Synthesis and X-ray structure of stable 2*H*-isoindoles

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Stable 2*H*-isoindoles with electron-withdrawing groups were prepared using the reaction of dinitrobenzene derivatives with isocyanoacetate in the presence of DBU. The use of acetonitrile as the solvent or a phosphazene base (BTPP) as a non-ionic base improved the yields. The structure was confirmed by X-ray crystallographic analysis of the compound **2e′**. According to the X-ray analysis, this substance existed in the solid phase only as the 2*H*-isomer.

Introduction

Pyrroles fused with polyaromatic hydrocarbons have been widely investigated as precursors of highly conjugated porphyrins and of electronically conducting polypyrroles. Recent developments in the efficient synthesis of these compounds have afforded a variety of polyaromatic annulated pyrroles. One of the most convenient preparations of such compounds has been the reaction of polyaromatic nitro compounds with ethyl isocyanoacetate in the presence of DBU.[1]

Some polyaromatic nitro compounds and heteroaromatic nitro compounds showed low reactivity and in some cases, we could not obtain the expected pyrroles and the corresponding pyrimidine *N*-oxides were formed. These drawbacks could be largely overcome[1c] by using other non-ionic bases such as proazaphosphatrane[2] or iminophosphorane.[3] In spite of these studies, attempts to prepare the true 2*H*-isoindole type compounds by the condensation of simple nitro aromatic compounds with a carbanion derived from ethyl isocyanoacetate, were unsuccessful. Thus, the remaining challenge in this field was the synthesis of isoindoles derived from simple nitro aromatic compounds.

Results and discussion

Isoindoles without nitrogen substituents are particularly reactive because of the occurrence of tautomeric equilibria with the 1*H*-isomer (imine-type compound). Unsubstituted isoindole was first synthesized[4] by the pyrolysis of *N*-methoxycarbonyloxyisoindoline and was isolated in 1972, but this compound was extremely labile and rapidly decomposed at ambient temperature.

Thus, the preparation of more stable isoindoles has been the object of extensive research. Most of the isoindoles so far prepared have been classified into two groups, that is, *N*-substituted[5] and 1,3-disubstituted[6] isoindoles. *N*-Substituted isoindoles are sufficiently stable and can be alkylated at the α-position.[7] Although these stabilizations were convenient and effective, the resulting isoindoles have not been utilized for the synthesis of conducting polymers and porphyrins.

So long as we used the standard reaction conditions, our approach to prepare the stable 2*H*-isoindole from 1,3- or 1,4-dinitrobenzenes was unproductive owing to the low yields and difficult separation of the pyrrolic compounds from the resulting mixture. Therefore, we examined the effect of several solvents and bases under various conditions.

Table 1 Preparation of nitro isoindoles **2**, **3** and nitro pyrrole **4**

Substrate	Solvent	Isocyano-acetate	Reaction Time/h	Product (%)[a]
1a	THF	$CNCH_2CO_2Et$	24	**2a** (9)
1a	CH_3CN	$CNCH_2CO_2Et$	24	**2a** (18)
1a	DMF	$CNCH_2CO_2Et$	24	**2a** (9)
1a	DMSO	$CNCH_2CO_2Et$	24	**2a** (8)
1a	THF	$CNCH_2CO_2Et$	24	**2a**[b] (29)
1b	THF	$CNCH_2CO_2Et$	48	**2b**[b] (9)
1c	CH_3CN	$CNCH_2CO_2Et$	4	**2c** (7) **3c** (2) **4** (3)
1c	CH_3CN	$CNCH_2CO_2t$-Bu	6	**2c′** (16) **3c′** (7)
1d	CH_3CN	$CNCH_2CO_2Et$	7	**2d** (16) **3d** (5) **4** (3)
1e	CH_3CN	$CNCH_2CO_2Et$	5	**2e** (64)
1e	CH_3CN	$CNCH_2CO_2t$-Bu	3	**2e′** (55)
1f	CH_3CN	$CNCH_2CO_2Et$	24	**2f** (7) **5** (27)

[a] Yields refer to pure isolated products. [b] BTPP was used instead of DBU.

To our surprise, we found that 1,3-dinitrobenzene **1a** undergoes nucleophilic addition and sequential cyclization using 2 equivalents of the reagent (See Table 1). A typical procedure was as follows: 1,3-dinitrobenzene (1 mmol) and 2 equivalents of ethyl isocyanoacetate were dissolved in 2 ml of THF, then 2.2 equivalents of DBU was added dropwise into the solution at 0 °C. The resulting mixture was stirred for 24 h after which it was worked up (experimental) and purified by silica gel column chromatography (ethyl acetate–hexane) to give pure ethyl 5-nitro-2*H*-isoindole-1-carboxylate **2a** in 10% yield (Scheme 1).

When this reaction was conducted in acetonitrile under similar conditions, the yield of **2a** was raised to 18%. Other solvents such as DMF and DMSO were not so effective. Thus, it may be concluded that acetonitrile is the most suitable solvent for these reactions. When THF was chosen as the solvent, the use of *tert*-butyliminotri(pyrrolidino)phosphorane (BTPP) as base improved the yield of **2a** to 29%. In all cases, the product was free of the possible isomer, ethyl 7-nitro-2*H*-isoindole-1-carboxylate. The reaction of 2,4-dinitrotoluene **1b** at room temperature for 48 h gave ethyl 6-methyl-5-nitro-2*H*-isoindole-1-carboxylate **2b** as the sole pyrrolic compound in 9% yield with a large

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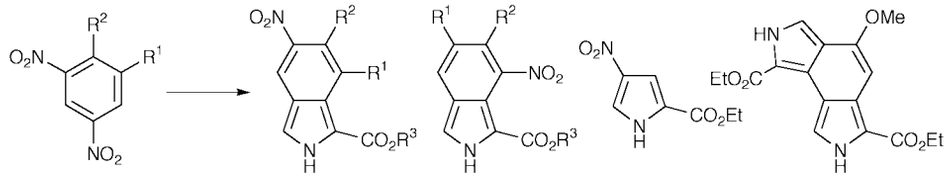


1 **2** **3** **4** **5**

a	R^1 = H	R^2 = H	R^3 = Et	**d**	R^1 = CO_2Et	R^2 = H	R^3 = Et
b	R^1 = H	R^2 = CH_3	R^3 = Et	**e**	R^1 = CN	R^2 = H	R^3 = Et
c	R^1 = CO_2Me	R^2 = H	R^3 = Et	**e′**	R^1 = CN	R^2 = H	R^3 = *t*-Bu
c′	R^1 = CO_2Me	R^2 = H	R^3 = *t*-Bu	**f**	R^1 = H	R^2 = OMe	R^3 = Et

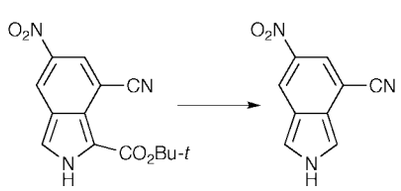
Scheme 1 *Reagents and conditions*: $CNCH_2CO_2Et$ or $CNCH_2CO_2t$-Bu, DBU or BTPP, solvent, RT.

amount of tarry matter. Unfortunately, 1,2- or 1,4-dinitrobenzenes and other electron-deficient aromatics such as methyl nitrobenzoate and dimethyl nitroterephthalate afforded complex mixtures.

Methyl 3,5-dinitrobenzoate **1c** reacted with ethyl isocyanoacetate in the presence of DBU in acetonitrile to give a mixture of ethyl 7-methoxycarbonyl-5-nitro-2*H*-isoindole-1-carboxylate **2c** and ethyl 5-methoxycarbonyl-7-nitro-2*H*-isoindole-1-carboxylate **3c** in yields of 7% and 2%, respectively. The reaction of ethyl 3,5-dinitrobenzoate **1d** gave a similar mixture with slightly better yields. In both cases, the unexpected nitropyrrole **4** was formed as an impurity. The mechanism of the formation of **4** is not clear at present.

3,5-Dinitrobenzonitrile **1e** was reacted smoothly with ethyl isocyanoacetate in the presence of DBU, giving ethyl 7-cyano-5-nitro-2*H*-isoindole-1-carboxylate **2e** as the sole product in 64% yield (Table 1).

The nitroisoindoles prepared here have an ester function at the α-position and, therefore, they have no potential as precursors for porphyrins and polypyrroles as they stand. Decarboxylation was attempted by heating with KOH in ethylene glycol at 170 °C, but the desired α-free pyrroles were not obtained. In order to effect decarboxylation, the reaction of **1c** and **1e** was conducted with *tert*-butyl isocyanoacetate and the corresponding pyrroles **2c′** and **2e′** were prepared. The compound **2e′** was successfully converted to the α-free pyrrole **6e′** by treatment with toluene-*p*-sulfonic acid in toluene at reflux temperature for 5 min in 27% yield (Scheme 2). This compound



2e′ **6e′**

Scheme 2 *Reagents and conditions*: toluene-*p*-sulfonic acid, toluene, reflux, 5 min.

was not so labile as compared with the unsubstituted isoindole because of the existence of two electron-withdrawing substituents (nitro and cyano). On the NMR timescale, it is stable in air at ambient temperature.

X-Ray diffraction-grade single crystals of compound **2e′** were grown by careful recrystallization from a dilute CH_2Cl_2 solution of the isoindole (Fig. 1). The resulting X-ray structure reveals that there are two isoindole molecules and one solvent molecule in the unit cell. The solvent molecule is disordered and shares one position between two orientations in a half-and-half fashion, the equivalent temperature factors of two Cl atoms show relatively large values. Existence of a dichloromethane molecule in the single crystals of compound **2e′** was confirmed

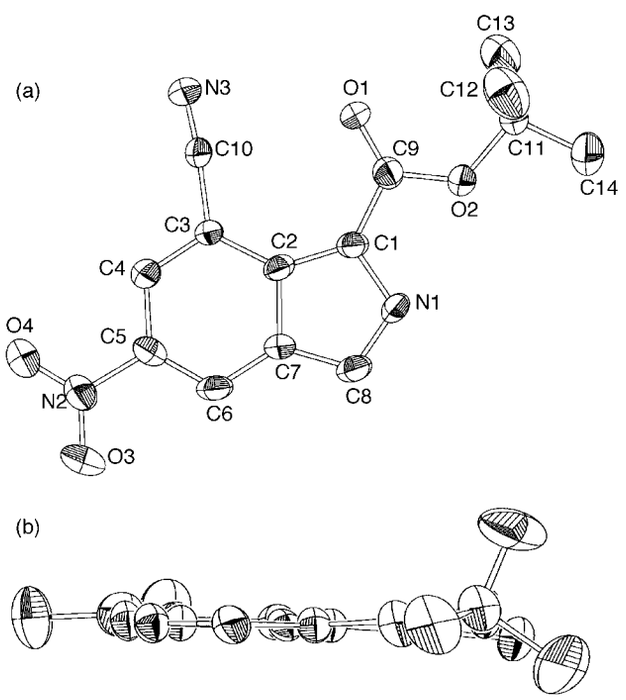


Fig. 1 (a) X-Ray crystal structure of isoindole **2e′**. Hydrogens and solvent are omitted for clarity. Bond distance (Å) and angles (°): N1–C1 1.381, N1–C8 1.320, C1–C2 1.387, C7–C8, 1.388; C1N1C8 112.0°, N1C1C2 106.5°, N1C8C7 108.5°, C1C2C7 107.0°, C2C7C8 106.5°. (b) Edge-on view of **2e′**.

by the ^{1}H NMR and elemental analysis of these single crystals (Anal. Calcd. for $C_{14}H_{13}N_3O_4 \cdot 1/2CH_2Cl_2$: C, 52.82; H, 4.28; N, 12.74; Found: C, 52.69; H, 4.26; N, 12.65%). When single crystals were grown from a $CHCl_3$ solution, a chloroform molecule was incorporated in the single crystals and the proportion of **2e′** and solvent was the same as that of dichloromethane containing single crystals.

When the bond length of N(1)–C(1) 1.380(9) Å is compared with that of N(1)–C(8) 1.319(9) Å, there is a small difference, which is mainly attributed to the contribution of the polarized canonical structure derived from the existence of the α-carbonyl group.[8] Thus, in this case, the possibility of the occurrence of tautomeric equilibrium with the 1*H*-isomer (imine-type structure) is not observed in the solid phase. According to the ^{1}H NMR result, the 2*H*-isomer is present almost exclusively in chloroform mainly because of the presence of nitro and cyano groups on the six-membered ring.[9] The isoindole ring is fairly planar and the dihedral angle between the nitro group and the benzene plane of the isoindole unit is 173.46°. The imino proton of pyrrole is linked by a hydrogen bond to the nitrile nitrogen of the neighboring molecule.

In all the reactions of dinitro arenes described above, only one of the nitro alkene moieties reacted with isocyanoacetate. However, when 2,4-dinitroanisole **1f** was reacted with 1 equiv. of ethyl isocyanoacetate in the presence of DBU, it gave a mixture of the monocyclization product, ethyl 6-methoxy-5-nitroisoindole-1-carboxylate **2f** and the double cyclization product, diethyl 4-methoxy-2,7-dihydropyrrolo[3,4-*e*]isoindole-1,6-dicarboxylate **5** in 7% and 27% yields respectively.

In conclusion, stable isoindoles were obtained from highly electron-deficient nitroarenes with isocyanoacetate using acetonitrile or THF as the solvent in the presence of DBU or BTPP as the base. Only 2,4-dinitroanisole **1f** reacted with isocyanoacetate to give the double cyclization product **5**. The decarboxylation of *tert*-butyl ester **2e′** was successful, and the resulting α-free isoindole **6e′** was a stable 2*H*-isoindole without any substituent on the α- and N-positions.

Experimental

General procedures

Melting points were measured by a Yanaco hot stage apparatus and are uncorrected. NMR spectra were recorded on a JEOL-JNM-GSX 270 or JNM-EX 400 spectrometer at ambient temperature by using $CDCl_3$, acetone-d_6 or DMSO-d_6 as a solvent and tetramethylsilane as an internal standard for ^1H and ^{13}C and *J* values are given in Hz. IR spectra were obtained with a Hitachi 270-30 spectrophotometer. Mass spectra were measured with a Hitachi M80B-LCAPI spectrometer under the following ionizing conditions: electron impact, 20 eV; high boiling PFK as a standard. THF was freshly distilled from sodium benzophenone ketyl. Ethyl isocyanoacetate was prepared from ethyl *N*-formylglycinate using $POCl_3$ and triethylamine.[10] Unless otherwise specified, all nitro aromatics which were not commercially available were prepared by the conventional nitration methods of aromatics using HNO_3–Ac_2O or HNO_3–H_2SO_4.

Ethyl 5-nitro-2*H*-isoindole-1-carboxylate 2a

tert-Butyliminotri(pyrrolidino)phosphorane (BTPP) (0.687 g, 2.2 mmol) was added dropwise to a solution of 1,3-dinitrobenzene (0.168 g, 1 mmol) and ethyl isocyanoacetate (0.225 g, 2 mmol) in THF (2 cm^3) at 0 °C. The resulting mixture was stirred for 24 h at ambient temperature, after which it was treated with dilute hydrochloric acid (10 cm^3) and extracted with ethyl acetate (3 × 10 cm^3). The combined organic phase was washed with aq. sodium hydrogen carbonate, water and brine, dried over sodium sulfate and evaporated. The residue was purified by silica gel column chromatography (ethyl acetate–hexane) to give pure ethyl 5-nitro-2*H*-isoindole-1-carboxylate **2a** (0.068 g, 29% yield), mp 221–223 °C; ^1H-NMR (CD_3SOCD_3) δ 1.38 (3H, t, *J* 7.08, CH_3), 4.37 (2H, q, *J* 7.16, CH_2), 7.95 (1H, dd, *J* 9.28, 1.96, ArH), 8.08 (1H, d, *J* 4.39, ArH), 8.09 (1H, d, *J* 4.72, ArH), 8.83 (1H, d, *J* 1.95, ArH) and 13.90 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.46, 59.93, 111.96, 118.16, 120.77, 121.17, 122.36, 123.03, 127.47, 142.22 and 160.28; ν_{max} (KBr)/cm^{-1} 3216, 1676, 1530, 1434, 1366, 1302 and 1142; *m*/*z* (EI) 234 (M^+, 92%), 188 (M^+ − EtOH, 100), 206 (8), 158 (17) and 142 (28); Anal. Calcd. for $C_{11}H_{10}N_2O_4$: C, 56.41; H, 4.30; N, 11.96; Found: C, 56.26; H, 4.35; N, 11.84%.

Other isoindoles **2b** and **2e** were prepared by the similar procedures as described in the preparation of **2a** using appropriate base and solvent and the conditions are shown in Table 1.

Ethyl 6-methyl-5-nitro-2*H*-isoindole-1-carboxylate 2b

Yield 9%; mp 211–213 °C; ^1H-NMR (CD_3SOCD_3) δ 1.37 (3H, t, *J* 7.08, CH_3CH_2), 2.55 (3H, s, CH_3), 4.35 (2H, q, *J* 7.00, CH_2), 7.84 (1H, s, ArH), 7.92 (1H, d, *J* 3.42, ArH), 8.54 (1H, s, ArH) and 13.75 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.48, 20.89, 59.74, 110.83, 121.03, 121.18, 122.02, 122.27, 127.09, 127.22, 144.85 and 160.28; ν_{max} (KBr)/cm^{-1} 3200, 1676, 1632, 1558, 1506, 1442, 1420, 1386, 1340, 1320, 1292, 1172, 1142 and 768; *m*/*z* (EI) 248 (M^+, 56%), 231 (19), 203 (9), 185 (100), 156 (17) and 128 (10); Anal. Calcd. for $C_{12}H_{12}N_2O_4$: C, 58.06; H, 4.87; N, 11.29; Found: C, 57.65; H, 4.86; N, 11.15%.

Reaction of 1c,d with ethyl isocyanoacetate

To a stirred solution of **1c** or **1d** (2 mmol) and ethyl isocyanoacetate (0.450 g, 4 mmol), 1,8-diazabicyclo[5.4.0]undec-7-ene (0.66 ml, 4.4 mmol) was added dropwise at 0 °C and the resulting mixture was stirred for 24 h at ambient temperature. It was worked up and the products **2c**, **3c**, **4** or **2d**, **3d**, **4** were separated by silica gel column chromatography (ethyl acetate–hexane). The pure products could be obtained by the recrystallization of the resulting solids from chloroform solutions.

Ethyl 7-methoxycarbonyl-5-nitro-2*H*-isoindole-1-carboxylate 2c

Yield 7%; mp 182–183 °C; ^1H-NMR ($CDCl_3$) δ 1.42 (3H, t, *J* 7.17, CH_3CH_2), 3.98 (3H, s, CH_3), 4.41 (2H, q, *J* 7.12, CH_2), 7.84 (1H, d, *J* 3.67, ArH), 8.21 (1H, d, *J* 1.22, ArH), 8.70 (1H, d, *J* 1.22, ArH) and 11.30 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.28, 52.15, 60.28, 112.60, 118.50, 121.97, 122.69, 123.10, 124.13, 126.41, 141.01, 159.56 and 167.41; ν_{max} (KBr)/cm^{-1} 3216, 1736, 1652, 1336, 1292 and 1200; *m*/*z* (EI) 292 (M^+, 65%), 246 (M^+ − EtOH, 100), 215 (11) and 188 (54); Anal. Calcd. for $C_{13}H_{12}N_2O_6$: C, 53.42; H, 4.14; N, 9.59; Found: C, 53.38; H, 4.09; N, 9.51%.

Ethyl 5-methoxycarbonyl-7-nitro-2*H*-isoindole-1-carboxylate 3c

Yield 2%; mp 177–179 °C; ^1H-NMR ($CDCl_3$) δ 1.41 (3H, t, *J* 7.17, CH_3CH_2), 3.98 (3H, s, CH_3), 4.40 (2H, q, *J* 7.12, CH_2), 7.84 (1H, s, ArH), 8.21 (1H, d, *J* 1.22, ArH), 8.70 (1H, d, *J* 1.22, ArH) and 11.25 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.05, 51.85, 60.07, 112.59, 118.28, 121.79, 122.26, 122.75, 123.96, 126.32, 140.94, 159.41 and 167.19; ν_{max} (KBr)/cm^{-1} 3204, 1716, 1658, 1632, 1540, 1442, 1298, 1286, 1234 and 1202; *m*/*z* (EI) 292 (M^+, 100%), 246 (M^+ − EtOH, 94), 215 (14), 188 (13) and 171 (15); Anal. Calcd. for $C_{13}H_{12}N_2O_6$: C, 53.42; H, 4.14; N, 9.59; Found: C, 53.09; H, 4.04; N, 9.59%.

Ethyl 4-nitropyrrole-2-carboxylate 4

Yield 3%; mp 165–166 °C; ^1H-NMR ($CDCl_3$) δ 1.40 (3H, t, *J* 7.17, CH_3CH_2), 4.39 (2H, q, *J* 7.22, CH_2), 7.40 (1H, dd, *J* 2.44, 1.83, ArH), 7.77 (1H, dd, *J* 3.66, 1.53, ArH) and 9.96 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.98, 62.12, 110.50, 124.47, 124.88, 138.90 and 160.84; ν_{max} (KBr)/cm^{-1} 3268, 1716, 1688, 1510, 1422, 1390, 1366, 1324, 1208 and 756; *m*/*z* (EI) 184 (M^+, 99%), 156 (100) and 139 (M^+ − EtO, 94); Anal. Calcd. for $C_7H_8N_2O_4$: C, 45.65; H, 4.38; N, 15.22; Found: C, 45.40; H, 4.33; N, 15.15%.

Ethyl 7-ethoxycarbonyl-5-nitro-2*H*-isoindole-1-carboxylate 2d

Yield 16%; mp 160–163 °C; ^1H-NMR (CD_3SOCD_3) δ 1.29 (3H, t, *J* 7.08, CH_3CH_2), 1.32 (3H, t, *J* 7.16, CH_3CH_2), 4.30 (2H, q, *J* 7.08, CH_3CH_2), 4.35 (2H, q, *J* 7.16, CH_3CH_2), 8.00 (1H, s, ArH), 8.18 (1H, s, ArH), 8.96 (1H, s, ArH) and 14.08 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 13.89, 14.30, 60.23, 61.03, 112.66, 118.47, 121.98, 122.58, 123.06, 124.14, 126.62, 141.01, 159.55 and 166.93; ν_{max} (KBr)/cm^{-1} 3210, 1731, 1649, 1332, 1288 and 1203; *m*/*z* (EI) 306 (M^+, 87%), 260 (M^+ − EtOH, 46), 232 (91), 215 (13), 188 (100) and 142 (31); Anal. Calcd. for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15; Found: C, 54.83; H, 4.57; N, 9.12%.

Ethyl 5-ethoxycarbonyl-7-nitro-2*H*-isoindole-1-carboxylate 3d

Yield 5%; mp 152–154 °C; ^{1}H-NMR (CD_3SOCD_3) δ 1.30 (3H, t, *J* 7.08, CH_3CH$_2$), 1.35 (3H, t, *J* 7.16, CH_3CH$_2$), 4.26 (2H, q, *J* 7.08, CH$_3$CH_2), 4.35 (2H, q, *J* 7.16, CH$_3$CH_2), 8.05 (1H, s, ArH), 8.20 (1H, s, ArH), 8.76 (1H, s, ArH) and 14.17 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.00, 14.12, 60.38, 61.11, 111.06, 116.00, 119.80, 121.71, 121.90, 126.89, 130.09, 142.93, 159.54 and 164.59; ν_{max} (KBr)/cm^{-1} 3212, 1719, 1660, 1638, 1546, 1446, 1298, 1288, 1240 and 1225; *m*/*z* (EI) 306 (M$^+$, 100%), 260 (M$^+$ − EtOH, 81), 232 (15) and 215 (22); Anal. Calcd. for $C_{14}H_{14}N_2O_6$: C, 54.90; H, 4.61; N, 9.15; Found: C, 54.68; H, 4.54; N, 9.19%.

Ethyl 7-cyano-5-nitro-2*H*-isoindole-1-carboxylate 2e

Yield 64%; mp 235–238 °C; ^{1}H-NMR ($CDCl_3$) δ 1.52 (3H, t, *J* 7.17, CH$_3$), 4.59 (2H, q, *J* 7.12, CH$_2$), 7.96 (1H, d, *J* 3.66, ArH), 8.57 (1H, d, *J* 2.13, ArH), 8.95 (1H, d, *J* 2.13, ArH) and 11.13 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 13.78, 59.88, 103.10, 112.55, 116.75, 121.61, 123.61, 123.94, 125.33, 127.62, 140.51 and 159.09; ν_{max} (KBr)/cm^{-1} 3176, 1658, 1606, 1510, 1480, 1446, 1354, 1334, 1312, 1276 and 774; *m*/*z* (EI) 259 (M$^+$, 65%), 213 (M$^+$ − EtOH, 100), 183 (14), 167 (18) and 139 (17); Anal. Calcd. for $C_{12}H_9N_3O_4$: C, 55.60; H, 3.50; N, 16.21; Found: C, 55.61; H, 3.62; N, 15.94%.

tert-Butyl 7-cyano-5-nitro-2*H*-isoindole-1-carboxylate 2e′

Yield 55%; mp >300 °C; ^{1}H-NMR ($CDCl_3$) δ 1.60 (9H, s, *t*-Bu), 7.90 (1H, d, *J* 3.67, ArH), 8.53 (1H, d, *J* 1.83, ArH), 8.93 (1H, d, *J* 2.14, ArH) and 11.10 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 27.98, 82.07, 102.88, 113.84, 117.00, 120.93, 122.85, 123.78, 125.26, 127.27, 140.15 and 158.73; ν_{max} (KBr)/cm^{-1} 3232, 1700, 1608, 1510, 1392, 1342, 1290, 1278, 1196, 1164, 1138, 1044 and 1018; *m*/*z* (EI) 287 (M$^+$, 13%), 231 (M$^+$ − (CH$_3$)$_2$C=CH$_2$, 100), 213 (M$^+$ − *t*-BuOH, 79), 197 (4), 183 (6), 167 (8) and 141 (8); Anal. Calcd. for $C_{14}H_{13}N_3O_4$: C, 58.53; H, 4.56; N, 14.63; Found: C, 58.65; H, 4.56; N, 14.65%.

Reaction of 1f with ethyl isocyanoacetate

The typical reaction conditions were described above. The products **2f** and **5** could be obtained in pure form by silica gel column chromatography (ethyl acetate–hexane) and following recrystallization of the resulting solids from chloroform solutions.

Ethyl 6-methoxy-5-nitroisoindole-1-carboxylate 2f

Yield 7%; mp 226–229 °C; ^{1}H-NMR (CD_3SOCD_3) δ 1.38 (3H, t, *J* 7.08, CH$_3$), 3.92 (3H, s, CH_3O), 4.34 (2H, q, *J* 7.16, CH$_2$), 7.46 (1H, s, ArH), 7.85 (1H, s, ArH), 8.38 (1H, s, ArH) and 13.59 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.45, 56.03, 59.57, 99.84, 110.66, 117.91, 120.88, 121.20, 127.56, 138.47, 148.89 and 160.31; ν_{max} (KBr)/cm^{-1} 3180, 1668, 1628, 1558, 1528, 1506, 1480, 1436, 1422, 1346, 1324, 1292, 1266, 1232, 1218 and 1182; *m*/*z* (EI) 264 (M$^+$, 100%), 218 (M$^+$ − EtOH, 47), 188 (10) and 171 (21); Anal. Calcd. for $C_{12}H_{12}N_2O_5$: C, 54.55; H, 4.58; N, 10.60; Found: C, 54.28; H, 4.52; N, 10.57%.

Diethyl 4-methoxy-2,7-dihydropyrrolo[3,4-*e*]isoindole-1,6-dicarboxylate 5

Yield 27%; mp 274–277 °C; ^{1}H-NMR (CD_3SOCD_3) δ 1.38 (6H, m, CH$_3$), 3.92 (3H, s, CH_3O), 4.35 (4H, m, CH$_2$), 6.96 (1H, s, ArH), 7.47 (1H, d, *J* 3.42, ArH), 8.08 (1H, d, *J* 3.41, ArH), 12.30 (1H, br, NH) and 12.53 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 14.56, 14.60, 54.61, 59.17, 59.62, 91.09, 111.82, 112.52, 112.86, 116.71, 116.87, 119.91, 121.63, 128.00, 152.31, 160.57 and 160.98; ν_{max} (KBr)/cm^{-1} 3260, 1650, 1628, 1538, 1494, 1432, 1396, 1280, 1156, 1132, 1118, 1040 and 774; *m*/*z* (EI) 330 (M$^+$, 92%), 284 (M$^+$ − EtOH, 100) and 238 (87); Anal. Calcd. for $C_{17}H_{18}N_2O_5$: C, 61.81; H, 5.49; N, 8.48; Found: C, 61.45; H, 5.54; N, 8.41%.

4-Cyano-6-nitro-2*H*-isoindole 6e′

A solution of isoindole *tert*-butyl ester (**2e′**) (0.0574 g, 0.2 mmol) and a catalytic amount of toluene-*p*-sulfonic acid in toluene (2 cm^3) was stirred at reflux temperature for 5 min. The resulting mixture was quenched with aq. sodium hydrogen carbonate and extracted with chloroform. The organic phase was washed with water and brine, dried and evaporated. The residue was purified by silica gel column chromatography (ethyl acetate–hexane) to give pure title compound **6e′**.

Yield 27%; ^{1}H-NMR (CD_3COCD_3) δ 7.65 (1H, s, ArH), 8.05 (1H, s, ArH), 8.15 (1H, d, *J* 1.95, ArH), 9.00 (1H, dd, *J* 1.96, 0.98, ArH) and 12.56 (1H, br, NH); ^{13}C-NMR (CD_3SOCD_3) δ 102.40, 109.63, 117.00, 118.73, 120.89, 121.34, 121.92, 126.00 and 140.05; *m*/*z* (EI) 187 (M$^+$, 100%), 157 (M$^+$ − NO, 8), 141 (M$^+$ − NO$_2$, 95), 129 (18) and 114 (41).

Crystal data for **2e′**·1/2CH_2Cl_2: $C_{14.5}H_{14}N_3O_4Cl$, M = 329.74, monoclinic, space group $P2_{1/a}$, a = 9.5471(7), b = 14.619(1), c = 11.4954(8) Å, β = 97.993(5)°, U = 1588.8(2) Å^3, Z = 4, D_c = 1.378 g cm^{-3}, μ = 23.40 cm^{-1}, Cu-Kα radiation, λ = 1.54178 Å, T = 296 K, 2737 determined 2570 independent, 1384 observed reflections [$I > 2\sigma(I)$], R = 0.080, Rw = 0.075. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were included but not refined. CCDC 207/398. See http://www.rsc.org/suppdata/p1/a9/a908641b/ for crystallographic files in .cif format.

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