Reaction of diimines and azines with diphenylcyclopropenone

Mohsen Abdel-Motaal Gomaa

Chemistry Department, Faculty of Science, Minia University, 61519 El-Minia, Egypt

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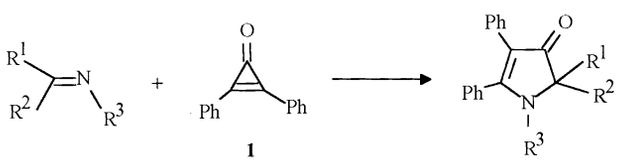
1-Cyclohexyl-2-cyclohexylaminomethylene-4,5-diphenyl-1,2-dihydropyrrol-3-one **4a** and 1-aryl-2-arylamino-methylene-4,5-diphenyl-1,2-dihydropyrrol-3-ones **4b**,**c** as the *E*-form are synthesized by the reaction between *N*,*N*′-dicyclohexylethane-1,2-diylidenediamine **2a** and *N*,*N*′-diarylethane-1,2-diylidenediamines **2b**,**c** with diphenylcyclopropenone **1** through a formal [2 + 3] cycloaddition reaction. The structure assignment of **4a** is confirmed on the basis of an X-ray crystal-structure determination. Similarly, diaryl azines **8a**–**c** react with **1** through a formal [2 + 3] cycloaddition reaction to give the non-isolable product Δ^4-pyrrolin-3-ones **10a**–**c** which undergo oxidative rearrangement to afford ultimately the indenone derivatives **9a**–**c**.

Introduction

The fascinating chemistry of cyclopropenones has attracted the attention of numerous researchers over the past three decades,[1,2] with special emphasis on the behaviour of diphenylcyclopropenone **1**.[3] Diphenylcyclopropenone has been found to react with a wide range of imines, amidines, guanidines and other compounds containing the C=N moiety to form azacyclopentenones (pyrrolinones) *via* a formal [2 + 3] cycloaddition reaction (Fig. 1).[4–9] Similarly, 2-amino-1-azetines



1

R^1 = H, Ph, NR_2; R^2 = Ar, NR_2; R^3 = H, Alkyl

Fig. 1

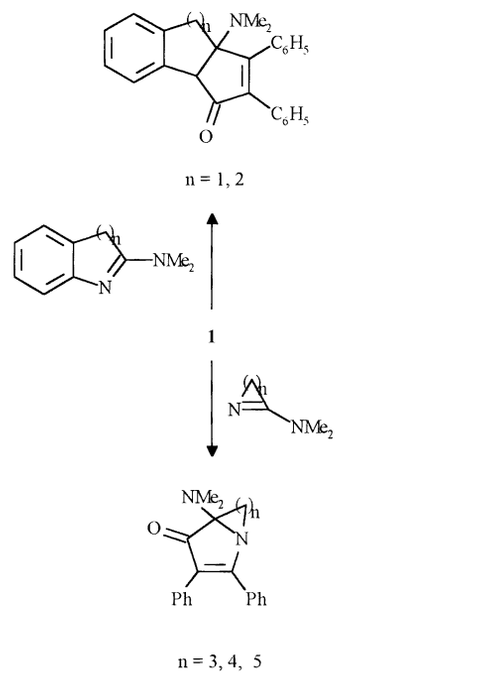
reacted with **1** to afford azeto[1,2-*a*]pyrroles.[10] Diphenylcyclopropenone **1** was used to synthesize the annelated heterocycles by its reaction with cyclic amidines to give rise to bi- and tricyclic pyrrolinones (Fig. 2).[11] Moreover, thiazolo[3,2-*a*]pyrimidones were synthesized from the reaction of diphenylcyclopropenone **1** with 2-aminothiazoles.[12] Similarly, tetrasubstituted 4(3*H*)-pyridones were produced from the reaction of **1** with 3-amino-2,2-dimethyl-2*H*-azirines (Fig. 3).[13]

As part of our programme to develop efficient procedures for the synthesis of heterocyclic compounds *via* the nucleophilic reactions of an amidine group (–HN–CR=N–) with π-deficient compounds[14–17] we have synthesized trisubstituted pyridin-2(1*H*)-ones from the reaction of N^1,N^2-diarylacetamidines with π-deficient dibenzoylacetylene.[18] Recently we also prepared 1,4,5,6-tetrahydropyridines by reaction of N^1,N^2-diarylacetamidines with benzylidenemalononitriles.[19]

Results and discussion

Herein I report the reaction of the diimines **2a**–**c** and the aromatic azines **8a**–**c** with the selected π-deficient diphenylcyclopropenone **1**.

First we undertook to investigate the reaction of *N*,*N*′-dicyclohexyl- **2a** and diaryl-ethane-1,2-diylidenediamines **2b**,**c** with diphenylcyclopropenone **1**. Thus diimines **2a**–**c** and the

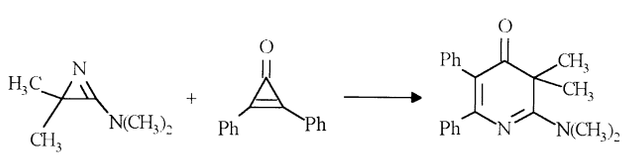


n = 1, 2

1

n = 3, 4, 5

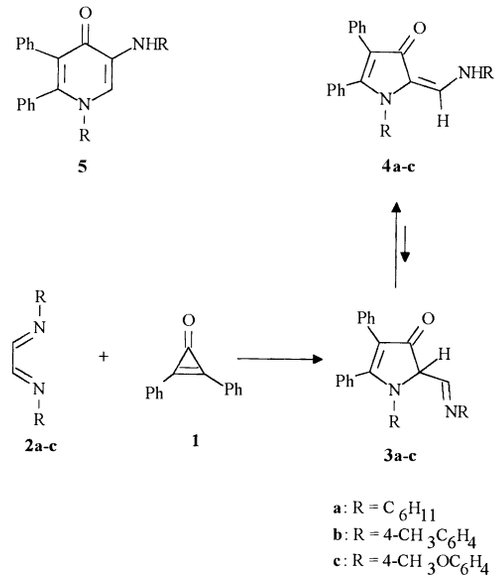
Fig. 2



1

Fig. 3

cyclopropenone **1** were heated in ethanol for 2–5 h to give the pyrrolinone derivatives **4a**–**c** in 42–67% yield (Scheme 1). ^{13}C NMR spectra showed a characteristic peak at δ_C 175.96–177.33 for the carbonyl groups, and the aliphatic carbon atoms (of **4a**) of the cyclohexyl rings appeared as two peaks at δ_C 56.05 and 56.33 for the cyclohexyl tertiary carbon atoms (CH) adjacent to the nitrogen atoms. A ^{13}C DEPT spectrum of **4a** showed six peaks with a negative amplitude that were assigned for the cyclohexyl-CH_2 carbon atoms. ^{1}H NMR spectroscopy showed signals between δ 7.42–7.98 that were assigned to the NH group. IR spectroscopy showed absorptions at 3380–3410 cm^{-1}



Scheme 1

for the amino groups and at 1645–1650 cm^{-1} for the C=O groups for structures **4**. We expected to obtain the structures **3a**–**c** but, in the ^1H NMR spectra, the H-2 methine hydrogen atom was not observed. To distinguish between arrangements of the tautomeric structure of **3a**–**c**, *i.e.* **4a**–**c**, and an alternative, *e.g.*, **5** an X-ray crystal-structure analysis of **4a** was carried out (Fig. 4). It clearly demonstrates the five-membered

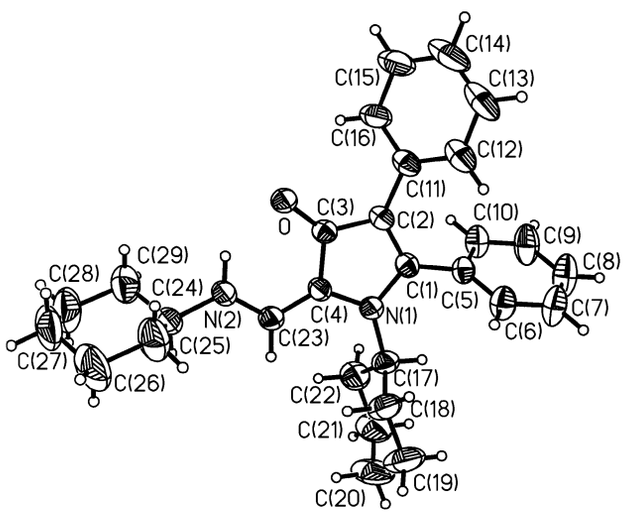


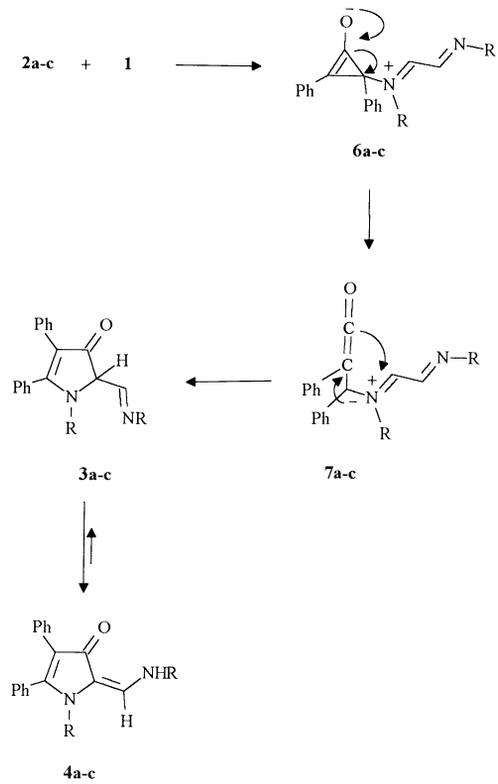
Fig. 4 Molecular structure of **4a** in the crystal phase (the crystallographic numbering does not reflect the systematic numbering).

structure and shows that the adduct is a tautomer (enamine-like structure) of **3a**–**c** in the *E*-configuration.

It is clear that the pyrrolinone structures **3a**–**c** tautomerize to the enaminone structures **4a**–**c** which are more stable, having extended conjugation and hydrogen bonding.

Formation of Δ^4-pyrrolinones **4a**–**c** may be rationalized as an initial attack of one of the imino nitrogen atoms of **2a**–**c** on the electrophilic carbon C-2 or C-3 of cyclopropenone **1** giving the immoniumbetaine **6a**–**c**, followed by ring opening to afford the ketene intermediate **7a**–**c**. Subsequent cyclization by attack of the ketene onto the iminium function (electrocyclization) leads to imines **3a**–**c** and hence to isomeric enaminones **4a**–**c** (Scheme 2).

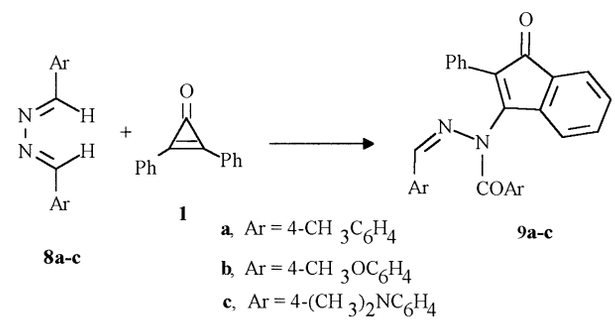
The reaction of dienophilic compounds with diaryl azines represents a valuable enlargement to synthetic heterocyclic chemistry.[20,21] Aldazines derived from aromatic aldehydes undergo the so-called criss-cross addition with two mol equiv.



Scheme 2

of dienophilic compounds to yield 1,5-diazabicyclo[3.3.0]-octane derivatives (derivatives of pyrazolo[1,2-*a*]pyrazoles), while the addition of equimolar amounts of the same reagents leads to the formation of the corresponding azomethine imines and pyrazoles. Recently, aromatic azines have been shown to react with dibenzoylacetylene to afford unexpected [4 + 2] cycloadducts such as 4,5-dibenzoyl-3,6-diarylpyridazines.[22]

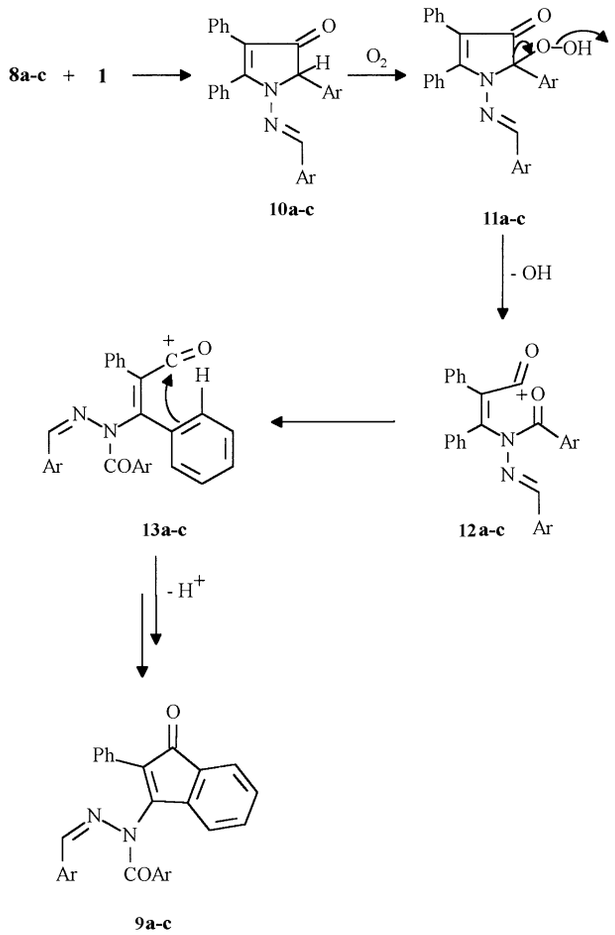
From the above findings it may be appropriate to investigate the reactivity of diarylaldazines **8a**–**c** towards the diphenylcyclopropenone **1** to compare their reactivity with **2a**–**c**. Thus two mol equivalents of **1** together with one mol equivalent of an aldazine **8a**–**c** were kept in ethanol at reflux for 12 h to afford solid inden-1-one derivatives **9a**–**c** (Scheme 3). The structure of



Scheme 3

products **9a**–**c** was assigned on the basis of their spectral data. ^1H NMR spectra showed only one imine-proton (CH=N), at δ 7.97–8.03. ^{13}C NMR spectra showed a signal between δ_C 195.80–195.94 that was assigned for the carbonyl group of the indenone system, and another signal at higher field between δ_C 170.44 and 170.72 was assigned to the amidic carbonyl group, in addition to a signal between δ_C 144.22–145.28 that was attributed to the imine carbon atom.

The formation of products **9a**–**c** was rationalized as a formal [2 + 3] cycloaddition reaction between **1** and **8a**–**c** to give the Δ^4-pyrrolin-3-ones **10a**–**c**, which undergo an oxidative rearrangement to afford ultimately the indenone derivatives **9a**–



Scheme 4

c *via* the intermediates **11a**–**c**–**13a**–**c** (Scheme 4). Eicher *et al.* have isolated indenones as a result of oxidative processes during the reaction of benzylidene azines with **1**.[23] Thus the aldazines **8a**–**c** react with the dienophiles like **1** as do imines *via* a [2 + 3] cycloaddition reaction but not as azines *via* the criss-cross addition reaction.

Conclusions

The present investigation clearly indicates that diaryl azines react with diphenylcyclopropenone through a formal [3 + 2] cycloaddition reaction giving the non-isolable Δ^4-pyrrolin-3-ones **10a**–**c** products, which undergo oxidative processes to afford ultimately the indenone derivatives **9a**–**c**. Similarly, diimines react with diphenylcyclopropenone to afford the Δ^4-pyrrolin-3-one derivatives which are more stable against air oxidation due to high conjugation.

Experimental

Uncorrected melting points were determined on a Griffin & George apparatus. Elemental analyses were carried out by the Microanalysis Center at Cairo University. IR spectra (KBr) were recorded on a Shimadzu 470 spectrophotometer. 400 MHz ^{1}H NMR and 100 MHz ^{13}C NMR spectra were observed on a Bruker AM 400 spectrometer. Mass spectra (70 eV, electron-impact mode) were recorded on a JEOL JMS600 instrument. Preparative thin-layer chromatography (PLC) used air-dried 1.0 mm thick layers of slurry-applied silica gel Merck PF_{254} on 48 cm wide and 20 cm high glass plates and toluene–ethyl acetate (2 : 1) as developing solvent. Zones were detected by the colour or by quenching of indicator fluorescence upon exposure to 254 nm light and eluted with acetone.

Starting materials

N,*N*′-Diarylethane-1,2-diylidenediamines **2b**,**c** and *N*,*N*′-dicyclohexylethane-1,2-diylidenediamine **2a**[24,25] and diaryl azines **8a**–**c**[26] were prepared as reported.

Reaction of *N*,*N*′-dicyclohexylethane-1,2-diylidenediamine 2a and *N*,*N*′-diarylethane-1,2-diylidenediamines 2b,c with diphenylcyclopropenone 1 (general procedure)

A solution of **1** (206 mg, 1.0 mmol) in ethanol (10 cm^3) was added to solutions of a diimine **2a**–**c** (1.0 mmol) in ethanol (20 cm^3). The mixture was heated to reflux temperature for 2–5 h. After this period, orange crystals of the corresponding enaminone **4a**–**c** precipitated, which were filtered off and recrystallized from ethanol and identified as follows.

(*E*)-1-Cyclohexyl-2-cyclohexylaminomethylene-4,5-diphenyl-1,2-dihydropyrrol-3-one [(*E*)-4a]. Yield 180 mg (42%), mp 259–260 °C as orange crystals (from ethanol); ^{1}H NMR (d_6-DMSO) δ 0.95–1.92 (m, 20 H, cyclohexyl-CH_2), 3.52–3.54 (m, 2 H, cyclohexyl-CH), 6.99 (s, 1 H, CH), several multiplets at 7.03, 7.13, 7.27 and 7.27 (10 H, ArH), 7.98 (s, 1 H, NH); ^{13}C NMR (d_6-DMSO) δ 24.10, 24.35, 24.97, 26.10, 31.63, 33.97 (cyclohexyl-CH_2), 56.05 and 56.33 (cyclohexyl-CH), 111.42, 114.05, 124.04, 127.34, 128.24, 127.66, 128.96, 129.64 (all Ar–CH and vinylic CH), 129.18, 132.56, 134.20, 140.99, 148.82, 176.39; IR (KBr) 3380 (NH), 1645 (CO) cm^{-1}; MS (70 eV) *m*/*z* (%) 426 (M^+, 100), 425 (15), 409 (5), 383 (7), 369 (5), 344 (51), 327 (57), 261 (19), 248 (14), 178 (15), 55 (24), 41 (14), [Calc. for $C_{29}H_{34}N_2O$ (426.6): C, 81.65; H, 8.03; N, 6.57. Found: C, 81.50; H, 7.95; N, 6.51%].

(*E*)-1-(4-Methylphenyl)-2-(4-methylphenylaminomethylene)-4,5-diphenyl-1,2-dihydropyrrol-3-one [(*E*)-4b]. Yield 264 mg (60%), mp 208–210 °C as orange crystals (from ethanol); ^{1}H NMR (d_6-DMSO) δ 2.22 (s, 3 H, CH_3), 2.25 (s, 3 H, CH_3), 6.95 (s, 1 H, CH), several multiplets at 7.07, 7.13, 7.17 and 7.23 (18 H, ArH), 7.46 (s, 1 H, NH); ^{13}C NMR (d_6-DMSO) δ 20.33, 20.63 (2 × CH_3), 116.40, 125.18, 127.72, 128.39, 128.46, 129.06, 129.92, 130.14, 130.28 and 131.0 (all Ar–CH and vinylic CH), 113.39, 120.86, 128.5, 131.15, 132.71, 134.20, 137.17, 137.95, 152.14, 177.33; IR (KBr) 3400 (NH), 1650 (CO) cm^{-1}; MS (70 eV) *m*/*z* (%) 442 (M^+, 100), 336 (7), 221 (6), 212 (4), 178 (5), 118 (9), 91 (11), 65 (4) [Calc. for $C_{31}H_{26}N_2O$ (442.6): C, 84.13; H, 5.92; N, 6.33. Found: C, 84.31; H, 5.83; N, 6.30%].

(*E*)-1-(4-Methoxyphenyl)-2-(4-methoxyphenylaminomethylene)-4,5-diphenyl-1,2-dihydropyrrol-3-one [(*E*)-4c]. Yield 315 mg (67%), mp 170–172 °C as orange crystals (from ethanol); ^{1}H NMR (d_6-DMSO) δ 3.70 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 6.68 (s, 1 H, CH), several multiplets at 6.89, 7.0, 7.10, 7.18 and 7.25 (18 H, ArH), 7.42 (s, 1 H, NH); ^{13}C NMR (d_6-DMSO) δ 55.19, 55.30 (2 × OCH_3), 114.31, 114.58, 114.97, 117.84, 123.22, 124.94, 127.57, 128.24, 128.80, 129.92, 130.04, and 131.94 (all Ar–CH and vinylic CH), 112.81, 120.71, 129.09, 130.94, 132.92, 133.82, 151.12, 157.51, 158.25, 175.96; IR (KBr) 3410 (NH), 1650 (CO) cm^{-1}; MS (70 eV) *m*/*z* (%) 474 (M^+, 100), 458 (6), 352 (7), 237 (4), 178 (5), 134 (6), 123 (3), 77 (5) [Calc. for $C_{31}H_{26}N_2O_3$ (474.6): C, 78.46; H, 5.52; N, 5.90. Found: C, 78.62; H, 5.40; N, 5.81%].

Reaction of diarylaldazines 8a–c with diphenylcyclopropenone 1 (general procedure)

A solution of **1** (206 mg, 1.0 mmol) in ethanol (10 cm^3) was added to a solution of an aldazines **8a**–**c** (0.5 mmol) in ethanol (20 cm^3) or toluene (30 cm^3). The mixture was heated to reflux temperature for 12 h before being concentrated and the residue was subjected to PLC using toluene–ethyl acetate (2 : 1) as the developing solvent to give one or two main zones. The faster

moving one contained **9a**, **9b** or **9c** respectively, while the more slowly moving one contained the unchanged cyclopropenone **1**. The zonal components were extracted, crystallized, and identified as follows.

3-[1′-(4-Methylbenzoyl)-2′-(4-methylbenzylidene)hydrazino]-2-phenylinden-1-one 9a. Yield 120 mg (52%), mp 118–119 °C as yellow crystals (from cyclohexane); ^{1}H NMR ($CDCl_3$) δ 2.34 (s, 3 H, CH_3), 2.41 (s, 3 H, CH_3), several multiplets at 7.11, 7.16, 7.24, 7.49, 7.53 and 7.61 (17 H, ArH), 8.03 (s, 1 H, CH=N); ^{13}C NMR ($CDCl_3$) δ 21.12, 21.35, 91.75, 108.75, 125.59, 126.07, 126.87, 127.84, 127.91, 129.07, 129.14, 129.36, 129.81, 130.52, 130.60, 131.60, 132.17, 138.69, 139.51, 144.27, 170.65, 195.96; IR (KBr) 1690 (CO), 1645 (CO) cm^{-1}; MS (70 eV) *m*/*z* (%) 457 (1), 456 (M^+, 48), 440 (14), 429 (4), 412 (2), 341 (72), 337 (58), 325 (44), 310 (65), 222 (68), 191 (28), 177 (82), 164 (18), 120 (37), 118 (100), 105 (37), 91 (87) [Calc. for $C_{31}H_{24}N_2O_2$ (456.6): C, 81.55; H, 5.30; N, 6.14. Found: C, 81.42; H, 5.18; N, 6.10%].

3-[1′-(4-Methoxybenzoyl)-2′-(4-methoxybenzylidene)-hydrazino]-2-phenylinden-1-one 9b. Yield 118 mg (48%), mp 85–89 °C as yellow crystals (from cyclohexane); ^{1}H NMR ($CDCl_3$) δ 3.75 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), several multiplets at 6.75, 6.88, 7.09, 7.11, 7.24, 7.35, 7.49, 7.53, 7.58 and 7.85 (17 H, ArH), 7.99 (s, 1 H, CH=N); ^{13}C NMR ($CDCl_3$) δ 55.26, 55.27, 91.52, 108.55, 113.89, 114.54, 126.15, 126.48, 127.12, 127.63, 127.92, 127.99, 128.43, 129.37, 130.58, 131.53, 132.73, 144.22, 158.96, 160.67, 170.72, 195.80; IR (KBr) 1690 (CO), 1645 (CO) cm^{-1}; MS (70 eV) *m*/*z* (%) 489 (1), 488 (M^+, 20), 467 (14), 354 (18), 340 (44), 326 (65), 223 (68), 209 (12), 196 (20), 152 (82), 150 (18), 137 (100), 123 (70), 121 (48), 105 (33), 91 (77) [Calc. for $C_{31}H_{24}N_2O_4$ (488.6): C, 76.21; H, 4.95; N, 5.74. Found: C, 76.11; H, 4.89; N, 5.63%].

3-{1′-[4-(Dimethylamino)benzoyl]-2′-[4-(dimethylamino)-benzylidene]hydrazino}-2-phenylinden-1-one 9c. Yield 130 mg (50%), mp 176–178 °C as orange crystals (from cyclohexane); ^{1}H NMR ($CDCl_3$) δ 2.91 (s, 6H, NCH_3), 2.92 (s, 6H, NCH_3), several multiplets at 6.52, 6.55, 6.67, 6.69, 7.11, 7.22, 7.26, 7.35, 7.44, 7.58, 7.60 (17 H, ArH), 7.97 (s, 1 H, CH=N); ^{13}C NMR ($CDCl_3$) δ 40.21, 40.33 (4 × NCH_3), 91.88, 107.81, 111.67, 112.70, 121.70, 123.07, 125.81, 126.68, 127.83, 127.88, 128.34, 129.08, 129.86, 130.30, 130.68, 131.02, 145.28, 150.62, 151.23, 170.44, 195.94; IR (KBr) 1690 (CO), 1645 (CO) cm^{-1}; MS (70 eV) *m*/*z* (%) 514 (M^+, 20), 499 (2), 484 (2), 471 (8), 425 (11), 365 (80), 338 (65), 322 (18), 294 (18), 282 (11), 264 (11), 263 (27), 193 (13), 178 (25), 164 (32), 149 (100), 134 (55), 121 (32), 105 (50), 91 (17), 84 (54), 77 (49) [Calc. for $C_{33}H_{30}N_4O_2$ (514.6): C, 77.02; H, 5.88; N, 10.89. Found: C, 76.91; H, 5.79; N, 10.73%].

Crystal structure determination of compound 4a

Crystal data. $C_{29}H_{34}N_2O$, M = 426.60. Trigonal, a = 32.814(2), c = 12.309(1) Å, α = 90.00°, T = 293 K, V = 11 478.1(14) Å^3, Mo-Kα radiation (λ = 0.710 73 Å), space group R-3, Z = 18, D_x = 1.111 Mg m^{-3}. Dark orange prisms. Crystal dimensions: 0.50 × 0.43 × 0.25 mm, μ(Mo-Kα) = 0.067 mm^{-1}, F(000) = 4140.

Data collection and processing. Nonius-Kappa CCD diffractometer, graphite-monochromator Mo-Kα (radiation; 6293 reflections measured (θ = 24.18°), 4039 unique) merging at R = 0.0317, linear and approx. isotropic crystal decay, *ca.* 23% corrected during processing. Refinements on F^2, $R1$ = 0.0769 for 2411 reflections with $I > 2\sigma(I)$, 291 variables, $wR2$ = 0.2018 for all unique data, SHELXL program package.

Atomic coordinates, bond lengths and angles, and parameters have been deposited at the Cambridge Crystallographic Data Centre.†

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† CCDC reference number(s) 170858. See http://www.rsc.org/suppdata/p1/b1/b109711n/ for crystallographic files in .cif or other electronic format.

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