{-1}]	^{1}H-N.M.R. (CDCl$_3$)[b] δ [ppm]
2a	47 (87)	154–155° (150–151°)[1]	$C_{15}H_9NO$ (219.2)	1720	6.75 (s, 1H); 7.28–8.25 (m, 8H)
2b	42 (83)	171–173°	$C_{16}H_{11}NO$ (233.3)	1720	2.42 (s, 3H); 6.60 (s, 1H); 7.10–8.07 (m, 7H)
2c	16 (85)	157.5–158.5°	$C_{16}H_{11}NO$ (233.3)	1720	2.50 (s, 3H); 6.47 (s, 1H); 6.93–8.00 (m, 7H)
2d	43 (82)	247–249°	$C_{15}H_8ClNO$ (253.7)	1720	6.90 (s, 1H); 7.42–8.40 (m, 7H)
2e	7 (80)	227–229°	$C_{15}H_8ClNO$ (253.7)	1720	6.80 (s, 1H); 7.33–8.27 (m, 7H)

[a] All products gave satisfactory microanalyses (C ±0.29, H ±0.19).

[b] See footnotes b and c to Table 1.

evaporated to give a brown oily residue. The residue is chromatographed on a silica gel column with petroleum ether/benzene to give **1**; colorless prisms from *n*-hexane/ether (Table 1).

6-Oxo-6*H*-isoindolo[2,1-*a*]indoles (2a–2e):

A solution of 1-aroylindole **1** (1.0 mmol) and palladium acetate (0.5 mmol) in acetic acid (40 ml) is stirred at 110° under nitrogen for 15 h. The reaction mixture is evaporated to give a dark brown oily residue which is then chromatographed on a silica gel plate developed by chloroform to give **2**; **2a**, **2b**, and **2c**, yellow needles from *n*-hexane/chloroform; **2d** and **2e**, yellow prisms from chloroform (Table 2).

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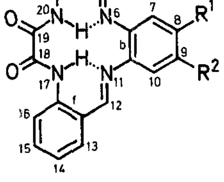
Errata

C. Giordano, A. Belli, V. Bellotti, *Synthesis* **1978** (6), 443–445.
The pressure of hydrogen sulphide given in the experimental procedures (pp. 444–445) should be 1.2 ata (912 torr) not 1.2 atm.

C. Skötsch, E. Breitmaier, *Synthesis* **1978** (9), 680–681.
The numbering for compounds **3a–c** (see Scheme, p. 680) should be as shown below.



3a $R^1 = R^2 = H$
b $R^1 = H$; $R^2 = t\text{-}C_4H_9$
c $R^1 = R^2 = CH_3$

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[1] W. Carruthers, E. Evans, *J. Chem. Soc. Perkin Trans. 1* **1974**, 1523.

[2] T. Itahara, T. Sakakibara, *Synthesis* **1978**, 607.

[3] R. Weissgerber, *Ber. Dtsch. Chem. Ges.* **43**, 3520 (1910).

[4] D. R. Julian, G. D. Tringham, *J. Chem. Soc. Chem. Commun.* **1973**, 13.

[5] W. J. Welstead, H. F. Stauffer, L. F. Sancilio, *J. Med. Chem.* **17**, 544 (1974).