ORIGINAL PAPER

Preparation and X-Ray Crystal Structure of 3-(4-(Dimethylamino)phenyl)-2-(phenylamino)isoquinolin-1(2*H*)-one, 3-(4-Methoxyphenyl)-2-(phenylamino)isoquinolin-1(2*H*)-one, and 2-Methyl-*N'*-(4-methylbenzoyl)-*N'*-phenylbenzohydrazide from Polylithiated 2-methylbenzoic Acid Phenylhydrazide and Methyl 4-dimethylaminobenzoate, Methyl 4-methoxybenzoate, or Methyl 4-methylbenzoate

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Abstract 2-Methylbenzoic acid phenylhydrazide was polylithiated with excess lithium diisopropylamide, and the resulting polylithiated intermediate was condensed with methyl 4-dimethylaminobenzoate or methyl 4-methoxybenzoate to afford C-acylated intermediates that were immediately acid cyclized to afford 3-(4-(dimethylamino)phenyl)-2-(phenylamino)isoquinolin-1(2H)-one C₂₃H₂₁N₃O or 3-(4-methoxyphenyl)-2-(phenylamino)isoquinolin-1(2H)one $C_{22}H_{18}N_2O_2$. The polylithiated intermediate underwent N-acylation when it was condensed with methyl 4-methylbenzoate to give 2-methyl-N'-(4-methylbenzoyl)-N'phenylbenzohydrazide C22H20N2O2. Crystals of C23H21N3O 4a are triclinic, $P = \overline{1}$, a = 9.138(2) Å, b = 10.519(2) Å, c = 11.082(2) Å, $\alpha = 91.55(3)^\circ$, $\beta = 108.92(3)^\circ$, $\gamma = 111.16(3)^\circ$, $Z = 2, V = 927.1(3) \text{ Å}^3, R_1 = 0.0711 \text{ and } wR_2 = 0.1828$ for reflections with $I > 2\sigma(I)$; crystals of C₂₂H₁₈N₂O₂ **4b** are monoclinic, $P2_1/c$, a = 8.821(1) Å, b = 13.276(2) Å, c = 15.482(3) Å, $\beta = 105.271(4)^\circ$, Z = 4, V = 1748.9(5) Å³, $R_1 = 0.0416$ and $wR_2 = 0.1030$ for reflections with $I > 2\sigma(I)$; crystals of C₂₂H₂₀N₂O₂ **3** are orthorhombic, *Pbca*, a = 13.505(3) Å, b = 9.733(2) Å, c = 28.601(6) Å,

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D. G. VanDerveer · W. T. Pennington Department of Chemistry, Clemson University, Clemson, SC 29634, USA Z = 8, V = 3759.4(13) Å³, $R_1 = 0.1683$ and $wR_2 = 0.3526$ for reflections with $I > 2\sigma(I)$.

Keywords Multiple anion synthesis · Isoquinolinones · *N*-acylated hydrazide

Introduction

The syntheses, biological potential and other uses of variously substituted isoquinolin-1(2H)-ones (isocarbostyrils) have recently been intensively studied and reviewed [1-6]. There are some recent reports dealing with the strong base multiple anion preparation of 3-substituted or 4-substituted and related substituted isoquinolin-1(2H)-ones [7–11]. While there is an abundance of information concerning 4-substituted isoquinolin-1(2H)-ones, there are fewer reports dealing with the preparation of 2-substituted and 2,3-disubstituted isoquinolin-1(2H)-ones, especially amino and anilino substituted [12-16]. For select isoquinolinones only 2-amino-3-phenylisoquinolin-1(2H)-one, 3-phenylamino-, and 4-phenylaminoisoquinolin-1(2H)-ones have been reported [12-16]; 2-phenylaminoisoquinolin-1(2H)ones have not. Relatively recent molecular modeling studies of select 3-arylisoquinolin-1(2H)-one antitumor agents with some X-ray studies have been reported. Recently the X-ray crystal analysis of 3-phenylisoquinolin-1(2H)-one has been documented [17].

Our attention has been focused on the strong base multiple anion preparation of these compounds [18, 19]. The 2,3-disubstituted isoquinolin-1(2H)-ones have been

Scheme 1 Preparation of 3-aryl-2-(phenylamino)isoquinolin-1(2*H*)-ones 4a and 4b and 2-methyl-*N*'-(4-methylbenzoyl)phenylbenzohydrazide 3



prepared in this laboratory by multiple anion synthesis procedures involving polylithiated 2-methylbenzamides [18], and 2-(methylphenyl)hydrazinecarboxylic acid esters 32

procedures involving polylithiated 2-methylbenzamides [18], and 2-(methylphenyl)hydrazinecarboxylic acid esters [19]. Additional methods of preparation by others involved *O*-methyl benzohydroxamates [8] or dilithiated *N*-methylbenzamides condensed with aromatic nitriles [7], followed by hydrolysis-cyclization of intermediates. Other strong base syntheses have involved lateral lithiation reactions [9], cyclization of dilithiated *N*,2-dimethylbenzamide, and intramolecular olefination of 2-trimethylsilylmethyl-*N*-acyl-*N*-alkylbenzamides [10].

Results and Discussion

During this investigation 2-methylbenzoic acid phenylhydrazide 1 [6] was trilithiated with excess lithium diisopropylamide (LDA) to afford reactive polylithiated intermediate 2. This polylithiated intermediate 2 was condensed with methyl 4-dimethylaminobenzoate to afford *C*-acylated intermediate compound that was not isolated, but illustrated in Scheme 1. It was immediately cyclized with 3 *M* hydrochloric acid to afford 2-phenylaminoisoquinolin-1(2*H*)-one **4a** in a 97 % yield. A follow up reaction of trilithiated hydrazide 2 with methyl 4-methoxybenzoate followed by acid cyclization of the *C*-acylated intermediate resulted in the preparation of 3-(4-methoxyphenyl)-2-(phenylamino)isoquinolin-1(2*H*)-one **4b** in 96 % yield. Absorption spectra was indicative of structure with several readily identifiable absorptions: IR (cm⁻¹), 3233 for **4a**; 3244 for **4b**; (NH); 1652 for **4a** and 1646 for **4b** (C=O); ¹H NMR (δ) 6.47 for **4a**; 6.56 for **4b** (C₄–H); ¹³C NMR 162.2 for **4a**; 160.6 for **4b** (C=O); 105.8 for **4a**; 107.1 for **4b** (C4). The general structure was also clearly confirmed by X-ray crystal analysis of isoquinolinones **4a** and **4b**. Both of the compounds **4a** and **4b** are new, and combustion analysis for C, H, and N provided additional support.

While the cyclization of *C*-acylated intermediate (bracketed in Scheme) to benzodiazapinone **5** is a possibility, estimated relative stability calculations indicate that **4b** is greater than 6 kcal mol⁻¹ more stable than **5** [20, 21].¹ Other spectral estimates, primarily ¹H and ¹³C NMR, also ruled out benzodiazepinone **5**.

Even though the procedures for **4a** and **4b** are reproducible in very good yield, methyl 4-methylbenzoate underwent *N*-acylation at the nitrogen bonded to the benzene ring and this resulted in *N*-acylated hydrazide **3**, 2-methyl-N'-(4-methylbenzoyl)-phenylbenzohydrazide in 67 % yield. This indicates that lithiation of the 2-methyl carbon to form the trianion did not occur probably due to

¹ Comparison of the enthalpies of formation calculated for isolated molecules of **4b** and **5** using MOPAC PM6 theory indicates that the **4b** isomer is more stable than the **5** isomer by slightly greater than 6 kcal mol⁻¹. Additional calculations using density functional theory (B3LYP/6-31G(d)) indicate that the **4b** isomer is more stable by slightly greater than 10 kcal mol⁻¹.

Fig. 1 ORTEP diagram (50 % ellipsoids for non-hydrogen atoms), 3-[4- dimethylamino)phenyl]-2- (phenylamino)isoquinolin- 1(2H)-one C₂₃H₂₁N₃O **4a** [23], and conventional illustration

Fig. 2 ORTEP diagram (50 % ellipsoids for non-hydrogen atoms), 3-(4-methoxyphenyl)-2-(phenylamino)isoquinolin-1(2*H*)-one C₂₂H₁₈N₂O₂ **4b** [23], and conventional illustration

contamination, and acylation occurred at next most reactive *N*-anion site. (see crystal studies on structurally related *N*-acylhydrazides [22]).

The molecular structure of 4a is shown in Fig. 1 and for 4b in Fig. 2. Selected bond distances and angles are listed in Table 1 for 4a and Table 2 for 4b. For 4a, the bond lengths agree with the assignment of the double bond shown between C1 and C2 (see the ORTEP diagram for numbering of atoms). The least squares best planes representing the rings containing N1 and C10 and the rings containing N1 and C16 are nearly perpendicular with angles of 88.2° and 75.6°, respectively, between them. Each molecule forms two hydrogen bonds with a second molecule in which the H atom on the N2 atom of each molecule is bonded at a distance of 2.002 Å to the O1 atom on the other molecule as shown in Fig. 3. The structure of 4b is nearly identical to that of 4a with the angles of the least squares best planes of 87.1° and 71.7°, respectively. The hydrogen bonding in 4b is identical to that of 4a except the distance is 2.115 Å.

The single crystal X-ray analysis (see the ORTEP diagram illustrated in Fig. 4) obtained for *N*-acylated product **3** indicated that cyclization between C2 and C3 did not occur. Instead of C2 bonding to N2, it attached to N1. The molecular structure of **3** is shown in Fig. 4 and selected bond distances and angles are listed in Table 3. The angles between the least squares best planes representing the rings containing C9 and C10 and containing C10 and C16 are 89.60° and 41.66° , respectively. Figure 5 shows the hydrogen bonding in which each molecule is hydrogen bonded to two molecules: the O2 atom is bonded at a distance of 2.109 Å to the H atom on N2 atom on the first molecule and the H atom on the N2 atom to the O2 atom on the second.

Experimental

Melting points were obtained with a Mel-Temp II melting point apparatus in open capillary tubes and are uncorrected. Fourier Transform infrared spectra were obtained with a Mattson Genesis II FT-IR with Specac Golden Gate Accessory. Proton and ¹³C NMR spectra were obtained with a Varian Associates Mercury Oxford (300 MHz for ¹H and 75 MHz for ¹³C) NMR spectrometer, and chemical shifts are recorded in δ ppm downfield from an internal tetramethylsilane (TMS) standard. Mass spectra were recorded using a Finnigan LCQ ESI-MS system.



Table 1 Selected bond distances (Å) and angles (°), C₂₃H₂₁N₃O 4a

C1–C2	1.352(4)	C1-C2-C3	121.5(3)
C2–C3	1.449(4)	C2-C1-N1	118.6(3)
C8–C9	1.467(4)	C1-N1-C9	125.1(3)
C9-N1	1.397(4)	N1-C9-C8	115.1(3)
N1-C1	1.399(4)	C1-N1-N2	116.8(2)
C1-C16	1.481(4)	C9-N1-N2	117.8(3)
C19-N3	1.376(4)	N1-N2-C10	114.4(2)
N3-C22	1.452(4)	N1-C1-C16	118.0(3)
N3-C23	1.453(4)	C19-N3-C22	120.5(3)
N1-N2	1.409(3)	C19-N3-C23	119.0(3)
N2-C10	1.418(4)	C22-N3-C23	118.6(3)
C901	1.224(4)		

Table 2 Selected bond distances (Å) and angles (°), $C_{22}H_{18}N_2O_2$ 4b

C1-C2	1.351(2)	C1-C2-C3	121.5(1)
C2–C3	1.434(2)	C2-C1-N1	119.1(1)
C8–C9	1.464(2)	C1-N1-C9	124.3(1)
C9-N1	1.392(2)	N1-C9-C8	115.8(1)
N1-C1	1.398(2)	C1-N1-N2	117.4(1)
C1-C16	1.484(2)	C9-N1-N2	117.9(1)
N1-N2	1.409(2)	N1-N2-C10	114.8(1)
N2-C10	1.414(2)	N1C1C16	118.9(1)
C901	1.229(2)		

Combustion analyses were performed by Quantitative Technologies, Inc., P.O. Box 470, Whitehouse, NJ 08888.

Preparation of 2-Phenylamino-3-arylisoquinolin-1(2*H*)ones **4a** and **4b**

Ratio of reagents—hydrazide: LDA: ester 1:5:1 for **4a** and 1:4:1 for **4b**.

In a typical reaction sequence, LDA was prepared by the addition of 40 mL for 4a [33 mL for 4b] of 1.60 M n-butyllithium [and 0.0630 mol for 4a and 0.0525 mol for 4b] in hexanes to a three-neck round-bottomed flask (e.g., 500 mL), equipped with a nitrogen inlet tube, and a sidearm addition funnel (e.g., 125 mL). The flask was cooled in an ice water bath, 6.41 g (0.0630 mol) for 4a and 5.34 g (0.0525 mol) for **4b** of diisopropylamine (99.5 %-Aldrich Chem. Co.), dissolved in 25-35 mL of dry THF (freshly distilled from sodium) was added from the addition funnel at a fast drop wise rate during a 5 min (0 °C, N_2) period. The solution was stirred for an additional 15-20 min, and then treated via the addition funnel, during 5 min, with 2-methylbenzoic acid phenylhydrazide [6], 3.39 g (0.0150 mol) dissolved in 40–60 mL of THF. After 3-4 h, a solution of 2.83 g of methyl 4-dimethylaminobenzoate for 4a and 2.62 g of methyl 4-methoxybenzoate for 4b (0.0158 mol 5 % molar excess)





Fig. 3 Intermolecular hydrogen bonding in 4a. The distance between the H atom on the N2 atom of each molecule to the O1 atom on the other molecule is 2.002 Å

dissolved in 25-35 mL of THF was added, during 5 min, to trilithiated intermediate 2, and the solution was stirred for 1-2 h. This was followed by rapid addition of 100 mL of 3 M hydrochloric acid, and heating the well stirred mixture under reflux for 30 min. The mixture was added to a large flask containing ice. Before neutralization with solid sodium bicarbonate, an additional 100 mL of solvent grade ether was added to the mixture, and the two-phase mixture was separated, followed by extraction of the aqueous layer with ether $(2 \times 50 \text{ mL})$. The combined organic fractions were extracted with 25 mL of 5 % sodium bicarbonate solution, then 25 mL water. The resulting organic solution was dried with MgSO₄, decanted, and evaporated [rotoevap. temp of water bath ~ 40 °C]. An oil or a solid resulted; the solid was recrystallized and the oil was taken up in an approximate equal volume of methanol or ethanol. Upon refrigeration of this solution/mixture, crystallization occurred.

3-[4-(Dimethylamino)phenyl]-2-(phenylamino)isoquinolin-1(2*H*)-one (**4a**)

Compound **4a** was obtained in a 97 % yield, 229–230 °C (methanol) from condensation-cyclization of **2** with methyl

Fig. 4 ORTEP diagram (50 % ellipsoids for non-hydrogen atoms), 2-methyl-N'-(4-methylbenzoyl)-N'- phenylbenzohydrazide C₂₂H₂₀N₂O₂ **3** [23], and conventional illustration



Table 3 Selected bond distances (Å) and angles (°), $C_{22}H_{20}N_2O_2$ 3

C1–C9	1.475(14)	C9-C1-N2	114.0(10)
C101	1.232(15)	C1-N2-N1	118.3(9)
C1-N2	1.362(13)	N2-N1-C10	116.7(8)
N2-N1	1.402(10)	N2-N1-C2	121.6(8)
N1-C10	1.443(12)	N1-C2-C16	117.7(9)
N1-C2	1.357(13)	N1-N2-C1-C9	179.4(8)
C2–O2	1.201(11)	C10-N1-N2-C1	100.4(10)
C2-C16	1.497(13)	C2-N1-N2-C1	-61.8(12)
		N2-N1-C2-C16	-24.4(14)



Fig. 5 Intermolecular hydrogen bonding in 3. The distances between the O2 atom and the H atom on the N2 atom are 2.109 Å

4-dimethylaminobenzoate. IR: 1598, 1652, 3023, 3233 cm⁻¹. ¹H-NMR (DMSO-d₆): δ 3.36 (s, 6H, CH₃), 6.47 (d, 2H, CH, J = 7.8 Hz), 6.64 (d, 2H, CH, J = 8.7 Hz), 6.65 (s, 1H, CH), 6.70 (d, 2H, CH, J = 7.2 Hz), 7.05 (t, 2H, CH, J = 7.8 Hz), 7.34 (s, 1H,

CH), 7.42 (d, 1H, CH, J = 8.7 Hz), 7.46 (m, 2H, CH), 7.70 (m, 1H, CH), 8.15 (d, 1H, CH, J = 8.1 Hz), 8.92 (s, 1H, NH). ¹³C-NMR (DMSO-d₆): δ 41.0, 105.8, 111.6, 113.0, 120.0, 122.5, 125.3, 126.8, 127.1, 127.8, 129.0, 130.7, 133.5, 137.4, 147.3, 149.0, 151.0, 162.2. Anal. Calcd for C₂₃H₂₁N₃O·1/8 H₂O: C, 77.23; H, 5.99; N, 11.75. Found: C, 77.09; H, 5.85; N, 11.56.

Single Crystal X-ray Structure Determination, 4a

Yellow crystals of C₂₃H₂₁N₃O **4a** were recrystallized from an ethanol–water solution in order to give satisfactory crystals for X-ray determination. Crystal data for X-ray studies [24] were collected at 168 K on a Mercury CCD area detector coupled with a Rigaku AFC8 diffractometer with graphite monochromated Mo-K α radiation. Data were collected in 0.5° oscillations in ω with 30 s exposures. A sweep of data was done using ω oscillations from -40.0° to 90.0° at $\chi = 45^{\circ}$ and $\phi = 0.0^{\circ}$; a second sweep was performed using ω oscillations from -40.0° to 90.0° at $\chi = 45^{\circ}$ and $\phi = 90.0^{\circ}$. The crystal-to-detector distance was 27.728 mm. Details of the data collection are reported Table 4. Data were collected, processed, and corrected for Lorentz polarization and for absorption using CrystalClear (Rigaku) [24, 25].

The non-hydrogen atoms were refined anisotropically. Ideal hydrogen atom coordinates for the rings containing C3, C10, and C16 (see numbering of atoms in ORTEP diagram, Fig. 1); C2; and the methyl groups containing C22 and C23 were calculated and the hydrogen atoms were allowed to ride on their respective carbon atoms. The hydrogen atom on N2 was located on a difference electron density map. The temperature factors of all hydrogen atoms were varied isotropically. Structure solution, refinement, and the calculation of derived results were performed using

Table 4 Crystallographic Data, C23H21N3O 4a

CCDC deposit number ^a	778252
Color/shape	Yellow/prism
Crystal dimensions (mm)	$0.34 \times 0.24 \times 0.10$
Formula	$C_{23}H_{21}N_3O$
Formula mass	355.43
<i>T</i> (K)	168
Crystal system	Triclinic
Space group	P 1
<i>a</i> (Å)	9.138(2)
<i>b</i> (Å)	10.519(2)
<i>c</i> (Å)	11.082(2)
α (°)	91.55(3)
β (°)	108.92(3)
γ (°)	111.16(3)
V (Å ³)	927.1(3)
Ζ	2
$d_{\rm calc} \ ({\rm g \ cm^{-3}})$	1.273
λ (Å)	0.71073
$\mu \ (\mathrm{mm}^{-1})$	0.080
<i>F</i> (000)	376
θ range (°)	2.90-25.15
Reflections collected	7002
Miller indices	$-10 \le h \le 10, -12 \le k \le 12, \\ -13 \le l \le 11$
Unique reflections	3284
Unique reflections $I > 2\sigma(I)$	2116
Max and min transmission	1.000, 0.521
Data, restraints, parameters	3284, 0, 250
Final <i>R</i> indices $I > 2\sigma(I)$	$R_1 = 0.0711, wR_2 = 0.1828$
R indices all data	$R_1 = 0.1109, wR_2 = 0.2379$
Goodness of fit on F^2	1.028
Largest diff peak and hole (e $Å^{-3}$)	0.378, -0.317

CCDC 778252 for **4a**, CCDC 882827 for **4b** and CCDC 828909 for **3** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

the *SHELX-97* [26] package of computer programs. Neutral atom scattering factors were those of Cromer and Waber [27], and the real and imaginary anomalous dispersion corrections were those of Cromer [27].

3-(4-Methoxyphenyl)-2-(phenylamino)isoquinolin-1(2*H*)-one (**4b**)

Compound **4b** was obtained in a 96 % yield, 177–178° C (ethanol) from the condensation-cyclization of **2** with methyl 4-methoxybenzoate. IR: 1510, 1600, 1646, 2964, 3244 cm⁻¹. ¹H-NMR (DMSO-d₆): δ 3.77 (s, 3H, OCH₃), 6.56 (s, 1H, CH), 6.65 (d, 2H, CH, J = 7.8 Hz), 6.85 (d, 2H,

CH, J = 8.7 Hz), 7.12 (t, 1H, CH, J = 7.5 Hz), 7.47 (m, 3H, CH), 7.56 (d, 2H, CH, J = 7.5 Hz), 7.66 (t, 2H, CH, J = 8.1 Hz), 8.38 (d, 1H, CH, J = 7.8 Hz). ¹³C-NMR (DMSO-d₆): δ 55.4, 107.1, 113.4, 114.3, 122.0, 125.2, 126.3, 126.7, 127.1, 128.2, 129.2, 130.8, 136.8, 145.2, 147.6, 160.1, 162.6. LCMS, exact mass, 342.39: (M + H)⁺, 343.05. Anal. Calcd for C₂₂H₁₈N₂O₂·1/2 H₂O: C, 75.20; H, 5.45; N, 7.97. Found C, 75.18; H, 5.20; N, 7.95.

Single Crystal X-ray Structure Determination, 4b

Colorless crystals of **4b**, $C_{22}H_{18}N_2O_2$ were recrystallized from an ethanol–water solution in order to give satisfactory crystals for X-ray determination. Crystal data for X-ray studies were collected at 188 K on the system described above using the same data collection parameters except the exposure times were 20 s and the second ω sweep range was -30.0° to 80.0° . The crystal-to-detector distance was 26.804 mm. Details of the data collection are reported Table 5. Data were collected, processed, and corrected as described above.

The non-hydrogen atoms were refined anisotropically. Ideal hydrogen atom coordinates for the rings containing C3, C10, and C16 (see numbering of atoms in ORTEP diagram, Fig. 2) and the methyl group containing C22 were calculated and the hydrogen atoms were allowed to ride on their respective carbon atoms. The hydrogen atoms on C2 and N2 were located on a difference electron density map. The temperature factors of all hydrogen atoms were varied isotropically. Structure solution, refinement, and other calculations are described above.

2-Methyl-*N*'-(4-methylbenzoyl)-*N*'-phenylbenzohydrazide (**3**)

Compound **3** was obtained [hydrazide:LDA:ester—1:4:1] in a 67 % yield, 159–160 °C (ethanol) from the condensation-cyclization of presumed **2** with methyl 4-methylbenzoate. IR: 1647, 1679, 2924, 3070, 3296 cm⁻¹. ¹H-NMR (DMSO-d₆): δ 3.43 (s, 3H, CH₃), 6.72 (t, 1H, CH, J = 7.2 Hz), 6.83 (d, 2H, CH, J = 8.7 Hz), 7.09 (s, 1H, CH), 7.21 (d, 2H, CH, J = 7.5 Hz), 7.36 (m, 3H, CH), 7.49 (d, 2H, CH, J = 7.5 Hz), 7.79 (t, 1H, CH, J = 7.8 Hz), 7.85 (d, 1H, CH, J = 8.1 Hz), 7.93 (d, 1H, CH, J = 3.6 Hz), 11.31 (s, 1H, NH), ¹³C-NMR (DMSO-d₆): δ 21.7, 112.9, 124.7, 126.3, 127.6, 128.5, 129.5, 129.9, 130.0, 131.0, 131.3, 131.4, 133.1, 134.2, 136.7, 141.1, 142.7, 168.2. Anal. Calcd for C₂₂H₁₈N₂O·1/8 H₂O: C, 76.22; H, 5.89; N, 8.08. Found C, 76.24; H, 5.88; N, 8.14.

Single Crystal X-ray Structure Determination, 3

Light yellow crystals of **3**, $C_{22}H_{20}N_2O_2$ were recrystallized from an ethanol–water solution in order to give satisfactory

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Table 5Crystallographic data, $C_{22}H_{18}N_2O_2$ 4b		Table 6Crystallographic data, $C_{22}H_{20}N_2O_2$ 3		
CCDC deposit number ^a	882827	CCDC deposit number ^a	828909	
Color/shape	Colorless/prism	Color/shape	Yellow/prism	
Crystal dimensions (mm)	$0.48 \times 0.36 \times 0.31$	Crystal dimensions (mm)	$0.29 \times 0.19 \times 0.10$	
Formula	$C_{22}H_{18}N_2O_2$	Formula	$C_{22}H_{20}N_2O_2$	
Formula mass	342.38	Formula mass	344.40	
<i>T</i> (K)	188	<i>T</i> (K)	173	
Crystal system	Monoclinic	Crystal system	Orthorhombic	
Space group	P21/c	Space Group	Pbca	
<i>a</i> (Å)	8.821(1)	a (Å)	13.505(3)	
<i>b</i> (Å)	13.276(2)	b (Å)	9.733(2)	
<i>c</i> (Å)	15.481(3)	c (Å)	28.601(6)	
β (°)	105.271(4)	$V(\text{\AA}^3)$	3759.4(13)	
V (Å ³)	1748.9(5)	Ζ	8	
Ζ	4	$d_{\rm calc}~({\rm g~cm^{-3}})$	1.217	
$d_{\rm calc} \ ({\rm g} \ {\rm cm}^{-3})$	1.300	λ (Å)	0.71073	
λ (Å)	0.71073	$\mu \ (\mathrm{mm}^{-1})$	0.079	
$\mu \ (\mathrm{mm}^{-1})$	0.084	<i>F</i> (000)	1456	
<i>F</i> (000)	720	θ range (°)	2.95–25.15	
θ range (°)	2.84–25.14	Reflections collected	15186	
Reflections collected	$11490 = -10 \le h \le 10 = -14 \le h \le 15$	Miller indices	$-16 \le h \le 12, -11 \le k \le 9, -34 \le l \le 34$	
White indices	$-18 \le l \le 18$	Unique reflections	3280	
Unique reflections	3108	Unique reflections $I > 2\sigma(I)$	1182	
Unique reflections $I > 2\sigma(I)$	2764	Max and min transmission	1.000, 0.3577	
Max and min transmission	1.000, 0.879	Data, restraints, parameters	3280, 0.237	
Data, restraints, parameters	3108, 0, 244	Final <i>R</i> indices $I > 2\sigma(I)$	$R_1 = 0.1683, wR_2 = 0.3526$	
Final <i>R</i> indices $I > 2\sigma(I)$	$R_1 = 0.0416, wR_2 = 0.1030$	R indices all data	$R_1 = 0.3152, wR_2 = 0.4897$	
R indices all data	$R_1 = 0.0463, wR_2 = 0.1098$	Goodness of fit on F^2	1.185	
Goodness of fit on F^2	1.069	Largest diff peak and hole (e ${\rm \AA}^{-3})$	0.547, -0.433	
Largest diff peak and hole (e $Å^{-3}$)	0.176, -0.219	CCDC 779252 for 40, CCDC 99292	7 few 4 h and CCDC 929000 few 2	

CCDC 778252 for **4a**, CCDC 882827 for **4b** and CCDC 828909 for **3** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

crystals for X-ray determination. Crystal data for X-ray studies were collected at 173 K on the system described above using the same data collection parameters with 120 s exposures. The crystal-to-detector distance was 27.267 mm. Details of the data collection are reported Table 6. Data were collected, processed, and corrected as described above.

The non-hydrogen atoms were refined anisotropically. Ideal coordinates for all hydrogen atoms were calculated and the hydrogen atoms were allowed to ride on their respective carbon atoms. The temperature factors of all hydrogen atoms were varied isotropically. Structure solution, refinement, and other calculations are described above.

The R factors for this compound are unusually high. Although we collected data using 120 s frames, the data CCDC 778252 for **4a**, CCDC 882827 for **4b** and CCDC 828909 for **3** contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

above 30° were still quite weak. There are no solvent voids and we are unable to explain the poor crystal quality. However, the atom connectivity, bond lengths and angles, and other molecular parameters determined from these data are sufficiently precise to be meaningful.

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