One-Pot Synthesis of Pyrrolo[2,1-*a*]isoquinoline-1-carboxamide Derivatives via a Four-Component Reaction

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Received 9 July 2007; revised 20 November 2007

Abstract: An effective route to functionalized 1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide derivatives is described. This involves reaction of *N*-alkyl-3-oxobutanamides, which result from the addition of amines to diketene, and dibenzoylacetylene in the presence of isoquinoline. The reactive 1:1 intermediate obtained from the addition of isoquinoline to dibenzoylacetylene is trapped by OH acids such as *N*-alkyl-3-oxobutanamides to produce the pyrrolo[2,1-*a*]isoquinoline-1-carboxamide derivatives.

Key words: amine, diketene, dibenzoylacetylene, isoquinoline, multicomponent reaction, pyrroloisoquinoline

Recently, multicomponent condensation reactions have become one of the most powerful methods for the synthesis of small molecule libraries, due to the fact that products are formed in a single step by simultaneous reaction of several reagents and that the molecular diversity required for such combinatorial libraries can be achieved by simply varying each component.[1]

Pyrrolidinoisoquinoline alkaloids are abundant in plant products, and many exhibit interesting biological activity.[2] Accordingly, much attention has focused on the development of general approaches to these alkaloids.[3] Syntheses of the pyrrolidinoisoquinoline ring subunit have also been described in the literature.[4] Boekelheide and Godfrey synthesized racemic pyrrolidinoisoquinoline using the Bischler–Napieralski reaction of 2-oxo-1-(2-phenylethyl)pyrroline.[4e] Optically active (+)-pyrrolidinoisoquinoline was first obtained by the degradative reduction of the alkaloid norsecurinine during structural elucidation.[4b] However, it is surprising that only a few examples of the asymmetric synthesis of the pyrrolidinoisoquinoline skeleton have been demonstrated.[5]

We wish to report a simple, one-pot, four-component reaction between amine, diketene and dibenzoylacetylene in the presence of isoquinoline leading to 1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide derivatives **2**.

Reaction of the *N*-alkyl-3-oxobutanamides **3**, which are derived from the addition of a primary amine **1** to diketene, with dibenzoylacetylene in the presence of isoquinoline proceeds in dichloromethane at ambient temperature, to produce the 1-acetyl-N^1-alkyl-2-hydroxy-3-[(*E*)-2-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide derivatives **2** (Table 1).

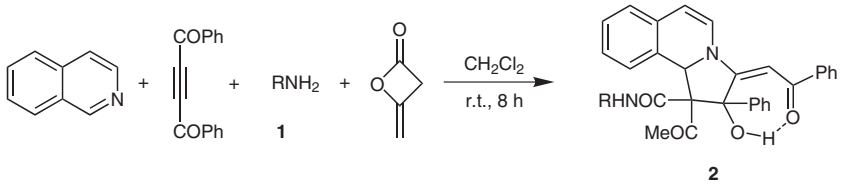
The structure of compounds **2a**–**g** was deduced from their elemental analyses, IR spectra, and high-field ^{1}H and ^{13}C NMR spectra. The mass spectrum of **2a** displayed the molecular ion peak at *m*/*z* 520, which is consistent with the 1:1:1:1 adduct of *sec*-butylamine, diketene, isoquinoline and dibenzoylacetylene. The ^{1}H NMR spectrum of **2a** exhibited nine signals readily recognized as arising from three methyl groups (δ = 0.79, d, $^3J_{HH}$ = 6.6 Hz; δ = 1.02, t, $^3J_{HH}$ = 7.6 Hz; δ = 2.10, s), one methylene group (δ = 1.56, m), two methine groups (δ = 3.66, m; δ = 6.44, s), and vinylic CH (δ = 6.16, s), NH (δ = 6.26, t, $^3J_{HH}$ = 5.5 Hz) and OH (δ = 9.56, s) protons, while the aromatic moieties gave rise to characteristic signals in the aromatic region of the spectrum. The proton-decoupled ^{13}C NMR spectrum of **2a** showed 29 distinct resonances, in agreement with the pyrrolidinoisoquinoline structure. Partial assignment of these resonances is given in the experimental section. The ^{1}H and ^{13}C NMR spectra of compounds **2b**–**g** are similar to those of **2a**, except for the amine moiety which exhibits characteristic signals with appropriate chemical shifts (see experimental).

Although the mechanism of the reaction between isoquinoline and dibenzoylacetylene in the presence of *N*-alkyl-3-oxobutanamides **3**, which are derived from the addition of primary amines to diketene, has not yet been established in an experimental manner, a possible explanation is proposed in Scheme 1. Based on the well-established chemistry of isoquinoline as a nucleophile,[6–10] it is reasonable to assume that **2** results from initial addition of isoquinoline to dibenzoylacetylene and subsequent protonation of the 1:1 adduct **4** by the *N*-alkyl-3-oxobutanamide **3** as OH acid. Then, the positively charged ion **5** might be attacked by the conjugate base of the OH acid to form intermediate **6**, which in turn is converted into enol **7**. Finally, cyclization of enol **7** leads to compound **2**.

In conclusion, the present method carries the advantages that not only is the reaction performed under neutral conditions, but also the substances can be mixed without any activation or modification. The simplicity of the present procedure makes it an interesting alternative to complex multistep approaches.[11,12]

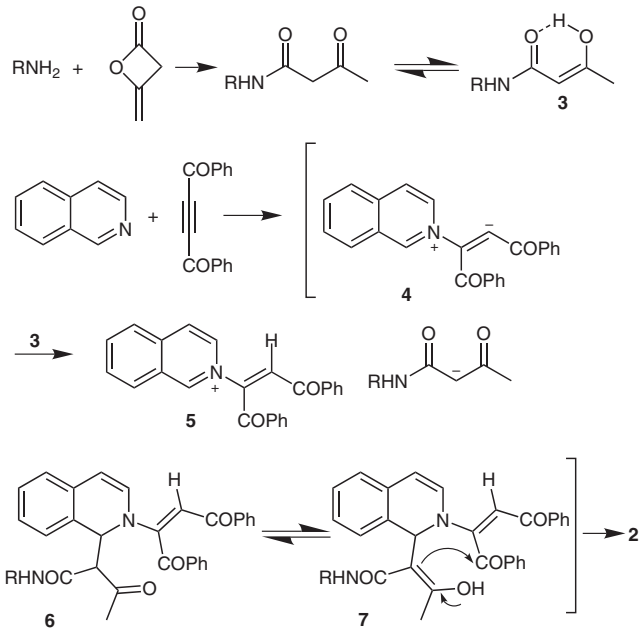
SYNTHESIS 2008, No. 3, pp 0429–0432
Advanced online publication: 10.01.2008
DOI: 10.1055/s-2008-1032033; Art ID: Z16407SS

Table 1 Reaction of Amine **1**, Diketene and Dibenzoylacetylene in the Presence of Isoquinoline



2

1,2	R	Yield (%) of **2**
a	*s*-Bu	78
b	*i*-Bu	80
c	*t*-Bu	85
d	allyl	85
e	Bn	80
f	2-$ClC_6H_4CH_2$	84
g	$CH_3(CH_2)_3CH(CH_2CH_3)CH_2$	85



Scheme 1

Amines and diketene were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Dibenzoylacetylene was prepared according to a literature procedure.[13,14] Melting points were measured on an Electrothermal 9100 apparatus. Elemental analyses for C, H and N were performed using a Heraeus CHN-O-Rapid analyzer. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 20 eV. ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$ solution) with a Bruker DRX-500 Avance spectrometer at 500.1 and 125.7 MHz, respectively. IR spectra were recorded on a Shimadzu IR-460 spectrometer. Chromatography columns were prepared from Merck silica gel, 230–240 mesh.

1-Acetyl-*N*^{1}-(*sec*-butyl)-2-hydroxy-3-[(*E*)-2-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide (2a); Typical Procedure

To a magnetically stirred soln of *s*-$BuNH_2$ (0.073 g, 1 mmol) and diketene (0.084 g, 1 mmol) in anhyd CH_2Cl_2 (5 mL) was added, after 5 h, isoquinoline (0.129 g, 1 mmol), and finally a soln of dibenzoylacetylene (0.234 g, 1 mmol) in anhyd CH_2Cl_2 (3 mL) was added dropwise at r.t. over 10 min. The reaction mixture was then allowed to stir for 2 h. The solvent was removed under reduced pressure and the residue was subjected to silica gel column chromatography (hexane–EtOAc, 7:1). The separated pyrroloisoquinoline was recrystallized (EtOH).

Yield: 0.41 g (78%); yellow crystals; mp 180–182 °C (dec).

IR (KBr): 3390 (OH), 3040 (NH), 1740 (COMe), 1656 (COPh), 1610 (CONH), 1594 (C=C), 1565 and 1502 cm^{-1} (Ar).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.79 (d, *J* = 6.6 Hz, 3 H, $CHCH_3$), 1.02 (t, *J* = 7.6 Hz, 3 H, CH_2CH_3), 1.56 (m, 2 H, CH_2CH_3), 2.10 (s, 3 H, CH_3), 3.66 (m, 1 H, C*H*NH), 6.16 (s, 1 H, NC=CH), 6.26 (t, *J* = 5.5 Hz, 1 H, NH), 6.36 (d, *J* = 7.6 Hz, 1 H, C^{6}H), 6.44 (s, 1 H, C^{10b}H), 6.90 (d, *J* = 7.5 Hz, 1 H, C^{5}H), 7.04 (t, *J* = 7.2 Hz, 1 H, CH of isoquinoline), 7.15 (t, *J* = 7.3 Hz, 2 H, 2 × CH of isoquinoline), 7.23 (t, *J* = 7.4 Hz, 1 H, CH of isoquinoline), 7.26 (t, *J* = 7.4 Hz, 1 H, CH of Ph), 7.31 (t, *J* = 7.4 Hz, 2 H, 2 × CH of Ph), 7.37 (t, *J* = 7.6 Hz, 2 H, 2 × CH of Ph), 7.46 (t, *J* = 7.1 Hz, 1 H, CH of Ph), 7.53 (d, *J* = 7.2 Hz, 2 H, 2 × CH of Ph), 7.82 (d, *J* = 7.9 Hz, 2 H, 2 × CH of Ph), 9.56 (s, 1 H, OH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 10.35 (CH_2CH_3), 19.55 ($CHCH_3$), 31.00 (CH_3), 31.04 (CH_2CH_3), 47.60 (CHNH), 64.51 (C^{10b}), 77.26 (C^1), 85.58 (COH), 89.21 (NC=*C*H), 116.74 (C^{6}H), 121.25 (C^{5}H), 125.74 (CH of Ph), 125.82 (CH of isoquinoline), 126.10 (2 × CH of Ph), 127.84 (2 × CH of Ph), 128.11 (2 × CH of Ph), 128.25 (CH of isoquinoline), 128.30 (2 × CH of Ph), 128.55 (CH of isoquinoline), 129.13 (CH of isoquinoline), 129.87 (C^{10a}), 130.50 (C^{6a}), 131.93 (CH of Ph), 138.29 (C_{ipso}COH), 139.79 (C_{ipso}-CO), 165.30 (N*C*=CH), 166.99 (CONH), 188.86 (*C*OPh), 202.20 (*C*OMe).

MS: *m*/*z* (%) = 520 (2) [M$^+$], 421 (8), 368 (85), 364 (22), 360 (80), 316 (22), 298 (12), 185 (15), 154 (12), 130 (50), 105 (100), 77 (90), 58 (9), 43 (47).

Anal. Calcd for $C_{33}H_{32}N_2O_4$ (520.62): C, 76.13; H, 6.20; N, 5.38. Found: C, 76.31; H, 6.40; N, 5.49.

1-Acetyl-2-hydroxy-*N*^{1}-isobutyl-3-[(*E*)-2-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide (2b)

Yield: 0.42 g (80%); yellow crystals; mp 163–165 °C (dec).

IR (KBr): 3395 (OH), 3040 (NH), 1699 (COMe), 1659 (COPh), 1620 (CONH), 1593 (C=C), 1564 and 1501 cm^{-1} (Ar).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.92 (d, *J* = 6.7 Hz, 3 H, CH_3 of *i*-Bu), 0.97 (d, *J* = 6.7 Hz, 3 H, CH_3 of *i*-Bu), 1.77 (sept, *J* = 6.7 Hz, 1 H, CH of *i*-Bu), 2.11 (s, 3 H, CH_3), 2.61 (m, 1 H, C*H*$_2$NH), 3.09 (m, 1 H, C*H*$_2$NH), 6.20 (s, 1 H, NC=CH), 6.35 (d, *J* = 7.6 Hz, 1 H, C^{6}H), 6.44 (s, 1 H, C^{10b}H), 6.49 (t, *J* = 6.0 Hz, 1 H, NH), 6.92 (d, *J* = 7.6 Hz, 1 H, C^{5}H), 7.00 (d, *J* = 7.5 Hz, 1 H, CH of isoquinoline), 7.15 (t, *J* = 8.0 Hz, 2 H, 2 × CH of isoquinoline), 7.22 (t, *J* = 7.5 Hz, 1 H, CH of Ph), 7.26 (d, *J* = 7.4 Hz, 1 H, CH of isoquinoline), 7.32 (t, *J* = 7.8 Hz, 2 H, 2 × CH of Ph), 7.38 (t, *J* = 7.5 Hz, 2 H, 2 × CH of Ph), 7.46 (t, *J* = 7.4 Hz, 1 H, CH of Ph), 7.50 (d, *J* = 7.3 Hz, 2 H, 2 × CH of Ph), 7.82 (d, *J* = 7.8 Hz, 2 H, 2 × CH of Ph), 9.48 (s, 1 H, OH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 20.35 (CH_3 of *i*-Bu), 20.37 (CH_3 of *i*-Bu), 28.22 (CH of *i*-Bu), 31.00 (CH_3), 47.44 (CH_2NH), 64.21 (C^{10b}), 77.28 (C^1), 85.79 (COH), 89.22 (NC=*C*H), 116.61 (C^{6}H), 121.20 (C^{5}H), 125.64 (2 × CH of Ph), 125.96 (CH of Ph), 126.13 (CH of isoquinoline), 127.84 (2 × CH of Ph), 128.02 (2 × CH of Ph), 128.31 (2 × CH of Ph), 128.32 (CH of isoquinoline), 128.59 (CH of isoquinoline), 129.13 (CH of isoquinoline), 129.82 (C^{10a}), 130.34 (C^{6a}), 131.95 (CH of Ph), 138.15 (C_{ipso}COH), 139.78 (C_{ipso}-CO), 165.78 (N*C*=CH), 166.64 (CONH), 188.90 (*C*OPh), 202.27 (*C*OMe).

MS: *m*/*z* (%) = 520 (4) [M$^+$], 403 (5), 360 (8), 342 (15), 298 (7), 185 (18), 170 (14), 142 (9), 129 (24), 105 (100), 77 (72), 58 (12), 43 (55).

Anal. Calcd for $C_{33}H_{32}N_2O_4$ (520.62): C, 76.13; H, 6.20; N, 5.38. Found: C, 76.10; H, 6.30; N, 5.40.

1-Acetyl-*N*^{1}-(*tert*-butyl)-2-hydroxy-3-[(*E*)-2-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide (2c)

Yield: 0.44 g (85%); yellow crystals; mp 175–177 °C (dec).

IR (KBr): 3405 (OH), 3025 (NH), 1701 (COMe), 1665 (COPh), 1620 (CONH), 1591 (C=C), 1560 and 1495 cm^{-1} (Ar).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.13 [s, 9 H, C(CH_3)$_3$], 2.09 (s, 3 H, CH_3), 6.11 (s, 1 H, NH), 6.15 (s, 1 H, NC=CH), 6.36 (d, *J* = 7.6 Hz, 1 H, C^{6}H), 6.39 (s, 1 H, C^{10b}H), 6.89 (d, *J* = 7.6 Hz, 1 H, C^{5}H), 7.09 (d, *J* = 7.6 Hz, 1 H, CH of isoquinoline), 7.14 (d, *J* = 7.3 Hz, 1 H, CH of isoquinoline), 7.18 (t, *J* = 7.5 Hz, 1 H, CH of isoquinoline), 7.23 (t, *J* = 7.1 Hz, 1 H, CH of isoquinoline), 7.27 (t, *J* = 7.4 Hz, 1 H, CH of Ph), 7.34 (t, *J* = 8.0 Hz, 2 H, 2 × CH of Ph), 7.37 (t, *J* = 7.8 Hz, 2 H, 2 × CH of Ph), 7.46 (t, *J* = 7.3 Hz, 1 H, CH of Ph), 7.55 (d, *J* = 7.6 Hz, 2 H, 2 × CH of Ph), 7.82 (d, *J* = 7.4 Hz, 2 H, 2 × CH of Ph), 9.63 (1 H, s, 1 H, OH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 28.10 [C(*C*H$_3$)$_3$], 31.05 (CH_3), 51.41 [*C*(CH$_3$)$_3$], 64.63 (C^{10b}), 77.51 (C^1), 85.34 (COH), 89.20 (NC=*C*H), 116.90 (C^{6}H), 121.28 (C^{5}H), 125.75 (2 × CH of Ph), 126.07 (CH of Ph), 126.22 (CH of isoquinoline), 127.85 (2 × CH of Ph), 128.16 (2 × CH of Ph), 128.20 (CH of isoquinoline), 128.31 (2 × CH of Ph), 128.39 (CH of isoquinoline), 129.18 (CH of isoquinoline), 129.83 (C^{10a}), 130.55 (C^{6a}), 131.94 (CH of Ph), 138.74 (C_{ipso}COH), 139.77 (C_{ipso}CO), 164.91 (N*C*=CH), 167.07 (CONH), 188.83 (*C*OPh), 202.03 (*C*OMe).

MS: *m*/*z* (%) = 520 (2) [M$^+$], 342 (31), 130 (19), 105 (100), 77 (76), 57 (54), 51 (26), 43 (73).

Anal. Calcd for $C_{33}H_{32}N_2O_4$ (520.62): C, 76.13; H, 6.20; N, 5.38. Found: C, 76.32; H, 6.31; N, 5.30.

1-Acetyl-*N*^{1}-allyl-2-hydroxy-3-[(*E*)-2-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide (2d)

Yield: 0.43 g (85%); yellow crystals; mp 185–187 °C (dec).

IR (KBr): 3395 (OH), 3040 (NH), 1699 (COMe), 1663 (COPh), 1605 (CONH), 1592 (C=C), 1563 and 1498 cm^{-1} (Ar).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.11 (s, 3 H, CH_3), 3.50 (m, 1 H, C*H*$_2$NH), 3.81 (m, 1 H, C*H*$_2$NH), 5.15 (d, *J* = 10.2 Hz, 1 H, C*H*$_2$=CH), 5.31 (d, *J* = 17.1 Hz, 1 H, C*H*$_2$=CH), 5.72 (m, 1 H, CH$_2$=C*H*), 6.20 (s, 1 H, NC=CH), 6.35 (d, *J* = 7.6 Hz, 1 H, C^{6}H), 6.43 (s, 1 H, C^{10b}H), 6.50 (t, *J* = 6.0 Hz, 1 H, NH), 6.92 (d, *J* = 7.6 Hz, 1 H, C^{5}H), 7.00 (d, *J* = 7.4 Hz, 1 H, CH of isoquinoline), 7.16 (t, *J* = 7.9 Hz, 2 H, 2 × CH of isoquinoline), 7.23 (t, *J* = 7.1 Hz, 1 H, CH of Ph), 7.26 (d, *J* = 7.1 Hz, 1 H, CH of isoquinoline), 7.32 (t, *J* = 7.1 Hz, 2 H, 2 × CH of Ph), 7.38 (t, *J* = 7.5 Hz, 2 H, 2 × CH of Ph), 7.46 (t, *J* = 7.0 Hz, 1 H, CH of Ph), 7.49 (d, *J* = 7.6 Hz, 2 H, 2 × CH of Ph), 7.82 (d, *J* = 7.0 Hz, 2 H, 2 × CH of Ph), 9.48 (s, 1 H, OH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 30.96 (CH_3), 42.46 (CH_2NH), 64.16 (C^{10b}), 77.40 (C^1), 85.78 (COH), 89.26 (NC=*C*H), 116.59 (*C*H$_2$=CH), 116.72 (C^{6}H), 121.18 (C^{5}H), 125.73 (2 × CH of Ph), 125.98 (CH of Ph), 126.15 (CH of isoquinoline), 127.84 (2 × CH of Ph), 128.06 (2 × CH of Ph), 128.31 (CH of isoquinoline), 128.59 (2 × CH of Ph), 128.60 (CH of isoquinoline), 129.14 (CH of isoquinoline), 129.81 (C^{10a}), 130.21 (C^{6a}), 131.97 (CH of Ph), 133.72 (CH$_2$=*C*H), 138.07 (C_{ipso}COH), 139.76 (C_{ipso}CO), 165.72 (N*C*=CH), 166.51 (CONH), 188.94 (*C*OPh), 202.11 (*C*OMe).

MS: *m*/*z* (%) = 504 (3) [M$^+$], 444 (4), 406 (3), 364 (6), 360 (10), 342 (12), 254 (6), 236 (10), 185 (12), 170 (14), 143 (11), 129 (49), 105 (100), 88 (77), 43 (73).

Anal. Calcd for $C_{32}H_{28}N_2O_4$ (504.58): C, 76.17; H, 5.59; N, 5.55. Found: C, 76.19; H, 5.63; N, 5.43.

1-Acetyl-*N*^{1}-benzyl-2-hydroxy-3-[(*E*)-2-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide (2e)

Yield: 0.44 g (80%); yellow crystals; mp 165–168 °C (dec).

IR (KBr): 3395 (OH), 3040 (NH), 1696 (COMe), 1665 (COPh), 1600 (CONH), 1595 (C=C), 1565 and 1501 cm^{-1} (Ar).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.14 (s, 3 H, CH_3), 3.99 (dd, *J* = 15.0, 4.4 Hz, 1 H, C*H*$_2$Ph), 4.49 (dd, *J* = 14.9, 4.1 Hz, 1 H, C*H*$_2$Ph), 6.21 (s, 1 H, NC=CH), 6.36 (d, *J* = 7.5 Hz, 1 H, C^{6}H), 6.47 (s, 1 H, C^{10b}H), 6.73 (br, 1 H, NH), 6.93 (d, *J* = 7.6 Hz, 1 H, C^{5}H), 7.07 (d, *J* = 7.5 Hz, 1 H, CH of isoquinoline), 7.16 (t, *J* = 7.3 Hz, 1 H, CH of isoquinoline), 7.18 (t, *J* = 7.2 Hz, 1 H, CH of isoquinoline), 7.24 (t, *J* = 7.3 Hz, 1 H, CH of Ph), 7.28–7.39 (m, 10 H, 10 × CH of Ar), 7.44–7.48 (m, 3 H, 3 × CH of Ph), 7.82 (d, *J* = 7.6 Hz, 2 H, 2 × CH of Ph), 9.50 (s, 1 H, OH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 31.04 (CH_3), 44.15 (CH_2NH), 64.19 (C^{10b}), 77.39 (C^1), 85.77 (COH), 89.28 (NC=*C*H), 116.67 (C^{6}H), 121.22 (C^{5}H), 125.66 (2 × CH of Ph), 126.02 (CH of Ph), 126.22 (CH of isoquinoline), 127.35 (CH of Ph), 127.87 (2 × CH of Ph), 127.94 (2 × CH of Ph), 127.95 (CH of isoquinoline), 128.15 (2 × CH of Ph), 128.35 (2 × CH of Ph), 128.42 (CH of isoquinoline), 128.67 (2 × CH of Ph), 129.18 (CH of isoquinoline), 129.85 (C^{10a}), 130.13 (C^{6a}), 132.04 (CH of Ph), 137.66 (C_{ipso}CH$_2$NH), 137.98 (C_{ipso}COH), 139.69 (C_{ipso}CO), 166.03 (N*C*=CH), 166.52 (CONH), 188.94 (*C*OPh), 202.20 (*C*OMe).

MS: *m*/*z* (%) = 554 (2) [M$^+$], 493 (3), 360 (7), 342 (15), 236 (14), 185 (17), 170 (25), 129 (39), 105 (100), 91 (38), 77 (90), 58 (26), 43 (37).

Anal. Calcd for $C_{36}H_{30}N_2O_4$ (554.64): C, 77.96; H, 5.45; N, 5.05. Found: C, 77.90; H, 5.50; N, 5.10.

1-Acetyl-*N*^{1}-(2-chlorobenzyl)-2-hydroxy-3-[(*E*)-2-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide (2f)

Yield: 0.49 g (84%); yellow crystals; mp 180–182 °C (dec).

IR (KBr): 3300 (OH), 3040 (NH), 1697 (COMe), 1664 (COPh), 1617 (CONH), 1594 (C=C), 1564 and 1500 cm^{-1} (Ar).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (s, 3 H, CH_3), 4.26 (dd, *J* = 15.5, 5.2 Hz, 1 H, C*H*$_2$Ph), 4.50 (dd, *J* = 15.2, 6.2 Hz, 1 H, C*H*$_2$Ph), 6.22 (s, 1 H, NC=CH), 6.35 (d, *J* = 7.5 Hz, 1 H, C^{6}H), 6.44 (s, 1 H, C^{10b}H), 6.89 (br, 1 H, NH), 6.92 (d, *J* = 7.6 Hz, 1 H, C^{5}H), 7.05 (d, *J* = 7.3 Hz, 1 H, CH of isoquinoline), 7.16 (t, *J* = 7.4 Hz, 2 H, 2 × CH of isoquinoline), 7.20 (t, *J* = 7.3 Hz, 1 H, CH of isoquinoline), 7.20–7.27 (m, 5 H, 5 × CH of Ph), 7.36–7.39 (m, 4 H, 4 × CH of Ph), 7.44–7.47 (m, 3 H, 3 × CH of Ph), 7.82 (d, *J* = 7.5 Hz, 2 H, 2 × CH of Ph), 9.50 (s, 1 H, OH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 31.28 (CH_3), 41.67 (CH_2NH), 64.22 (C^{10b}), 77.38 (C^1), 85.70 (COH), 89.30 (NC=*C*H), 116.63 (C^{6}H), 121.23 (C^{5}H), 125.52 (2 × CH of Ph), 126.01 (CH of Ph), 126.21 (CH of isoquinoline), 127.09 (CH of 2-ClC_6H_4), 127.87 (2 × CH of Ph), 128.08 (2 × CH of Ph), 128.33 (2 × CH of Ph), 128.39 (CH of isoquinoline), 128.53 (CH of isoquinoline), 128.62 (CH of isoquinoline), 129.13 (CH of 2-ClC_6H_4), 129.33 (CH of 2-ClC_6H_4), 129.88 (C^{10a}), 130.08 (CH of 2-ClC_6H_4), 130.12 (C^{6a}), 132.02 (CH of Ph), 133.60 (C_{ipso}Cl), 133.63 (C_{ipso}CH$_2$NH), 137.50 (C_{ipso}COH), 139.70 (C_{ipso}CO), 166.21 (N*C*=CH), 166.54 (CONH), 188.93 (*C*OPh), 202.15 (*C*OMe).

MS: *m*/*z* (%) = 589 (2) [M$^+$], 417 (4), 402 (5), 375 (4), 298 (13), 273 (10), 190 (25), 129 (40), 105 (100), 89 (13), 77 (70), 43 (34).

Anal. Calcd for $C_{36}H_{29}ClN_2O_4$ (589.08): C, 73.40; H, 4.96; N, 4.76. Found: C, 73.50; H, 5.00; N, 4.59.

1-Acetyl-*N*^{1}-(2-ethylhexyl)-2-hydroxy-3-[(*E*)-oxo-2-phenylethylidene]-2-phenyl-1,2,3,10b-tetrahydropyrrolo[2,1-*a*]isoquinoline-1-carboxamide (2g)

Yield: 0.49 g (85%); yellow crystals; mp 175–78 °C (dec).

IR (KBr): 3405 (OH), 3045 (NH), 1699 (COMe), 1662 (COPh), 1610 (CONH), 1595 (C=C), 1565 and 1501 cm^{-1} (Ar).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.85–0.94 (m, 6 H, 2 × CH_3 of 2-ethylhexyl), 1.26–1.40 (m, 8 H, 4 × CH_2 of 2-ethylhexyl), 1.45 (m, 1 H, CH of 2-ethylhexyl), 2.11 (s, 3 H, CH_3), 2.71 (m, 1 H, C*H*$_2$NH), 3.22 (m, 1 H, C*H*$_2$NH), 6.19 (s, 1 H, NC=CH), 6.35 (d, *J* = 7.6 Hz, 1 H, C^{6}H), 6.42 (br, 1 H, NH), 6.45 (s, 1 H, C^{10b}H), 6.92 (d, *J* = 7.6 Hz, 1 H, C^{5}H), 6.98 (d, *J* = 7.9 Hz, 1 H, CH of isoquinoline), 7.15 (t, *J* = 7.5 Hz, 2 H, 2 × CH of isoquinoline), 7.22 (t, *J* = 7.6 Hz, 1 H, CH of Ph), 7.26 (d, *J* = 7.5 Hz, 1 H, CH of isoquinoline), 7.32 (t, *J* = 7.7 Hz, 2 H, 2 × CH of Ph), 7.39 (t, *J* = 7.7 Hz, 2 H, 2 × CH of Ph), 7.46 (t, *J* = 7.5 Hz, 1 H, CH of Ph), 7.49 (d, *J* = 7.6 Hz, 2 H, 2 × CH of Ph), 7.82 (d, *J* = 7.9 Hz, 2 H, 2 × CH of Ph), 9.48 (s, 1 H, OH).

^{13}C NMR (125.7 MHz, $CDCl_3$): δ = 10.94 (CH_3 of 2-ethylhexyl), 14.10 (CH_3 of 2-ethylhexyl), 23.08 (CH_2 of 2-ethylhexyl), 24.43 (CH_2 of 2-ethylhexyl), 28.84 (CH_2 of 2-ethylhexyl), 29.69 (CH_2 of 2-ethylhexyl), 31.15 (CH_3), 39.08 (CH of 2-ethylhexyl), 42.74 (CH_2NH), 64.23 (C^{10b}), 77.40 (C^1), 85.78 (COH), 89.21 (NC=*C*H), 116.61 (C^{6}H), 121.19 (C^{5}H), 125.59 (2 × CH of Ph), 125.95 (CH of Ph), 126.11 (CH of isoquinoline), 127.83 (2 × CH of Ph), 128.04 (2 × CH of Ph), 128.27 (CH of isoquinoline), 128.30 (2 × CH of Ph), 128.55 (CH of isoquinoline), 129.12 (CH of isoquinoline), 129.80 (C^{10a}), 130.38 (C^{6a}), 131.94 (CH of Ph), 138.21 (C_{ipso}COH), 139.79 (C_{ipso}CO), 165.75 (N*C*=CH), 166.42 (CONH), 188.89 (*C*OPh), 202.20 (*C*OMe).

MS: *m*/*z* (%) = 576 (3) [M$^+$], 365 (8), 360 (14), 343 (8), 236 (10), 212 (8), 185 (14), 170 (18), 154 (6), 142 (8), 129 (24), 115 (16), 105 (100), 85 (6), 77 (94), 57 (20), 43 (67).

Anal. Calcd for $C_{37}H_{40}N_2O_4$ (576.73): C, 77.06; H, 6.99; N, 4.86. Found: C, 77.10; H, 6.95; N, 4.71.

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