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Efficient Construction of Tri- and Tetracyclic Heterocycles from Linear 1,6-Dienes by a Domino Reaction

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Abstract: Tri- and tetracyclic heterocycle systems were constructed by a palladium-catalyzed domino reaction of linear 1,6-dienes that contain acryl groups with aryl halides through C–C coupling and aromatic C–H functionalization. Three different acrylamides have been shown to be very active for the reaction. The substituents on the aryl halides could be ethoxycarbonyl, ketyl, chloro, sulfonyl, cyano, etc. Thus, the ready accessibility of the starting materials, the wide range of compatibility of substrates including both dienes and aryl halides, and the generality of this process make the reaction highly valuable in view of the synthetic and medicinal importance of these kinds of heterocycles.

Keywords: 1,6-dienes · C–H activation · domino cyclizations · heterocycles · palladium

Introduction

Multistep sequential transformations—domino carbon–carbon bond formation[1] or cascade[2] reactions—are gaining steadily increasing importance and are receiving much attention as complex organic molecules can be obtained in a single operation.[3] The Heck coupling reaction is one of the most effective methods for the construction of C–C bonds and has been widely applied in the syntheses of materials, pharmaceuticals, and natural products.[4] Activation of carbon–hydrogen (C–H) bonds in hydrocarbons may provide chemists with an environmentally friendly method to construct C–C bonds and would aid the development of a direct methodology for the functionalization of C–H bonds, providing a great challenge to chemists.[5,6] In recent years, palladium-catalyzed activation of the aromatic C–H group has received considerable attention due to its application in the construction of a variety of condensed ring systems by using a nonfunctionalized aryl group.[7–9] The domino carbon–carbon bond formation through these processes is particularly useful as complex organic molecules can be directly obtained in a single operation. J. C. Carretero and Hiroaki Ohno and co-workers have reported a domino-cyclization reaction of alkenes and allenenes, respectively, for the synthesis of tri- and tetracyclic heterocycles.[10] More recently, a methodology for the construction of condensed aromatic rings by palladium(0)-catalyzed domino cyclization of alkyne-substituted phenyl iodide with a terminal alkyne was developed.[11] Therefore, they are efficient and elegant methods for the syntheses of complex organic molecules in both academic and industrial laboratories.[12–14] To the best of our knowledge, domino carbon–carbon bond formation that includes the C–H activation of an aromatic ring for the construction of multicyclic organic compounds by use of the linear 1,6-dienes compounds has scarcely been investigated.[15]

As a result of our interest in the development of palladium-catalyzed processes and direct C–H functionalization, we report herein the palladium-catalyzed reactions of *N*-benzyl-*N*-cinnamylacrylamide (**a**), *N*-cinnamyl-*N*-phenylacrylamide (**b**), and *N*-acryloyl-*N*-benzylcinnamamide (**c**) with different aryl halides, which provide a direct, efficient, and economic methodology for the construction of tri- and tetracyclic compounds through both C–C bond formation and the C–H bond activation.

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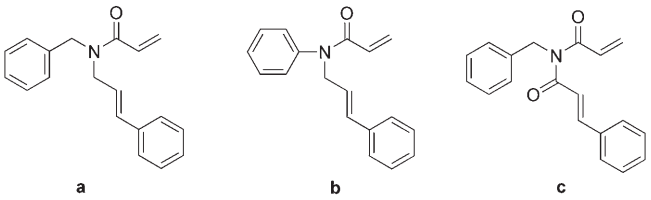
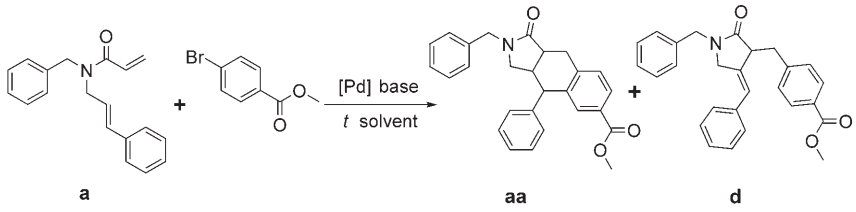


Results and Discussion

A survey of the reaction conditions by using *N*-benzyl-*N*-cinnamylacrylamide (**a**) and methyl 4-bromobenzoate as a test experiment was performed (Scheme 1, Table 1). In a typical experiment, reaction of **a** and methyl 4-bromobenzoate in DMF in the presence of catalyst [$Pd(OAc)_2$] produced the pyrrolidin-2-one **d** in 53% yield after 28 h at 120°C. By controlling the experimental conditions we discovered that 1) the efficiency of the domino reaction in producing product **aa** can be greatly enhanced by raising the reaction temperature to 155°C (Table 1, entry 6); 2) the base additive plays an important role in the overall efficiency of the reaction as we discovered by simply changing the base from tributylamine to potassium carbonate (entries 6, 7), with the unexpected isoindole **aa** produced in 83 and 16% yield when using tributylamine and potassium carbonate, respectively, under other identical conditions; 3) among the catalysts investigated (entries 10–12), the palladium(II) acetate/(triphenylphosphine) catalytic system was the most effective one (entries 6, 10–12); 4) DMF was a better solvent for this reaction than 1,4-dioxane (entries 6, 8–9). As shown in Table 1, the tricyclic compound **aa** was only isolated in yields of 29 and 22%, respectively, when the 1,4-dioxane was employed as a solvent, indicating temperature/solvent effects on the outputs of the reactions and on the formation of the final products. Thus, the following standard reaction conditions were used for carrying out the following studies: 1,6-diene (1 equiv) was reacted with different aryl halides (1.1 equiv) in the presence of palladium(II) catalyst (2 mol%) and Ph_3P (4 mol%) with (nBu)$_3$N (2 equiv) as an additive in DMF at 155°C.



Scheme 1. Synthesis of substituted tricyclic heterocycles.

To probe the scope and limitations of this novel domino reaction, a range of substituted aryl halides and acrylamides were examined (Table 2). It is found that the outputs of the domino reactions of *N*-benzyl-*N*-cinnamylacrylamide (**a**) and *N*-cinnamyl-*N*-phenylacrylamide (**b**) with aryl halides were strongly influenced by the electronic properties of the aryl halides. A variety of isoindoles were readily isolated in good to excellent yields (Table 2, entries 1–15) when the aryl halides with electron-withdrawing groups were employed. The electron-withdrawing groups could be ethoxycarbonyl, ketyl, chloro, sulfonyl, cyano, etc. However, the corresponding heterotricyclic compounds could not be isolated if the aryl halides had electron-donating substituents on the benzene ring, and considerable amounts of unidentified products were obtained when 4-bromotoluene, 2-bromotoluene, and 1-bromo-4-methoxybenzene were used, indicating that the aryl halides have an electronic effect on the reaction. It was found that the reaction of *N*-acryloyl-*N*-benzylcinnamamide (**c**) with aryl halides is compatible with either electron-donating or electron-withdrawing groups on the aryl halides, and the outputs of the reactions were good (entries 16–22).

Table 1. Palladium-catalyzed one-pot reaction for construction of the tricyclic heterocycles.[a]

Entry	[Pd] (mol%)	Base (equiv)	Solvent	t [h]	T [°C][b]	Yield [%][c]	
						aa	**d**
1	$[Pd(OAc)_2]/PPh_3$ (1:2)	(nBu)$_3$N (2)	DMF	18	110	–	–
2	$[Pd(OAc)_2]/PPh_3$ (2:4)	(nBu)$_3$N (2)	DMF	28	120	8	53
3	$[Pd(OAc)_2]/PPh_3$ (2:4)	(nBu)$_3$N (2)	DMF	26	130	15	25
4	$[Pd(OAc)_2]/PPh_3$ (1:2)	(nBu)$_3$N (2)	DMF	26	140	20	23
5	$[Pd(OAc)_2]/PPh_3$ (2:4)	(nBu)$_3$N (2)	DMF	25	150	54	19
6	**$[Pd(OAc)_2]/PPh_3$ (2:4)**	**(nBu)$_3$N (2)**	**DMF**	**24**	**155**	**83**	**14**
7	$[Pd(OAc)_2]/PPh_3$ (2:4)	K_2CO_3 (2)	DMF	24	155	16	11
8	$[Pd(OAc)_2]/PPh_3$ (2:4)	(nBu)$_3$N (2)	Dioxane	24	120	29	8
9	$[Pd(OAc)_2]/PPh_3$ (2:4)	(nBu)$_3$N (2)	Dioxane	24	110	22	6
10	$[Pd(OAc)_2]/PPh_3$ (2:4)	(nBu)$_3$N (2)	DMF	24	155	30	18
11	$[Pd(dba)_2]$[d] (2)	(nBu)$_3$N (2)	DMF	24	155	20	7
12	$[Pd(PPh_3)_4]$ (2)	(nBu)$_3$N (2)	DMF	24	155	16	27

[a] All reactions were carried out under argon by using **a** (1.0 equiv), methyl 4-bromobenzoate (1.1 equiv), $[Pd(OAc)_2]$ (2 mol%), PPh_3, base, and solvent (10 mL) at the indicated temperature. [b] Oil bath temperature. [c] Isolated yield. [d] dba: dibenzylidene acetone.

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Table 2. Palladium-catalyzed domino reaction for the formation of tricyclic heterocycles.[a]

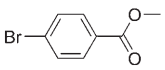
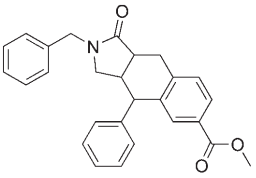
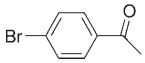
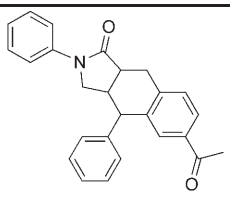
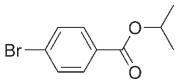
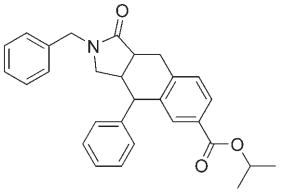
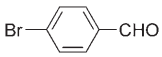
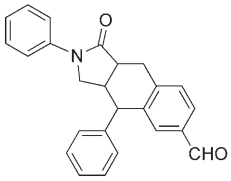
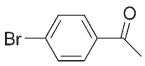
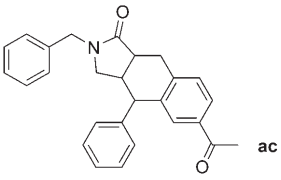
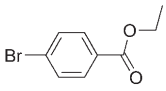
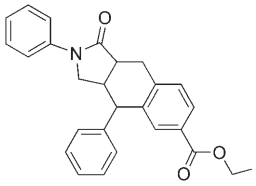
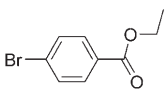
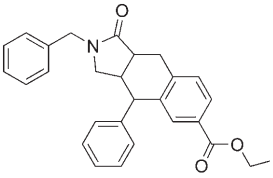
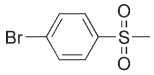
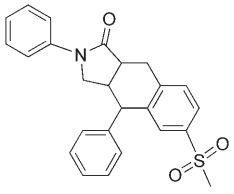
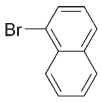
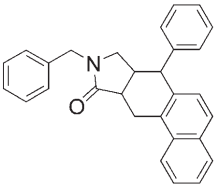
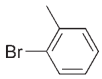
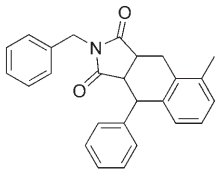
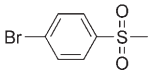
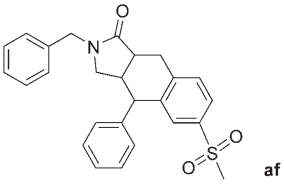
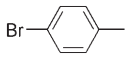
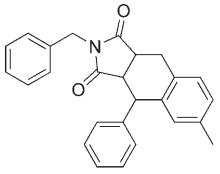
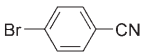
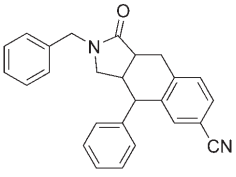
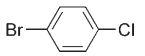
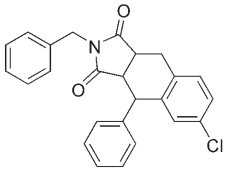
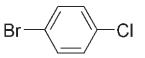
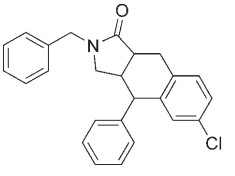
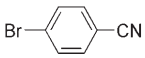
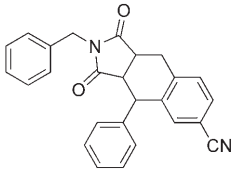
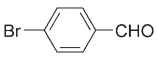
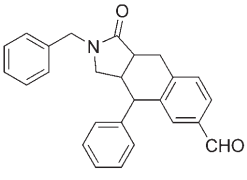
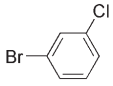
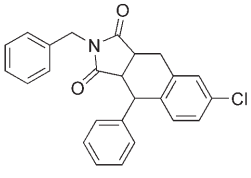
Entry	S[c]	ArX	Product	Yield [%][b]	Entry	S[c]	ArX	Product	Yield [%][b]
1	**a**		 **aa**	83	12	**b**		 **bb**	82
2	**a**		 **ab**	81	13	**b**		 **bc**	75
3	**a**		 **ac**	60	14	**b**		 **bd**	72
4	**a**		 **ad**	85	15	**b**		 **be**	82
5	**a**		 **ae**	71	16	**c**		 **ca**	81
6	a		 **af**	52	17	**c**		 **cb**	84
7	**a**		 **ag**	80	18	**c**		 **cc**	65
8	**a**		 **ah**	62	19	**c**		 **cd**	86
9	**a**		 **ai**	63	20	**c**		 **ce**	67

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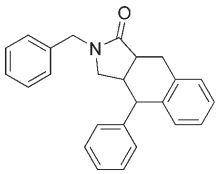
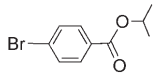
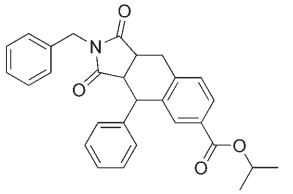
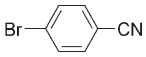
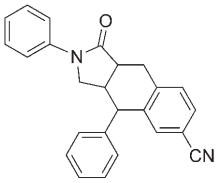
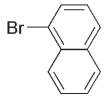
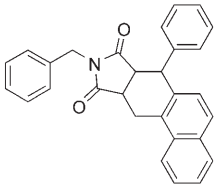
Table 2. (Continued)

Entry	S[c]	ArX	Product	Yield [%][b]	Entry	S[c]	ArX	Product	Yield [%][b]
10	**a**		 **aj**	60	21	**c**		 **cf**	83
11	**b**		 **ba**	78	22	**c**		 **cg**	79

[a] General conditions: **a**, **b**, **c** (1.0 equiv), ArX (X = Br; I) (1.1 equiv), $[Pd(OAc)_2]$ (2 mol %), PPh_3 (4 mol %), $(n-Bu)_3N$ (2 equiv), DMF 10 mL, 155 °C (oil bath temperature). [b] Isolated yield after flash column chromatography. [c] The substrates of the reactions.

In addition, the *ortho*-, *meta*-, and *para*-substituted aryl halides are suitable for the reactions (entries 16, 17, and 20). Interestingly, it was found that the C–Br bond could be selectively reacted with 1,6-dienes when both C–Br and C–Cl bonds are on the benzene ring (entries 8, 18, 20). When 1-bromonaphthalene was used in the reaction, a tetracyclic compound (**cg**) was obtained in 79 % yield (entry 22).

All the resulting tri- and tetracyclic compounds were confirmed by one- (^1H, ^{13}C), two-dimensional (COSY) NMR spectral analyses, and elemental or HRMS analyses. The representative compounds of **ab**, **bd**, and **cg** were additionally characterized by X-ray crystallographic analyses (the structures of the compounds are shown in Figures 1, 2, and 3). Further details can be obtained in the Supporting Information.[16] Although racemic products were obtained in all cases, it was strangely found that the 5,6-ring systems were in a *trans*-orientation in the case of reactions of **a** and **b** with aryl halides, and in the case of the reaction of **c** with aryl halides, *cis*-fused compounds were obtained; this is probably due to steric effects.

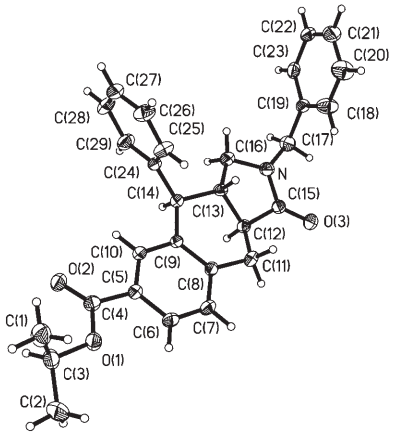


Figure 1. Molecular structure of compound **ab**.

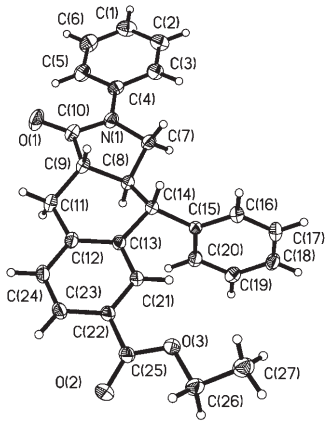


Figure 2. Molecular structure of compound **bd**.

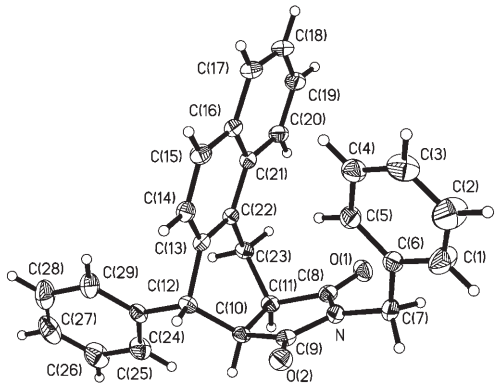


Figure 3. Molecular structure of compound **cg**.

The mechanism of this novel domino cyclization is proposed as follows (Scheme 2): insertion of arylpalladium(II) halide into an acrylamide moiety produced the intermediate

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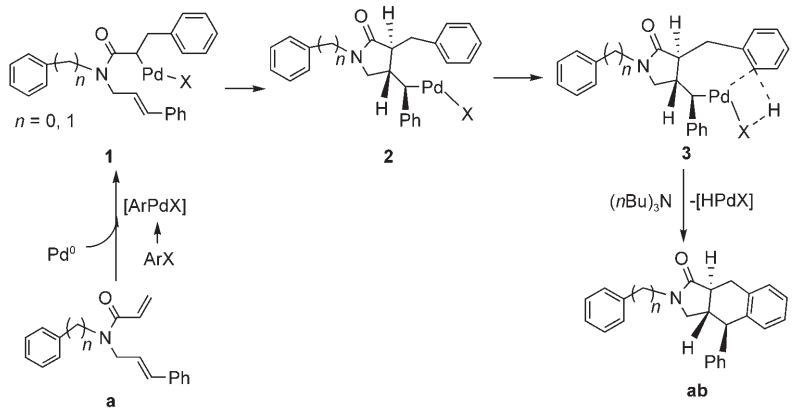

Scheme 2. Proposed mechanism of the reaction.

1, which then reacted with the carbon–carbon double bond through a carbopalladation reaction to afford **2**. σ-Bond metathesis onto the aryl group in **2** via the intermediate **3**, followed by a proton abstraction process by the base afforded the final products on the basis of the fact that the reaction is facilitated by electron-withdrawing substituents on the aromatic ring in the cases of acrylamides **a** and **b** being used, which is inconsistent with an electronic aromatic-substitution mechanism, and a proton abstraction mechanism for this kind of reaction has been proposed.[17] However, other plausible pathways can not be ruled out.

Conclusion

We have developed a novel domino reaction for the synthesis of tri- and tetracyclic heterocycles through multistep C–C bond formation and C–H activation of a benzene ring by treatment of linear 1,6-dienes that contain acryl groups with aryl halides catalyzed by a palladium catalyst. The ready accessibility of the starting materials, the wide range of compatibility of substrates, including both dienes and aryl halides, and the generality of this process make the reaction highly valuable in view of the synthetic and medicinal importance of these kinds of heterocycles. Further investigations to understand this catalytic transformation, to evaluate the process with a broader scope of substrates, and to construct more complex structures are in progress in our lab.

Experimental Section

General: All catalyzed reactions were performed under an argon atmosphere by using the oven-dried Schlenk flask. The chemicals were purchased from Alfa Aesar and Acros Chemical. All solvents and materials were pre-dried and redistilled or recrystallized before use. ^{1}H (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on Bruker Avance 300 M spectrometers with $CDCl_3$ as the solvent and TMS as the internal standard. Chemical shifts are reported in ppm by assigning the TMS resonance in the ^{1}H NMR spectrum as $\delta = 0.00$ ppm and the $CDCl_3$ resonance in the ^{13}C spectrum as $\delta = 77.0$ ppm. All coupling constants (J values) were reported in Hertz (Hz). Column chromatography was performed on silica gel 200–300 mesh. Melting points were determined by using a Gallenkamp melting point apparatus and are uncorrected. FTIR spectra were recorded from KBr pellets in the 4000–400 cm^{-1} range on a Nicolet 5DX spectrometer. Mass spectra were performed on Micaomass GCT-MS. 2D NMR and HRMS were performed at the State-Authorized Analytical Center at the University of Science and Technology of China. X-ray crystallographic diffraction data of **ab**, **bd**, and **cg** were collected at room temperature with a Bruker SMART Apex CCD diffractometer with $Mo_{K\alpha}$ radiation ($\lambda = 0.71073$ Å) and graphite monochromator by using the ψ and ω-scan mode. Data reductions and absorption corrections were performed with SAINT and SADABS software, respectively. The structure was solved by direct methods and refined on F^2 by full-matrix least-squares using SHELXTL.[18] All nonhydrogen atoms were treated anisotropically. The positions of hydrogen atoms were generated geometrically.

General procedures: A typical procedure for the palladium-catalyzed domino reaction of linear 1,6-dienes that contain acryl groups with aryl halides: *N*-Benzyl-*N*-cinnamylacrylamide (**a**) (0.97 g, 3.5 mmol), isopropyl 4-bromobenzoate (0.93 g, 3.85 mmol), [$Pd(OAc)_2$] (25.5 mg, 0.07 mmol), and PPh_3 (35.84 mg, 0.14 mmol) were added to a degassed solution of $(n\text{Bu})_3$N (1.67 mL, 7 mmol) in DMF (10 mL). After the mixture had been stirred for half an hour at room temperature, it was then heated at 155 °C for 30 h, and was then quenched with water and extracted with EtOAc (3×5 mL). The combined organic layers were washed with hydrochloric acid (5%), sodium carbonate (5%), and saturated sodium chloride solution. The mixture was then dried over $MgSO_4$ and concentrated. The residue was purified by flash chromatography column (4:1 petroleum ether/EtOAc) to give the corresponding isoindole.

Methyl 2-benzyl-1-oxo-4-phenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]-isoindole-6-carboxylate (aa): White solid; 1.19 g (83% yield); m.p. 164–165 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.78$ (d, 1H, $J = 8.0$ Hz; Ar–H), 7.43 (s, 1H; Ar–H), 6.99–7.24 (m, 11H; Ar–H), 4.59 (d, 1H, $J = 14.8$ Hz; Ar–CH_2–N), 4.25 (d, 1H, $J = 14.8$ Hz; Ar–CH_2–N), 3.94 (d, 1H, $J = 11.5$ Hz; Ar–CH–), 3.75 (s, 3H; –O–CH_3), 3.35 (dd, 1H, $J = 4.7$, 4.7 Hz; N–CH_2–CH–), 3.09–2.93 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.58–2.49 (m, 1H; O=C–CH–CH_2–), 2.35–2.29 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 174.1$, 166.5, 142.2, 141.0, 139.6, 136.1, 130.8, 129.7, 128.6, 128.3, 127.7, 127.2, 127.1, 126.9, 51.6, 50.7, 49.8, 46.3, 45.5, 43.9, 30.7 ppm; IR (KBr): $\tilde{\nu} = 3036$, 2931, 2881, 1716 (C=O), 1678 (C=O), 1600, 1566, 1496, 1481, 1435, 1357, 1303, 1284, 1242, 1195, 1145, 1122, 1095, 976, 759, 709, 613 cm^{-1}; HRMS: m/z: calcd for $C_{27}H_{25}NO_3$: 411.1834; found: 411.1829.

2-Benzyl-6-isobutyryl-4-phenyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]isoindol-1-one (ab): Colorless crystals; 356 mg (81% yield); m.p. 166–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.70$ (d, 1H, $J = 1.0$ Hz; Ar–H), 7.39 (s, 1H; Ar–H), 6.99–7.24 (m, 11H; Ar–H), 5.07–5.01 (m, 1H; –O–CH–CH_3), 4.50 (d, 1H, $J = 14.8$ Hz; Ar–CH_2–N), 4.25 (d, 1H, $J = 14.8$ Hz; Ar–CH_2–N), 3.92 (d, 1H, $J = 11.4$ Hz; Ar–CH–), 3.31 (dd, 1H, $J = 4.8$, 4.8 Hz; N–CH_2–CH–), 3.04–2.91 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.50–2.47 (m, 1H; O=C–CH–CH_2–), 2.34–2.32 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.5$, 165.9, 142.6, 141.1, 140.0, 136.6, 131.2, 129.2, 128.7, 128.5, 128.1, 127.6, 127.4, 127.3, 68.3, 51.2, 50.2, 46.7, 45.9, 44.3, 31.1, 21.9 ppm; IR (KBr): $\tilde{\nu} = 3028$, 2931, 2881, 2499, 1716 (C=O), 1678 (C=O), 1600, 1496, 1435, 1357, 1303, 1284, 1242, 1122, 976, 759, 709, 613 cm^{-1}; HRMS: m/z: calcd for $C_{29}H_{29}NO_3$: 439.2147; found: 439.2141.

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6-Acetyl-2-benzyl-4-phenyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]isoindol-1-one (ac): White solid; 0.83 g (60% yield); m.p. 147–148°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, 1H, J = 7.8 Hz; Ar–H), 7.28–6.97 (m, 12H; Ar–H), 4.53 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 4.23 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 3.92 (d, 1H, J = 11.1 Hz; Ar–CH–), 3.35 (dd, 1H, J = 4.8, 4.8 Hz; N–CH_2–CH–), 3.03–2.91 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.53–2.43 (m, 1H; O=C–CH–CH_2–), 2.29–2.07 (m, 1H; –CH_2–CH–CH–), 2.07 ppm (s, 3H; O=C–CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.2, 174.9, 143.0, 142.1, 140.7, 137.0, 136.1, 130.7, 130.5, 129.5, 129.2, 129.0, 128.5, 128.1, 127.8, 126.8, 51.6, 50.6, 47.1, 46.3, 44.7, 31.5, 26.9 ppm; IR (KBr): $\tilde{\nu}$ = 3029, 2958, 2928, 2870, 1685 (C=O), 1678 (C=O), 1600, 1492, 1423, 1357, 1273, 1242, 1114, 1072, 1030, 952, 918, 821, 756, 702, 601 cm^{-1}; HRMS: m/z: calcd for $C_{27}H_{25}NO_2$: 395.1885; found: 395.1882.

2-Benzyl-4-phenyl-6-propionyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]isoindol-1-one (ad): Colorless crystals; 1.26 g (85% yield); m.p. 167–168°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, 1H, J = 7.9 Hz; Ar–H), 7.49 (s, 1H; Ar–H), 7.31–7.07 (m, 11H; Ar–H), 4.63 (d, 1H, J = 14.8 Hz; Ar–CH_2–N), 4.34–4.21 (m, 1H; Ar–CH_2–N, 2H; O–CH_2–CH_3), 3.98 (d, 1H, J = 11.4 Hz; Ar–CH–), 3.45 (dd, 1H, J = 4.7, 4.7 Hz; N–CH_2–CH–), 3.13–2.98 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.59–2.57 (m, 1H; O=C–CH–CH_2–), 2.30 (m, 1H; –CH_2–CH–CH–), 1.29 ppm (t, 3H, J = 7.1, 7.1 Hz; –CH_2–CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.1, 166.0, 142.2, 140.9, 139.6, 136.1, 130.8, 129.6, 128.6, 128.4, 128.3, 128.1, 127.6, 127.0, 126.8, 60.4, 50.7, 49.8, 46.3, 45.5, 43.8, 30.7, 13.8 ppm; IR (KBr): $\tilde{\nu}$ = 3028, 2978, 2931, 2866, 1712 (C=O), 1685 (C=O), 1612, 1492, 1415, 1354, 1280, 1238, 1168, 1130, 941, 918, 825, 756, 702, 613 cm^{-1}; HRMS: m/z: calcd for $C_{28}H_{27}NO_3$: 425.1991; found: 425.1989.

9-Benzyl-7-phenyl-7,7a,8,9,10a,11-hexahydronaphtho[1,2-*f*]isoindol-10-one (ae): White solid; 1.01 g (71% yield); m.p. 168–169°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.1 (d, 1H, J = 8.4 Hz; Ar–H), 7.78 (d, 1H, J = 8.1 Hz; Ar–H), 7.55–6.82 (m, 14H; Ar–H), 4.55 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 4.20 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 3.80 (d, 1H, J = 7.5 Hz; Ar–CH–), 3.56 (dd, 1H, J = 8.1, 8.1 Hz; N–CH_2–CH–), 3.40–3.31 (m, 1H; N–CH_2–CH–, 1H; Ar–CH_2–CH–), 3.15–3.07 (m, 1H; Ar–CH_2–CH–), 3.04–2.97 (m, 1H; O=C–CH–CH_2–), 2.87–2.83 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.5, 141.1, 136.0, 135.7, 132.2, 128.5, 128.4, 128.2, 128.1, 127.5, 127.0, 126.5, 126.0, 125.0, 122.9, 50.4, 48.7, 46.1, 40.9, 36.4, 23.6 ppm; IR (KBr): $\tilde{\nu}$ = 3028, 2982, 2910, 2841, 1685 (C=O), 1492, 1440, 1352, 1325, 1273, 1080, 1026, 949, 882, 779, 746, 700, 673, 650, 630, 569, 530 cm^{-1}; HRMS: m/z: calcd for $C_{29}H_{25}NO$: 403.1936; found: 403.1931.

2-Benzyl-6-(methylsulfonyl)-4-phenyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]-isoindol-1-one (af): White solid; 0.78 g (52% yield); m.p. 186–187°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, 1H, J = 7.0 Hz; Ar–H), 7.46 (d, 1H, J = 8.1 Hz; Ar–H), 7.28–7.05 (m, 11H; Ar–H), 4.62 (d, 1H, J = 14.8 Hz; Ar–CH_2–N), 4.33 (d, 1H, J = 14.8 Hz; Ar–CH_2–N), 4.03 (d, 1H, J = 11.6 Hz; Ar–CH–), 3.43 (dd, 1H, J = 4.8, 4.8 Hz; N–CH_2–CH–), 3.15–2.94 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.89 (s, 3H; –S–CH_3), 2.60–2.58 (m, 1H; O=C–CH–CH_2–), 2.29–2.07 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.7, 142.1, 141.4, 141.2, 138.3, 136.0, 130.7, 128.8, 128.5, 128.4, 128.0, 127.6, 127.5, 127.3, 124.8, 50.8, 49.6, 46.3, 45.2, 44.0, 43.7, 30.7 ppm; IR (KBr): $\tilde{\nu}$ = 3028, 2924, 2877, 1685 (C=O), 1600, 1481, 1423, 1357, 1303, 1249, 1172, 1149, 1118, 1087, 964, 817, 763, 705, 609, 567, 543 cm^{-1}; HRMS: m/z: calcd for $C_{26}H_{25}NO_3S$: 431.1555; found: 431.1549.

2-Benzyl-1-oxo-4-phenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]isoindole-6-carbonitrile (ag): White solid; 1.05 g (80% yield); m.p. 159–160°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.35–6.95 (m, 13H; Ar-H), 4.52 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 4.23 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 3.87 (d, 1H, J = 11.4 Hz; Ar–CH–), 3.35 (dd, 1H, J = 4.8, 4.8 Hz; N–CH_2–CH–), 3.03–2.88 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.53–2.43 (m, 1H; O=C–CH–CH_2–), 2.35–2.25 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.7, 141.2, 140.9, 136.0, 133.4, 130.4, 129.4, 128.8, 128.1, 127.6, 127.3, 118.4, 109.9, 50.5, 49.6, 46.3, 44.9, 43.6, 30.7 ppm; IR (KBr): $\tilde{\nu}$ = 3028, 2962, 2897, 2858, 2222, 1693 (C=O), 1600, 1489, 1427, 1354, 1288, 1261, 1195, 1103, 1033, 898, 798, 759, 698, 613, 578 cm^{-1}; HRMS: m/z: calcd for $C_{26}H_{22}N_2O$ 378.1732; found: 378.1730.

2-Benzyl-6-chloro-4-phenyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]isoindol-1-one (ah): Straw-yellow liquid; 0.84 g (62% yield); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24–7.00 (m, 13H; Ar–H), 4.55 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 4.25 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 3.87 (d, 1H, J = 11.7 Hz; Ar–CH–), 3.23 (dd, 1H, J = 4.8, 4.8 Hz; N–CH_2–CH–), 3.02–2.86 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.51–2.42 (m, 1H; O=C–CH–CH_2–), 2.30–2.24 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.2, 142.0, 141.2, 136.1, 134.0, 131.6, 130.8, 129.0, 128.6, 128.4, 128.3, 128.0, 127.9, 127.6, 127.1, 126.9, 126.4, 122.9, 50.7, 49.7, 46.3, 45.1, 44.0, 29.9 ppm; IR (KBr): $\tilde{\nu}$ = 3024, 2928, 2870, 1689 (C=O), 1639, 1491, 1450, 1357, 1261, 1199, 1076, 1030, 744, 698, 528 cm^{-1}; HRMS: m/z: calcd for $C_{25}H_{22}ClNO$: 387.1390; found: 387.1387.

2-Benzyl-1-oxo-4-phenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]isoindole-6-carbaldehyde (ai): White solid; 0.84 g (63% yield); m.p. 104–105°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.30 (s, 1H; O=CH), 7.21–6.90 (m, 13H; Ar–H), 4.53 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 4.24 (d, 1H, J = 14.7 Hz; Ar–CH_2–N), 3.90 (d, 1H, J = 11.4 Hz; Ar–CH–), 3.29 (dd, 1H, J = 4.8, 4.8 Hz; N–CH_2–CH–), 3.03–2.88 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.53–2.43 (m, 1H; O=C–CH–CH_2–), 2.35–2.25 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 195.1, 173.9, 141.9, 140.4, 136.1, 131.6, 130.4, 128.7, 128.1, 127.8, 127.1, 126.6, 50.7, 49.7, 46.3, 45.3, 43.8, 30.9 ppm; IR (KBr): $\tilde{\nu}$ = 3028, 2928, 2858, 2719, 1693 (C=O), 1685 (C=O), 1600, 1562, 1492, 1423, 1361, 1284, 1257, 1215, 1180, 1033, 1072, 1030, 752, 702, 590 cm^{-1}; HRMS: m/z: calcd for $C_{26}H_{23}NO_2$: 381.1729; found: 381.1723.

2-Benzyl-4-phenyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]isoindol-1-one (aj): Straw-yellow liquid; 0.74 g (60% yield); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.24–6.99 (m, 13H; Ar–H), 4.52 (d, 1H, J = 7.8 Hz; Ar–CH_2–N), 4.23 (d, 1H, J = 14.8 Hz; Ar–CH_2–N), 3.87 (d, 1H, J = 11.4 Hz; Ar–CH–), 3.22 (dd, 1H, J = 2.9, 7.6 Hz; N–CH_2–CH–), 2.97–2.90 (m, 1H; N–CH_2–CH–, 2H; Ar–CH_2–CH–), 2.51–2.42 (m, 1H; O=C–CH–CH_2–), 2.30–2.24 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.6, 142.9, 140.7, 139.2, 136.2, 135.5, 129.5, 128.4, 128.1, 127.6, 127.2, 126.2, 120.4, 50.8, 49.9, 46.1, 45.6, 44.1, 30.7 ppm; IR (KBr): $\tilde{\nu}$ = 3024, 2928, 2870, 1689 (C=O), 1639, 1492, 1450, 1357, 1261, 1199, 1076, 1030, 744, 698, 528 cm^{-1}; HRMS: m/z: calcd for $C_{25}H_{23}NO$: 353.1780; found: 353.1775.

1-Oxo-2,4-diphenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]isoindole-6-carbonitrile (ba): White solid; 0.99 g (78% yield); m.p. 200–201°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.60–7.09 (m, 13H; Ar–H), 4.08 (d, 1H, J = 10.7 Hz; Ar–CH–), 3.67 (t, 1H, J = 9.6, 9.9 Hz; N–CH_2–CH–), 3.59 (t, 1H, J = 7.2, 8.8 Hz; N–CH_2–CH–), 3.44 (dd, 1H, J = 5.0, 5.1 Hz; Ar–CH_2–CH–), 3.20–3.11 (m, 1H; Ar–CH_2–CH–), 2.77–2.71 (m, 1H; O=C–CH–CH_2–), 2.54–2.51 ppm (m, 1H; –CH_2–CH–CH–); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 141.1, 140.7, 138.9, 133.4, 132.0, 130.5, 129.5, 129.0, 128.6, 128.4, 128.2, 124.4, 119.2, 118.4, 110.8, 50.8, 49.6, 46.3, 40.6, 30.7 ppm; IR (KBr): $\tilde{\nu}$ = 3066, 3020, 2889, 2225, 1716 (C=O), 1597 (C=O), 1492, 1384, 1357, 1300, 1230, 1180, 1103, 1068, 898, 864, 837, 759, 698, 574 cm^{-1}; HRMS: m/z: calcd for $C_{25}H_{20}N_2O$: 364.1576; found: 364.1573.

6-Acetyl-2,4-diphenyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]isoindol-1-one (bb): White solid; 1.09 g (82% yield); m.p. 206–207°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.76 (d, 1H, J = 7.9 Hz; Ar–H), 7.57 (d, 1H, J = 8.1 Hz; Ar–H), 7.44–7.11 (m, 11H; Ar–H), 4.12 (d, 1H, J = 11.3 Hz; Ar–CH–), 3.69 (t, 1H, J = 9.7, 9.9 Hz; N–CH_2–CH–), 3.58 (t, 1H, J = 2.5, 6.9 Hz; N–CH_2–CH–), 3.45 (dd, 1H, J = 5.0, 5.1 Hz; Ar–CH_2–CH–), 3.20–3.11 (m, 1H; Ar–CH_2–CH–), 2.77–2.73 (m, 1H; O=C–CH–CH_2–), 2.53–2.50 (m, 1H; –CH_2–CH–CH–); 2.42 ppm (s, 3H; O=C–CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.1, 166.5, 142.2, 141.0, 139.6, 136.1, 130.8, 129.7, 128.6, 128.3, 128.1, 127.6, 127.2, 127.1, 126.9, 51.6, 50.7, 45.5, 43.8, 31.4, 30.7 ppm; IR (KBr): $\tilde{\nu}$ = 3028, 2947, 2889, 1716 (C=O), 1705 (C=O), 1597, 1498, 1435, 1388, 1280, 1242, 1199, 1107, 987, 902, 759, 705 cm^{-1}; HRMS: m/z: calcd for $C_{26}H_{23}NO_2$: 381.1729; found: 381.1722.

1-Oxo-2,4-diphenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]isoindole-6-carbaldehyde (bc): White solid; 0.96 g (75% yield); m.p. 206–207°C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.81 (s, 1H; O=CH), 7.72 (d, 1H, J = 7.7 Hz; Ar–H), 7.58 (d, 1H, J = 7.9 Hz; Ar–H), 7.45–7.09 (m, 11H; Ar–H), 4.16 (d, 1H, J = 11.4 Hz; Ar–CH–), 3.70 (t, 1H, J = 9.7, 9.9 Hz; N–CH_2–CH–), 3.59 (t, 1H, J = 2.5, 6.9 Hz; N–CH_2–CH–), 3.50 (dd, 1H, J = 5.0, 5.1 Hz; Ar–CH_2–CH–), 3.23–3.14 (m, 1H; Ar–CH_2–CH–), 2.80–2.75

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(m, 1H; O=C−CH−CH_2−), 2.58–2.56 ppm (m, 1H; −CH_2−CH−CH−); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.5, 173.1, 142.6, 140.1, 131.6, 128.8, 127.7, 126.8, 124.1, 119.2, 51.6, 50.7, 44.9, 44.5, 30.8 ppm; IR (KBr): $\tilde{\nu}$ = 3028, 2966, 2862, 1689 (C=O), 1685 (C=O), 1597, 1496, 1392, 1300, 1203, 1099, 1068, 898, 829, 752, 690, 605, 513, 493 cm^{-1}; HRMS: *m/z*: calcd for $C_{25}H_{21}NO_2$: 367.1572; found: 367.1570.

Ethyl 1-oxo-2,4-diphenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]isoindole-6-carboxylate (bd): Colorless crystals; yield: 1.04 g (72%); m.p. 198–199 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88 (d, 1H, *J* = 8.0 Hz; Ar−H), 7.48 (s, 1H; Ar−H), 7.42–7.23 (m, 11H; Ar−H), 4.32–4.25 (q, 2H, *J* = 7.2, 7.1 Hz; O−CH_2−CH_3), 3.91 (d, 1H, *J* = 8.5 Hz; Ar−CH−), 3.49 (dd, 1H, *J* = 3.9, 3.8 Hz; N−CH_2−CH−), 3.31–3.20 (m, 1H; N−CH_2−CH−, 2H, Ar−CH_2−CH−), 3.18–3.08 (m, 1H; O=C−CH−CH_2−), 1.67 (m, 1H, −CH_2−CH−CH−), 1.29 ppm (t, 3H, *J* = 7.1, 7.1 Hz; −CH_2−CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.3, 166.0, 142.0, 140.6, 139.4, 139.1, 130.8, 129.7, 129.5, 128.9, 128.7, 128.4, 127.7, 127.1, 126.9, 124.3, 60.5, 53.4, 51.7, 49.3, 44.6, 30.6, 13.9 ppm; IR (KBr): $\tilde{\nu}$ = 3027, 2971, 2862, 1709 (C=O), 1688 (C=O), 1612, 1413, 1279, 1236, 1168, 1128, 942, 916, 823, 755, 703, 612 cm^{-1}; HRMS: *m/z*: calcd for $C_{27}H_{25}NO_3$: 411.1834; found: 411.1831.

6-(Methylsulfonyl)-2,4-diphenyl-2,3,3a,4,9,9a-hexahydrobenzo[*f*]isoindol-1-one (be): White solid; 1.19 g (82% yield); m.p. 205–206 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, 1H, *J* = 8.0 Hz; Ar−H), 7.57 (d, 1H, *J* = 7.9 Hz; Ar−H), 7.47–7.10 (m, 11H; Ar−H), 4.13 (d, 1H, *J* = 8.3 Hz; Ar−CH−), 3.68 (t, 1H, *J* = 9.7, 9.9 Hz; N−CH_2−CH−), 3.55 (t, 1H, *J* = 6.8, 6.9 Hz; N−CH_2−CH−), 3.48 (dd, 1H, *J* = 4.9, 5.0 Hz; Ar−CH_2−CH−), 3.17–3.21 (m, 1H; Ar−CH_2−CH−), 2.90 (s, 3H; O=S−CH_3), 2.77–2.73 (m, 1H; O=C−CH−CH_2−), 2.55–2.52 ppm (m, 1H; −CH_2−CH−CH−); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.9, 141.9, 140.9, 138.9, 130.7, 128.9, 128.4, 127.4, 124.9, 119.2, 51.5, 50.7, 44.8, 44.4, 44.0, 30.0 ppm; IR (KBr): $\tilde{\nu}$ = 3020, 2924, 2854, 1708 (C=O), 1597, 1496, 1392, 1300, 1176, 1145, 1107, 964, 898, 759, 694, 524 cm^{-1}; HRMS: *m/z*: calcd for $C_{25}H_{23}NO_3S$: 417.1399; found: 417.1393.

2-Benzyl-8-methyl-4-phenyl-3a,4,9,9a-tetrahydro-2*H*-benzo[*f*]isoindole-1,3-dione (ca): Colorless crystals; 1.08 g (81% yield); m.p. 149–150 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23–7.18 (m, 6H; Ar−H), 7.06–6.99 (m, 5H; Ar−H), 6.53–6.51 (m, 2H; Ar−H), 4.67 (s, 1H; Ar−CH−), 4.43 (d, 2H, *J* = 3.4 Hz; Ar-CH_2-N), 3.75–3.72 (m, 1H; O=C−CH−CH−), 3.31–3.26 (m, 1H; O=C−CH−CH_2−), 3.25–3.21 (m, 1H; Ar−CH_2−), 2.48–2.43 (m, 1H; Ar−CH_2−), 2.14 ppm (s, 3H; −CH_3−); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.9, 178.4, 138.4, 136.3, 135.1, 134.8, 131.1, 129.2, 128.4, 128.2, 127.6, 127.5, 127.0, 126.8, 126.6, 125.7, 44.7, 43.8, 41.9, 40.0, 29.2, 19.4 ppm; IR (KBr): $\tilde{\nu}$ = 3063, 3027, 2932, 2857, 1771 (C=O), 1697 (C=O), 1603, 1588, 1453, 1340, 1171 cm^{-1}; MS (EI, 70 ev): *m/z*: 380.9 (51.37) $[M]^+$, 214.0 (32.39), 219.0 (69.78), 91.0 (16.32), 58.0 (11.53), 43.0 (100.00); HRMS: *m/z*: calcd for $C_{26}H_{23}NO_2$: 381.1729; found: 381.1726.

2-Benzyl-6-methyl-4-phenyl-3a,4,9,9a-tetrahydro-2*H*-benzo[*f*]isoindole-1,3-dione (cb): White solid; 1.12 g (84% yield); m.p. 175–176 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.25–7.15 (m, 6H; Ar−H), 7.06–6.95 (m, 6H; Ar−H), 6.57–6.54 (d, 1H, *J* = 7.1 Hz; Ar−H), 4.71 (s, 1H; Ar−CH−), 4.44 (s, 2H; Ar−CH_2−N), 3.76–3.73 (d, *J* = 8.4 Hz, 1H; O=C−CH−CH−), 3.32–3.27 (t, *J* = 7.2, 7.5 Hz, 1H; O=C−CH−CH_2−), 3.01–2.96 (d, *J* = 14.7 Hz, 1H; Ar−CH_2−), 2.80–2.73 (q, *J* = 7.3, 7.3 Hz, 1H; Ar−CH_2−), 2.26 ppm (s, 3H; −CH_3); ^{13}C NMR (75.5 MHz, $CDCl_3$): δ = 178.9, 178.3, 140.0, 136.2, 134.6, 134.3, 129.2, 128.5, 128.3, 128.1, 127.9, 127.7, 127.4, 126.8, 126.5, 126.3, 45.3, 41.9, 39.7, 29.2, 19.4 ppm; IR (KBr): $\tilde{\nu}$ = 3060, 3026, 2926, 2851, 1772 (C=O), 1704 (C=O), 1602, 1448, 1342, 1170 cm^{-1}; HRMS: *m/z*: calcd for $C_{26}H_{23}NO_2$: 381.1729; found: 381.1725.

2-Benzyl-6-chloro-4-phenyl-3a,4,9,9a-tetrahydro-2*H*-benzo[*f*]isoindole-1,3-dione (cc): White solid; 0.91 g (65% yield); m.p. 168–169 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.18 (m, 6H; Ar−H), 7.14–7.03 (m, 5H; Ar−H), 6.63–6.61 (m, 2H; Ar−H), 4.72 (s, 1H; Ar−CH−), 4.51 (s, 2H; Ar−CH_2−N), 3.77–3.73 (d, *J* = 7.1 Hz, 1H; O=C−CH−CH−), 3.36–3.32 (t, *J* = 7.2 Hz, 1H; O=C−CH−CH_2−), 3.09–3.04 (d, *J* = 15 Hz, 1H; Ar−CH_2−), 2.85–2.75 ppm (q, *J* = 7.5, 7.5 Hz, 1H; Ar−CH_2−); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.7, 178.0, 145.2, 139.8, 138.6, 135.8, 134.2, 130.9, 128.5, 128.1, 127.9, 127.6, 126.5, 126.0, 119.7, 45.3, 44.8, 43.9, 39.6, 29.2 ppm; IR (KBr): $\tilde{\nu}$ = 3018, 2943, 2891, 1774 (C=O), 1691 (C=O), 1340, 1172 cm^{-1}; MS (EI, 70 ev): *m/z*: 400.8 (34.21) $[M]^+$, 238.9 (100.0), 203.9 (17.25), 91.0 (19.73); HRMS: *m/z*: calcd for $C_{25}H_{20}ClNO_2$: 401.1183; found: 401.1181.

2-Benzyl-1,3-dioxo-4-phenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]isoindole-6-carbonitrile (cd): White solid; 1.18 g (86% yield); m.p. 125–126 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63–7.60 (m, 2H; Ar−H), 7.34–6.83 (m, 10H; Ar−H), 6.65–6.62 (m, 2H; Ar−H), 4.80 (s, 1H; Ar−CH−), 4.54 (s, 2H; Ar−CH_2−N), 3.81–3.78 (d, *J* = 8.9 Hz, 1H; O=C−CH−CH−), 3.41–3.36 (t, *J* = 8.7 Hz, 1H; O=C−CH−CH_2−), 3.14–3.09 (d, *J* = 15 Hz, 1H; Ar−CH_2−), 2.77–2.70 ppm (q, *J* = 7.2, 7.2 Hz, 1H; Ar−CH_2−); ^{13}C NMR (75 Hz, $CDCl_3$): δ = 178.3, 177.6, 145.7, 134.9, 134.5, 134.2, 132.1, 129.1, 128.8, 128.6, 128.0, 127.8, 127.6, 127.0, 126.8, 126.5, 118.19, 110.5, 45.5, 45.1, 42.0, 39.7, 29.2 ppm; IR (KBr): $\tilde{\nu}$ = 3059, 3028, 2914, 2856, 2429, 1776 (C=O), 1703 (C=O), 1606, 1456, 1340, 1167 cm^{-1}; MS (EI, 70 ev): *m/z*: 391.9 (28.60) $[M]^+$, 230.0 (100.0), 91.0 (18.66); HRMS: *m/z*: calcd for $C_{26}H_{20}N_2O_2$: 392.1525; found: 392.1518.

2-Benzyl-7-chloro-4-phenyl-3a,4,9,9a-tetrahydro-2*H*-benzo[*f*]isoindole-1,3-dione (ce): White solid; 0.94 g (67% yield); m.p. 129–130 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.28–7.16 (m, 6H; Ar−H), 7.10–6.94 (m, 5H; Ar−H), 6.49 (d, *J* = 7.2 Hz, 2H; Ar−H), 4.50 (d, *J* = 5.7 Hz, 1H; Ar−CH−), 4.37 (s, 2H; Ar−CH_2−N), 3.25–3.23 (t, *J* = 1.8, 2.3 Hz, 1H; O=C−CH−CH−), 3.12–3.07 (d, *J* = 14.5 Hz, 1H; O=C−CH−CH_2−), 2.84–2.79 ppm (m, 2H; Ar−CH_2−); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.8, 168.7, 134.8, 134.2, 130.9, 128.5, 128.1, 127.7, 127.1, 126.8, 126.5, 119.7, 45.3, 44.8, 41.8, 39.7, 29.3 ppm; IR (KBr): $\tilde{\nu}$ = 3066, 3026, 2928, 2912, 2847, 1772 (C=O), 1697 (C=O), 1608, 1456, 1286, 1174 cm^{-1}; HRMS: *m/z*: calcd for $C_{25}H_{20}ClNO_2$: 401.1183; found: 401.1180.

Isopropyl 2–1,3-dioxo-4-phenyl-2,3,3a,4,9,9a-hexahydro-1*H*-benzo[*f*]-isoindole-6-carboxylate (cf): White solid; 1.32 g (83% yield); m.p. 165–166 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.90–7.88 (d, *J* = 8.1 Hz, 2H; Ar−H), 7.22–6.98 (m, 9H; Ar−H), 6.55–6.53 (d, *J* = 7.2 Hz, 2H; Ar−H), 5.20–5.12 (m, 1H; −O−CH−), 4.72 (s, 1H; Ar−CH−), 4.44 (s, 2H; Ar−CH_2−N), 3.76–3.74 (d, *J* = 7.2 Hz, 1H; O=C−CH−CH−), 3.31–3.26 (t, *J* = 7.5, 7.2 Hz, 1H, O=C−CH−CH_2−), 3.01–2.96 (d, *J* = 15 Hz, 1H; Ar−CH_2−), 2.73–2.65 (q, *J* = 7.2, 7.2 Hz, 1H; Ar−CH_2−), 1.30–1.26 ppm (m, 6H; −CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.6, 178.0, 165.3, 145.1, 135.7, 134.6, 134.3, 130.0, 129.5, 129.1, 128.6, 128.4, 128.1, 128.0, 127.6, 126.9, 126.8, 126.7, 126.5, 68.1, 45.4, 45.2, 42.0, 39.6, 39.5, 29.4, 29.2, 21.6 ppm; IR (KBr): $\tilde{\nu}$ = 3064, 3026, 2928, 2912, 2847, 1774 (C=O), 1716 (C=O), 1697 (C=O), 1608, 1454, 1286, 1174, 1028 cm^{-1}; HRMS: *m/z*: *m/z*: calcd for $C_{29}H_{27}NO_4$: 453.1940; found: 453.1945.

9-Benzyl-7-phenyl-7,7a,10a,11-tetrahydro-9*H*-naphtho[2,1-*f*]isoindole-8,10-dione (cg): Colorless crystals; 1.15 g (79% yield); m.p. 167–168 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.43 (m, 6H; Ar−H), 7.26–6.84 (m, 6H; Ar−H), 6.69–6.64 (m, 2H; Ar−H), 6.37–6.34 (d, *J* = 7.2 Hz, 2H; Ar−H), 4.88 (s, 1H; Ar−CH−), 4.34 (s, 2H; Ar−CH_2−N), 3.90–3.79 (m, 2H; O=C−CH−CH−, O=C−CH−CH_2−), 3.45–3.40 (t, *J* = 7.5, 7.7 Hz, 1H; Ar−CH_2−), 2.76–2.69 ppm (q, *J* = 7.1, 7.1 Hz, 1H; Ar−CH_2−); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 178.9, 178.3, 140.0, 134.4, 134.0, 133.1, 131.2, 130.3, 128.4, 128.3, 127.8, 127.5, 127.3, 126.8, 126.7, 126.4, 126.3, 125.4, 122.6, 45.9, 45.3, 41.9, 39.8, 23.6 ppm; IR (KBr): $\tilde{\nu}$ = 3061, 2989, 2926, 2889, 1774 (C=O), 1701 (C=O), 1606, 1494, 1338, 1166 cm^{-1}; MS (EI, 70 ev): *m/z*: 416.9 (89.01) $[M]^+$, 325.9 (11.76), 254.9 (100.00), 178.0 (10.85), 91.2 (47.45), 43.0 (20.74); HRMS: *m/z*: calcd for $C_{29}H_{23}NO_2$: 417.1729; found: 417.1733.

Mathyl 4-((1-benzyl-4-benzylidene-2-oxopyrrolidin-3-yl)methyl)benzoate (d): Colorless solid; 0.76 g (53% yield); m.p. 135–136 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.82 (d, 1H, *J* = 8.0 Hz; Ar−H), 7.01–7.49 (m, 11H; Ar−H), 4.59 (d, 1H, *J* = 14.7 Hz; Ar−CH_2−N), 4.25 (d, 1H, *J* = 14.7 Hz; Ar−CH_2−N), 6.46 (s, 1H; C=CH), 3.75 (s, 3H; −O−CH_3), 3.83–3.94 (m, 2H; N−CH_2−CH−), 3.51 (m, 1H; O=C−CH−CH_2−), 2.79–2.73 (m, 2H; Ar−CH_2−CH−); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.4, 166.3, 143.9, 139.6, 137.3, 137.1, 130.8, 129.7, 128.5, 128.2, 127.6, 127.4, 127.3, 127.1, 126.9, 124.2, 55.8, 51.6, 49.5, 35.9, 31.2 ppm; IR (KBr): ν = 3296, 3081, 2879, 1716 (C=O), 1678 (C=O), 1653, 1615, 1346, 1229, 1146, 1123, 1097, 757, 710, 615 cm^{-1}; HRMS: *m/z*: calcd for $C_{27}H_{25}NO_3$: 411.1834; found: 411.1830.

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[1] a) L. F. Tietze, U. Beifuss, *Angew. Chem.* **1993**, *105*, 137–170; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 131–163; b) L. F. Tietze, *Chem. Rev.* **1996**, *96*, 115–136; c) N. Hall, *Science* **1994**, *266*, 32–34; d) L. F. Tietze, G. Brasche, K. Gericke, *Domino Reactions in Organic Synthesis*, Wiley-VCH, Weinheim, **2006**; e) A. de Meijere, *Acc. Chem. Res.* **2005**, *38*, 413–422.

[2] a) D. Enders, M. R. M. Hüttl, C. Grondal, G. Raabe, *Nature* **2006**, *441*, 861–863; b) K. C. Nicolaou, T. Montagnon, S. A. Snyder, *Chem. Commun.* **2003**, 551–564; c) K. C. Nicolaou, Y. H. Lim, C. D. Papageorgiou, J. L. Piper, *Angew. Chem.* **2005**, *117*, 8131–8135; *Angew. Chem. Int. Ed.* **2005**, *44*, 7917–7921.

[3] a) *Metal-Catalyzed Cross-Coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, New York, **1998**; b) K. C. Nicolaou, E. J. Sorensen, *Classics in Total Synthesis*, Wiely-VCH, Weinheim, **1996**; c) K. C. Nicolaou, D. J. Edmonds, P. G. Bulger, *Angew. Chem.* **2006**, *118*, 7292–7344; *Angew. Chem. Int. Ed.* **2006**, *45*, 7134–7186; d) E. Negishi, J.-C. Shi, S. Huo, *Angew. Chem.* **2002**, *114*, 2245–2247; *Angew. Chem. Int. Ed.* **2002**, *41*, 2141–2143; e) T.-L. Ho, *Tandem Organic Reactions*, Wiley, New York, **1992**.

[4] a) S. Iimura, L. E. Overman, R. Paulini, A. Zakarian, *J. Am. Chem. Soc.* **2006**, *128*, 13095–13101; b) A. Madin, C. J. O'Donnell, T. Oh, D. W. Old, L. E. Overman, M. J. Sharp, *J. Am. Chem. Soc.* **2005**, *127*, 18054–18065; c) N. Miyaura, *Top. Curr. Chem.* **2002**, *219*, 11–59; d) B. M. Trost, P. A. Hipskind, *Tetrahedron Lett.* **1992**, *33*, 4541–4544; e) S. R. Chemler, D. Trauner, S. J. Danishefsky, *Angew. Chem.* **2001**, *113*, 4676–4701; *Angew. Chem. Int. Ed.* **2001**, *40*, 4544–4568.

[5] a) R. G. Bergman, *Nature* **2007**, *446*, 391–393; b) E. M. Ferreira, B. M. Stoltz, *J. Am. Chem. Soc.* **2003**, *125*, 9578–9579; c) X. Chen, J.-J. Li, X.-S. Hao, C. E. Goodhue, J.-Q. Yu, *J. Am. Chem. Soc.* **2006**, *128*, 78–79; d) B. Sezen, R. Franz, D. Sames, *J. Am. Chem. Soc.* **2002**, *124*, 13372–13373; e) N. Tsukada, T. Mitsuboshi, H. Setoguchi, Y. Inoue, *J. Am. Chem. Soc.* **2003**, *125*, 12102–12103; f) C. Zhou, R. C. Larock, *J. Am. Chem. Soc.* **2004**, *126*, 2302–2303; g) B. A. Arndtsen, R. G. Bergman, T. A. Mobley, T. H. Petersen, *Acc. Chem. Res.* **1995**, *28*, 154–162; h) M. Tobisu, N. Chatani, *Angew. Chem.* **2006**, *118*, 1713–1715; *Angew. Chem. Int. Ed.* **2006**, *45*, 1683–1684.

[6] a) Z. Shi, B. Li, X. Wan, J. Cheng, Z. Fang, B. Cao, C. Qin, Y. Wang, *Angew. Chem.* **2007**, *119*, 5650–5654; *Angew. Chem. Int. Ed.* **2007**, *46*, 5554–5558; b) G. Cai, Y. Fu, Y. Li, X. Wan, Z. Shi, *J. Am. Chem. Soc.* **2007**, *129*, 7666–7673; c) S. Yang, B. Li, X. Wan, Z. Shi, *J. Am. Chem. Soc.* **2007**, *129*, 6066–6067; d) Z. Shi, H. Chuan, *J. Org. Chem.* **2004**, *69*, 3669–3671; e) X. Wan, Z. Ma, B. Li, K. Zhang, S. Cao, S. Zhang, Z. Shi, *J. Am. Chem. Soc.* **2006**, *128*, 7416–7417.

[7] a) R. Grigg, V. Savic, V. Tambyrajah, *Tetrahedron Lett.* **2000**, *41*, 3003–3006; b) C. C. Hughes, D. Trauner, *Angew. Chem.* **2002**, *114*, 1639–1642; *Angew. Chem. Int. Ed.* **2002**, *41*, 1569–1572; c) E. J. Hennessy, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 12084–12085; d) B. Sezen, D. Sames, *J. Am. Chem. Soc.* **2003**, *125*, 10580–10585; e) B. S. Lane, D. Sames, *Org. Lett.* **2004**, *6*, 2897–2900; f) D. R. Stuart, K. Fagnou, *Science* **2007**, *316*, 1172–1175.

[8] a) T. Harayama, H. Yasuda, T. Akiyama, Y. Take Takeuchi, H. Abe, *Chem. Pharm. Bull.* **2000**, *48*, 861–864; b) T. Harayama, H. Akamatsu, K. Okamura, T. Miyagoe, T. Akiyama, H. Abe, Y. Takeuchi, *J. Chem. Soc. Perkin Trans. 1* **2001**, 523–528; c) M. A. Campo, Q. Huang, T. Yao, Q. Tian, R. C. Larock, *J. Am. Chem. Soc.* **2003**, *125*, 11506–11507; d) L.-C. Campeau, M. Parisien, M. Leb Leblanc, K. Fagnou, *J. Am. Chem. Soc.* **2004**, *126*, 9186–9187; e) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174–238; f) C. Jia, T. Kitamura, Y. Fujiwara, *Acc. Chem. Res.* **2001**, *34*, 633–639.

[9] a) D. E. Ames, A. Opalko, *Tetrahedron* **1984**, *40*, 1919–1925; b) J. E. Rice, Z.-W. Cai, *J. Org. Chem.* **1993**, *58*, 1415–1424; c) S. Pogodin, P. U. Biedermann, I. Agranat, *J. Org. Chem.* **1997**, *62*, 2285–2287; d) T. Iwaki, A. Yasuhara, T. Sakamoto, *J. Chem. Soc. Perkin Trans. 1* **1999**, 1505–1510; e) R. K. Thalji, J. A. Ellman, R. G. Bergman, *J. Am. Chem. Soc.* **2004**, *126*, 7192–7193.

[10] a) P. Mauleon, I. Alonso, P. Mauleon, I. Alonso, J. C. Carretero, *Angew. Chem.* **2001**, *113*, 1331–1333; *Angew. Chem. Int. Ed.* **2001**, *40*, 1291–1293; b) P. Mauleon, A. A. Nunez, I. Alonso, J. C. Carretero, *Chem. Eur. J.* **2003**, *9*, 1511–1520; c) I. Alonso, M. Alcamí, P. Mauleón, J. C. Carretero, *Chem. Eur. J.* **2006**, *12*, 4576–4583; d) H. Ohno, K. Miyamura, T. Mizutani, Y. Kadoh, Y. Takeoka, H. Hamaguchi, T. Tanaka, *Chem. Eur. J.* **2005**, *11*, 3728–3741; e) H. Ohno, T. Mizutani, Y. Kadoh, K. Miyamura, T. Tanaka, *Angew. Chem.* **2005**, *117*, 5243–5245; *Angew. Chem. Int. Ed.* **2005**, *44*, 5113–5115.

[11] a) A. Pinto, L. Neuville, J. Zhu, *Angew. Chem.* **2007**, *119*, 3355–3359; *Angew. Chem. Int. Ed.* **2007**, *46*, 3291–3295; b) G. Cuny, M. Choussy, J. Zhu, *Angew. Chem.* **2003**, *115*, 4922–4925; *Angew. Chem. Int. Ed.* **2003**, *42*, 4774–4777.

[12] a) B. M. Trost, *Angew. Chem.* **1995**, *107*, 285–307; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259–281; b) P. A. Wender, S. T. Handy, D. L. Wright, *Chem. Ind.* **1997**, 765–769; c) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695 –705; d) B. M. Trost, *Science* **1991**, *254*, 1471–1477.

[13] a) Q. Huang, A. Fazio, G. Dai, M. A. Campo, R. C. Larock, *J. Am. Chem. Soc.* **2004**, *126*, 7460–7461; b) M. A. Campo, Q. Huang, T. Yao, Q. Tian, R. C. Larock, *J. Am. Chem. Soc.* **2003**, *125*, 11506–11507; c) H.-Y. Thu, W.-Y. Yu, C.-M. Che, *J. Am. Chem. Soc.* **2006**, *128*, 9048–9049; d) R. Giri, N. Maugel, J.-J. Li, D.-H. Wang, S. P. Breazzano, L. B. Saunders, J.-Q. Yu, *J. Am. Chem. Soc.* **2007**, *129*, 3510–3511; e) J. Zhao, D. Yue, M. A. Campo, R. C. Larock, *J. Am. Chem. Soc.* **2007**, *129*, 5288–5295; f) J. Zhao, M. Campo, R. C. Larock, *Angew. Chem.* **2005**, *117*, 1907–1909; *Angew. Chem. Int. Ed.* **2005**, *44*, 1873–1875.

[14] a) D. Kalyani, N. R. Deprez, L. V. Desai, M. S. Sanford, *J. Am. Chem. Soc.* **2005**, *127*, 7330–7331; b) L. V. Desai, K. L. Hull, M. S. Sanford, *J. Am. Chem. Soc.* **2004**, *126*, 9542–9543; c) A. R. Dick, K. L. Hull, M. S. Sanford, *J. Am. Chem. Soc.* **2004**, *126*, 2301–2302; d) R. Giri, X. Chen, J. Q. Yu, *Angew. Chem.* **2005**, *117*, 2150–2153; *Angew. Chem. Int. Ed.* **2005**, *44*, 2112–2115.

[15] a) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* **2007**, *107*, 174–238; b) J.-P. Corbet, G. Mignani, *Chem. Rev.* **2006**, *106*, 2651–2710; c) M. Catellani, E. Motti, F. Faccini, R. Ferraccioli, *Pure Appl. Chem.* **2005**, *77*, 1243–1248.

[16] CCDC 664803 (**bd**), 664804 (**ab**), and 664805 (**cg**) 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.

[17] a) D. García-Cuadrado, P. D. Mendoza, A. A. C. Braga, F. Maseras, A. M. Echavarren, *J. Am. Chem. Soc.* **2007**, *129*, 6880–6886; b) D. GarcMa-Cuadrado, A. A. C. Braga, F. Maseras, A. M. Echavarren, *J. Am. Chem. Soc.* **2006**, *128*, 1066–1067.

[18] a) G. M. Sheldrick, SHELXL97, *Program for Crystal Structure Refinement*, University of Göttingen (Germany), **1997**; b) G. M. Sheldrick, SHELXS97, *Program for Crystal Structure Refinement*, University of Göttingen (Germany), **1997**; c) G. M. Sheldrick, *Acta Crystallogr. Sect. A* **1990**, *46*, 467–473.

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