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Syntheses of 1-Arylidenamino-2,4-disubstituted-2-imidazoline-5-ones. X-Ray Structure of 1-Benzylidenamino-2-phenyl-4-benzylidene-2-imidazoline-5-one

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Summary. The present paper deals with syntheses and study of 1-arylidenamino-2,4-disubstituted-2-imidazoline-5-ones. The compounds were prepared by cyclization of arylidenehydrazides of 2-benzoylamino-3-arylacrylic acid which were synthesized *via* condensation of hydrazides of 2-benzoylamino-3-arylacrylic acid with substituted benzaldehydes. The structure of 1-benzylidenamino-2-phenyl-4-benzylidene-2-imidazoline-5-one was determine by single crystal X-ray analysis. Geometry optimization of the above compound at the semi-empirical PM3 level is also presented and compared with the X-ray data.

Keywords. 1-Arylidenamino-2,4-disubstituted-2-imidazoline-5-ones; Syntheses; X-Ray structure; Semi-empirical quantum-chemical PM3 calculations.

Synthese von 1-Arylidenamino-2,4-disubstituierten-2-imidazolin-5-onen. Röntgenstrukturanalyse von 1-Benzylidenamino-2-phenyl-4-benzyliden-2-imidazolin-5-on

Zusammenfassung. Diese Arbeit beschäftigt sich mit Synthese und Untersuchung von 1-Arylidenamino-2,4-disubstituierten-2-imidazolin-5-onen. Die Verbindungen wurden durch Cyclisierung von Arylidenhydraziden von 2-Benzoylamino-3-arylacrylsäure hergestellt, welche durch Kondensation von 2-Benzoylamino-3-arylacrylsäure mit substituierten Benzaldehyden gewonnen wurden. Die Struktur von 1-Benzylidenamino-2-phenyl-4-benzyliden-2-imidazolin-5-on wurde mittels Einkristallröntgenstrukturanalyse bestimmt. Eine Geometrieoptimierung der Titelverbindung auf der semiempirischen PM3-Ebene wird ebenfalls vorgestellt und mit den Röntgendaten verglichen.

Introduction

2-Benzoylamino-3-phenylacrylic acid was first reported in 1948 by *Stodola* [1] who described its synthesis. It was used as a starting compound for the preparation

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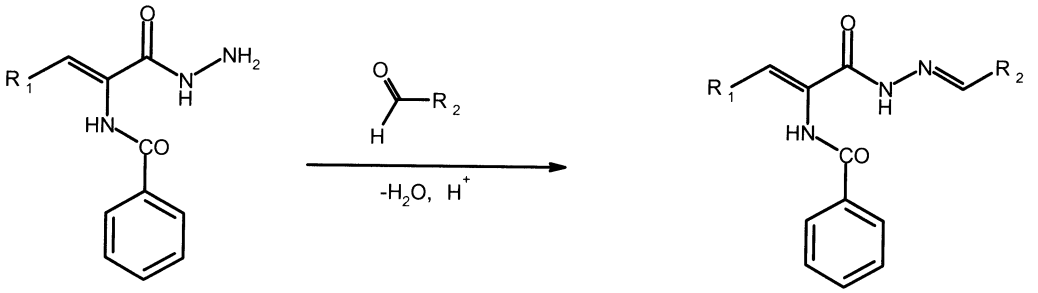
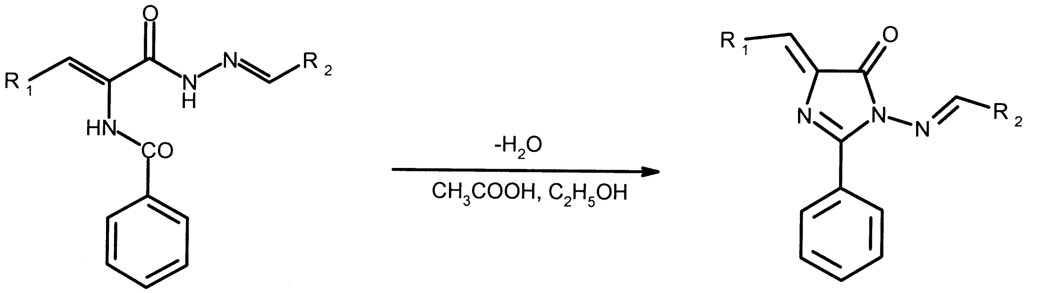


1a: R_1 = Ph	R_2 = Ph
1b: R_1 = 4-CH_3O-Ph	R_2 = Ph
1c: R_1 = 3,4-$(CH_3O)_2$-Ph	R_2 = Ph
1d: R_1 = Ph	R_2 = 2-NO_2-Ph
1e: R_1 = 4-CH_3O-Ph	R_2 = 4-CH_3O-Ph
1f: R_1 = 4-Cl-Ph	R_2 = 2-OH-Ph

Scheme 1



Scheme 2

of the benzylidenehydrazide of 2-benzoylamino-3-phenylacrylic acid (**1a**) and its substituted derivatives **1b**–**f** (Scheme 1) which were synthesized analogously to Ref. [2].

We now report the cyclization of compounds **1a**–**f** leading to the 1-arylidenamino-2,4-disubstituted-2-imidazoline-5-ones **2a**–**f** (Scheme 2) which to our knowledge have not been described in the literature so far.

Results and Discussion

The new compounds together with their chemical and analytical data are summarized in Table 1. Selected IR frequencies of **1a**–**f** and **2a**–**f** ((C=O), $(C-C)_{ar}$, (C–N), (C=N), and $(C-H)_{ar}$ vibrations [3]) are given in Table 2.

Table 1. Analytical data of **1a–f** and **2a–f**

					Found (Calcd.) (%)		
	Formula	M_r	M.P. (°C)	Yield (%)	C	H	N
1a	$C_{23}H_{19}N_3O_2$	369.4	237–239	87	74.6 (74.8)	5.0 (5.2)	11.3 (11.4)
1b	$C_{24}H_{21}N_3O_3$	399.4	231–233	89	72.2 (72.2)	5.3 (5.3)	10.3 (10.5)
1c	$C_{25}H_{23}N_3O_4$	429.1	174–176	64	69.8 (69.9)	5.5 (5.4)	9.6 (9.8)
1d	$C_{23}H_{18}N_4O_4$	414.4	184–186	91	66.4 (66.7)	4.1 (4.4)	13.1 (13.5)
1e	$C_{25}H_{23}N_3O_4$	429.5	238–241	87	69.6 (69.9)	5.5 (5.4)	9.7 (9.8)
1f	$C_{23}H_{18}N_3O_3Cl$	419.9	283–286	93	65.5 (65.8)	4.6 (4.3)	10.0 (10.0)
2a	$C_{23}H_{17}N_3O$	351.4	181–183	30	78.5 (78.6)	4.9 (4.9)	12.2 (12.0)
2b	$C_{24}H_{19}N_3O_2$	381.4	178–182	31	75.7 (75.6)	4.9 (5.0)	10.9 (11.0)
2c	$C_{25}H_{21}N_3O_3$	411.4	213–215	35	72.7 (73.0)	5.2 (5.1)	10.0 (10.2)
2d	$C_{23}H_{16}N_4O_3$	396.4	179–181	16	69.5 (69.7)	4.0 (4.1)	14.0 (14.1)
2e	$C_{25}H_{21}N_3O_3$	411.5	185–189	47	73.0 (73.0)	5.1 (5.1)	9.9 (10.2)
2f	$C_{23}H_{16}N_3O_2Cl$	401.9	230–234	32	69.0 (68.7)	3.8 (4.0)	10.2 (10.5)

Table 2. Selected IR data (cm^{-1}) of **1a–f** and **2a–f**

	ν(C=O)	ν(C=N)	$\nu(C-C)_{ar}$	ν(C−N)	$\delta(C-H)_{ar}$
1a	1645 s	1604 m	1476 s	1338 m	692 m
1b	1644 vs	1606 s	1488 m	1336 m	685 s
1c	1654 s	1601 s	1479 s	1337 m	694 m
1d	1643 vs	1603 m	1478 m	1341 m	689 m
1e	1640 s	1603 s	1480 s	1338 m	690 w
1f	1642 vs	1610 s sh	1482 m	1336 w	695 m
2a	1707 vs	1640 s[a]	1490 m	1336 s	687 m
2b	1701 s	1639 s[a]	1490 m	1336 s	691 s
2c	1694 vs	1644 s[a]	1489 s	1334 vs	698 vs
2d	1712 vs	1640 vs[a]	1489 s	1341 vs	694 s
2e	1698 s	1638 s[a]	1490 m	1341 m	691 m
2f	1706 vs	1644 s[a]	1544 m	1336 s	704 m

[a] Stretching vibration of the benzylidene C=N group

A single crystal X-ray analysis of **2a** (Fig. 1) corroborated the cyclization of **1a** and the formation of an imidazoline ring accompanied by elimination of water. Atomic coordinates and equivalent isotropic displacement parameters for **2a** are listed in Table 3, selected bond lengths and angles in Table 4. The crystal packing is shown in Fig 2.

There are no significant deviations from planarity in the aromatic rings [4] formed by N(1)-C(2)-N(3)-C(4)-C(5) (plane 1), C(21)C-(22)-C(23)-C(24)-C(25)-C(26) (plane 2), C(8)-C(9)-C(10)-C(11)-C(12)-C(13) (plane 3), and C(14)-C(15)-

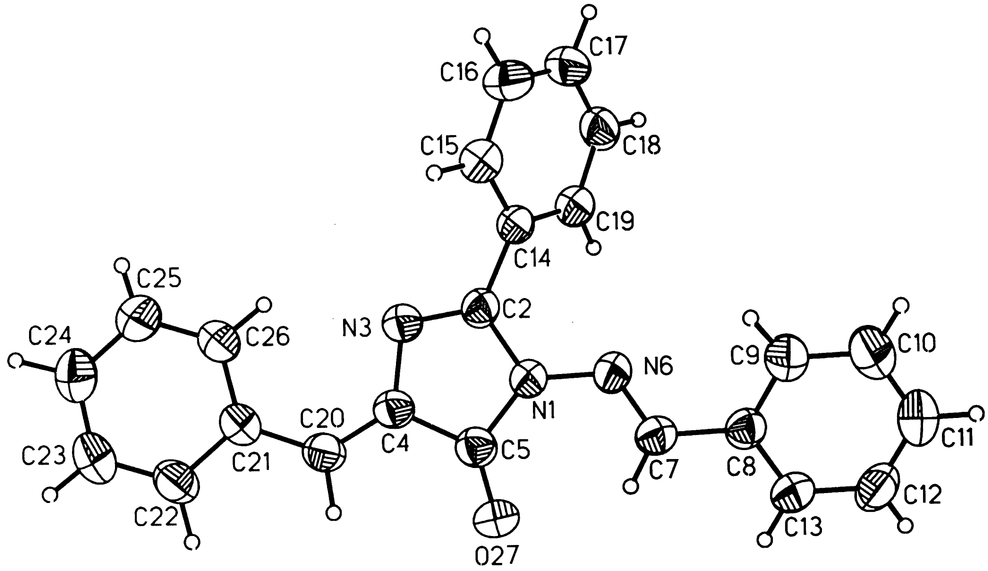


Fig. 1. Molecular structure of **2a**

C(16)-C(17)-C(18)-C(19) (plane 4). The dihedral angles between the rings amount to 5.4(5)° (plane 1–plane 2), 18.3 (5)° (plane 1–plane 3), 42.2(4)° (plane 1–plane 4), 22.9(6)° (plane 2–plane 3), 45.0(4)° (plane 2–plane 4) and 47.1(5)° (plane 3–plane 4). Possible intramolecular hydrogen bond interactions are presented in Table 5.

The presence of hydrogen bonds in **1f** and **2f** is also obvious from the ^{1}H NMR spectra. High values of the chemical shift of the OH hydrogen in **1f** and **2f** point to the existence of intramolecular hydrogen bonding between OH and the nitrogen atom of the *ortho*-CH=N group in both compounds even in *DMSO*. As to the IR spectra of **1f** and **2f**, the bands of intramolecularly bonded OH were not apparent; they are probably too broad to be measured. ^{1}H NMR data are summarized in Table 6.

In addition to the X-ray single crystal analysis, we performed semi-empirical quantum-chemical calculations of **2a** for reference purposes. The bond lengths and angles predicted by the PM3 method are compared with X-ray results in Table 3. The experimentally determined bond lengths are somewhat shorter (max. difference $<5.0\%$, average difference $= |0.56\%|$) than the theoretically calculated ones except for the C=O bond lengths (see Table 3) and the bond lengths and angles in the phenyl rings which are nearly identical. The maximum difference in bond angles amounts to 5.3%, the average difference in equal to $|0.49\%|$. Thus, we can conclude that semi-empirical calculations are in good agreement with X-ray results.

In the mass spectrum of **2a**, a peak at 352.4 $(M+1)^+$ was observed and isolated in the ionic trap. It was fragmented by a collision dissociation; a peak at 249.2 corresponds to a splitting of a neutral fragment of molecular formula C_7H_5N.

Table 3. Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($\text{Å}^2 \times 10^3$) for **2a**; U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor

Atom	*x*	*y*	*z*	U_{eq}
O (27)	2481 (3)	4011 (1)	1395 (1)	59 (1)
N (1)	2252 (3)	2978 (1)	2317 (1)	45 (1)
N (3)	5161 (3)	2197 (1	2152 (1)	45 (1)
N (6)	670 (3)	3232 (1)	2753 (1)	48 (1)
C (2)	3552 (4)	2293 (1)	2542 (1)	42 (1)
C (4)	5012 (4)	2842 (1)	1612 (1)	45 (1)
C (5)	3140 (4)	3378 (2)	1721 (1)	47 (1)
C (7)	−607 (4)	3814 (2)	2521 (1)	47 (1)
C (8)	−2267 (4)	4079 (2)	2988 (1)	46 (1)
C (9)	−2389 (6)	3777 (2)	3698 (2)	76 (1)
C (10)	−3984 (7)	4027 (3)	4116 (2)	99 (1)
C (11)	−5510 (6)	4582 (2)	3840 (2)	80 (1)
C (12)	−5402 (5)	4889 (2)	3140 (2)	67 (1)
C (13)	−3790 (4)	4644 (2)	2718 (2)	54 (1)
C (14)	3048 (4)	1716 (1)	3143 (1)	43 (1)
C (15)	4688 (4)	1414 (2)	3614 (1)	53 (1)
C (16)	4292 (5)	814 (2)	4147 (2)	66 (1)
C (17)	2292 (5)	511 (2)	4209 (2)	65 (1)
C (18)	650 (5)	807 (2)	3745 (2)	57 (1)
C (19)	1024 (4)	1416 (2)	3217 (2)	50 (1)
C (20)	6278 (4)	2963 (2)	1059 (1)	48 (1)
C (21)	8094 (4)	2480 (2)	862 (1)	46 (1)
C (22)	9280 (5)	2768 (2)	297 (2)	58 (1)
C (23)	11045 (5)	2339 (2)	99 (2)	67 (1)
C (24)	11640 (5)	1592 (2)	457 (2)	67 (1)
C (25)	10481 (5)	1290 (2)	1008 (2)	69 (1)
C (26)	8744 (5)	1718 (2)	1211 (2)	59 (1)

Attempts concerning the preparation of **2a–f** in dimethylformamide, acetanhydride, or in a mixture of acetic acid and hydrochloric acid were unsuccessful. Finally the syntheses were performed in a mixture of ethanol and acetic acid with satisfactory yields. The products are soluble in common organic solvents.

Experimental

Elemental analyses were performed on an EA 1108 instrument (Fisons). Melting points were determined on a Boetius block. IR spectra were recorded on an ATI Mattson Genesis Series FTIR spectrometer (KBr pellets). The mass spectrum was measured on an LCQ Finnigan MAT instrument. ^{1}H NMR spectra were recorded on a Bruker AMX 360 NMR spectrometer (**1a–f** in *DMSO*-d_6, $\delta = 2.55$ ppm; **2a–f** in $CDCl_3$, *HMDS* as internal standard, $\delta = 0.05$ ppm). The geometry optimization of **2a** was performed using the semi-empirical quantum-chemical PM3 module in the HyperChem

Table 4. Comparison of selected bond lengths (Å) and angles (deg) of **2a** as determined by single crystal X-ray analysis with values calculated by the semi-empirical quantum-chemical PM3 method

	X-Ray	PM3
O(27)–C(5)	1.212 (3)	1.213
N(1)–N(6)	1.376 (3)	1.403
N(1)–C(2)	1.396 (3)	1.460
N(1)–C(5)	1.400 (3)	1.473
N(3)–C(2)	1.288 (3)	1.315
N(3)–C(4)	1.405 (3)	1.443
N(6)–C(7)	1.271 (3)	1.300
C(2)–C(14)	1.467 (3)	1.466
C(4)–C(20)	1.339 (3)	1.343
C(4)–C(5)	1.477 (3)	1.489
C(7)–C(8)	1.454 (3)	1.467
C(20)–C(21)	1.441 (4)	1.456
N(6)–N(1)–C(2)	119.6 (2)	117.3
N(6)–N(1)–C(5)	131.3 (2)	124.3
C(2)–N(1)–C(5)	108.0 (2)	106.0
C(2)–N(3)–C(4)	106.3 (2)	110.3
C(7)–N(6)–N(1)	119.4 (2)	121.9
N(3)–C(2)–N(1)	113.8 (2)	111.4
N(3)–C(2)–C(14)	123.8 (2)	124.7
N(1)–C(2)–C(14)	122.4 (2)	123.8
C(20)–C(4)–N(3)	127.4 (2)	127.4
C(20)–C(4)–C(5)	123.1 (2)	125.6
N(3)–C(4)–C(5)	109.4 (2)	107.0
O(27)–C(5)–N(1)	126.7 (2)	124.0
O(27)–C(5)–C(4)	130.8 (2)	134.1
N(1)–C(5)–C(4)	102.5 (2)	104.8
N(6)–C(7)–C(8)	118.8 (2)	119.6
C(4)–C(20)–C(21)	129.8 (2)	127.6

5.0 molecular modeling program package [5]. The geometry optimization converged as follows: total energy: −86792.39 kcal/mol (−138.31 a.u.), binding energy: −5093.84 kcal/mol, heat of formation: 120.92 kcal/mol, criterion of RMS gradient: 0.008 kcal/(Å · mol).

X-Ray crystallography

Data were collected on a KUMA KM-4 kappa axis four-circles diffractometer. X-ray data for **2a**: yellow crystal (0.90×0.80×0.50 mm) obtained by recrystallization from ethanol, $C_{23}H_{17}N_3O$, $M_r =$ 351.40, monoclinic, $P2_1/c$, $Z = 4$, $a = 6.345(2)$, $b = 15.633(3)$, $c = 18.145(4)$ Å, $\beta = 93.72(2)^\circ$, $V = 1796.0)(7)$ Å^3, $T = 293$ K, $D_c = 1.300$ g.cm^{-3}, $F(000) = 736$, $\mu(\mathrm{Mo}K_\alpha) = 0.082$ mm^{-1}. The structure was solved by direct methods using SHELXS-96 [6] and refined anisotropically (313

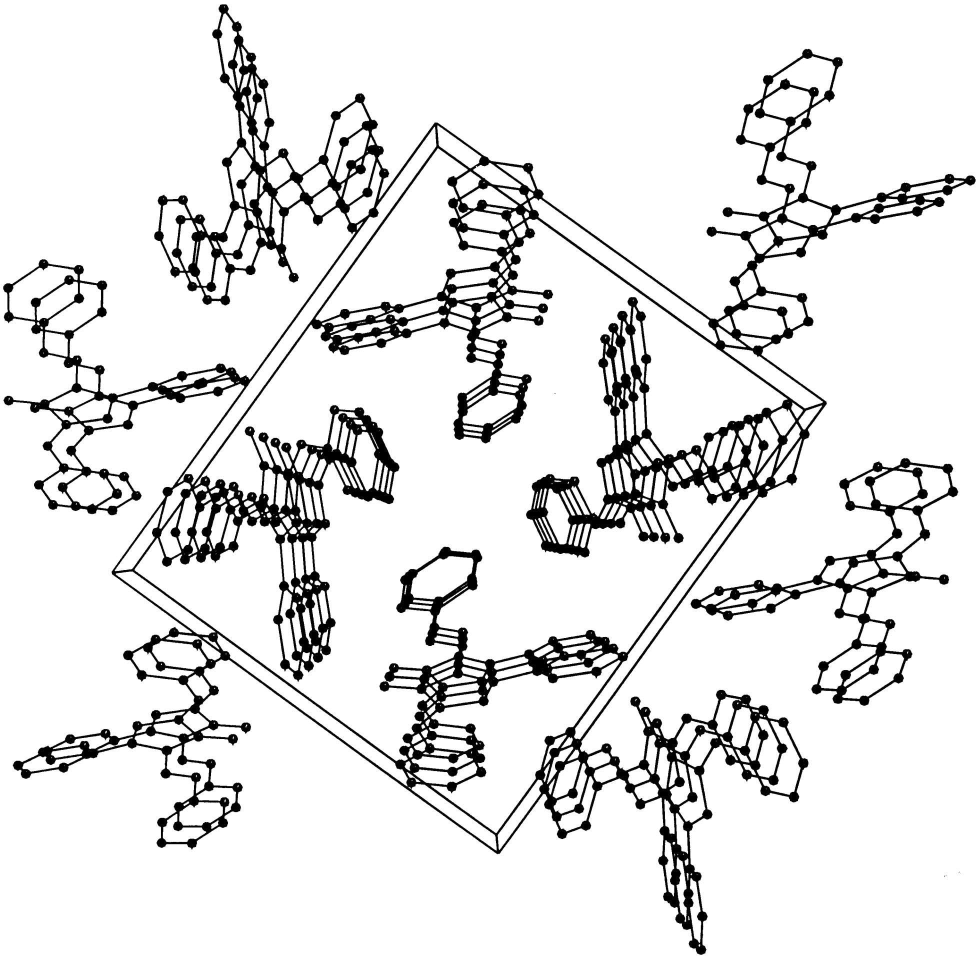


Fig. 2. Crystal packing of **2a**

Table 5. Possible intramolecular hydrogen interactions (distances in Å, angles in °) in **2a** (*D*: donor atom A: acceptor atom)

D–H···*A*	*D*–H	H···*A*	*D*–*A*	<*D*H*A*
C(7)–H(7)···O(27)	0.97(5)	2.3(3)	2.94(3)	123(3)
C(20)–H(20)···O(27)	1.01(9)	2.7(2)	3.00(3)	100(6)
C(9)–H(9)···N(6)	0.9(3)	2.4(2)	2.81(4)	103(5)
C(19)–H(19)···N(1)	0.9(2)	2.8(2)	3.06(1)	97(3)
C(19)–H(19)···N(6)	0.9(2)	2.58(8)	2.97(1)	105(4)
C(15)–H(15)···N(3)	1.0(3)	2.73(6)	2.96(1)	94(2)
C(26)–H(26)···N(3)	0.9(2)	2.3(2)	3.03(3)	131(4)

Table 6. ^{1}H NMR data for **1a–f** and **2a–f** (δ in ppm)

	OCH_3	Aromatic	Ph–CH=C	Ph–CH=N	–NH–
1a	–	7.22–8.01	7.22	8.48	10.17, 11.76
1b	3.81	7.00–8.11	7.22	8.47	10.09, 11.67
1c	3.60, 3.82	7.02–8.15	7.35	8.49	10.11, 11.65
1d	–	7.37–8.19	7.24	8.88	10.22, 12.14
1e	3.81, 3.85	7.00–8.11	7.22	8.41	10.01, 11.54
1f	–	6.95–8.09	7.25	8.66	10.23, 11.36, 12.06 (OH)
2a	–	7.40–8.27	7.26	9.64	–
2b	3.84	6.93–8.28	7.24	9.67	–
2c	3.92, 3.98	6.89–8.28	7.21	9.66	–
2d	–	7.23–8.27	7.28	10.20	–
2e	3.84, 3.86	6.93–8.27	7.23	9.54	–
2f	–	6.93–8.22	7.24	9.64	10.16(OH)

parameters) by the full-matrix least-squares procedure using SHELXL-96 [7]. All H-atom positions were found from differencial *Fourier* maps; their parameters were left free for refinement. 3027 refl. collected, 2939 independent refl.; $R_1 = 0.049$, $wR_2 = 0.121$ for $I > 2\sigma(I)$; $R_1 = 0.106$, $wR_2 = 0.151$ for all data, GOF = 0.995; extinction coeff. = 0.011(2). Largest differences in peak and hole are 0.231 and $-0.214\,\mathrm{e}\cdot\text{Å}^{-3}$, respectively. Additional material to the structure determination may be ordered from Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Federal Republic of Germany, referring to the deposition number CSD-408371.

Syntheses

1a–f

The hydrazide of 2-benzoylamino-3-phenylacrylic acid or 3-substituted phenylacrylic acid (10 mmol) was dissolved in 15 ml (**1a**, **1f**), 25 ml (**1b**, **1e**), or 40 ml (**1c**, **1d**) of concentrated acetic acid. The corresponding aldehyde (20 mmol) was added during stirring at room temperature. The reaction mixture was stirred for 10 min (in the case of **1d** for 1 min). The yellow solid formed was filtered off and washed with ethanol. White crystals were obtained after recrystallization from ethanol (**1a**) or ethanol/benzene (**1b–f**).

2a–f

Compounds **1a–f** (2.5 mmol) were refluxed for 3 h (**1a–1d**), 4 h (**1e**), and 10 h (**1f**) in a mixture of concentrated acetic acid and ethanol (45:90 ml for **1a**, **1c**, **1e**, 140:200 ml for **1b**, 90:45 ml for **1d**, and 90:90 ml for **1f**). The colour of the solution changed to yellow immediately. A yellow solid formed after concentrating and cooling the solution. In all cases, yellow crystals were obtained after recrystallization from ethanol (**2a**, **2b**, **2d**) or from a 1:1 mixture of ethanol/benzene (**2c**, **2e**, **2f**).

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