

# Regioselective Synthesis of Heterospirocyclic Isobenzofuranones and Medium-Sized Lactones by Multiple Anion Capture Reactions of 1,3-Dianions

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The multicomponent reaction of 1,3-dianions with ketones and oxalic acid dichloride or diethylmalonic dichloride afforded six- to eight-membered lactones. Treatment of the dianion of 3-acetylindole with benzophenone and diethylma-

lonic dichloride resulted in the formation of a cyclic 1,3,5-triketooctene. The reaction of 1,3-dianions with ketones and phthalic dichloride resulted in the formation of heterospirocyclic isobenzofuranones rather than of medium-sized rings.

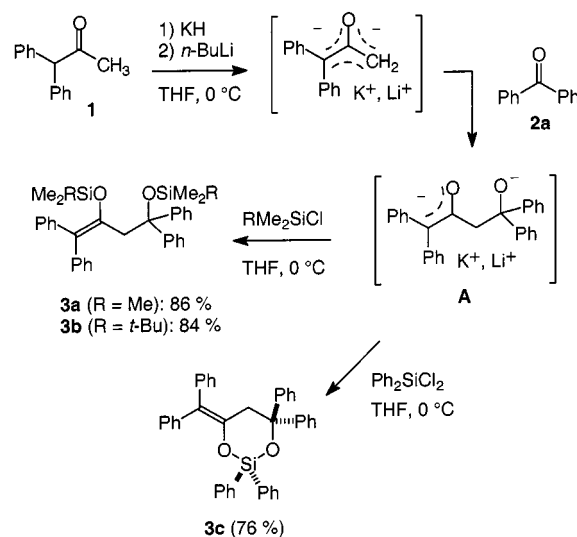
Domino and multi-component reactions have found widespread applications in organic synthesis.<sup>[1]</sup> Multiple anion capture reactions involve attack of a carbanion on a relais species to form an intermediate which is subsequently reacted with an electrophile. Recent examples include the reaction of carbon nucleophiles with allenes and subsequent cyclization with acrylates,<sup>[2]</sup> and reactions involving isocyanates<sup>[3]</sup> or allenyl isothiocyanates as the relais species.<sup>[4]</sup> Multiple anion capture reactions involving nitriles as the relais species have been observed in the reaction of bislithiated 2,3-methylbutadiene with benzonitrile,<sup>[5]</sup> and in the 1,4-addition of nitriles to (butadiene)zirconocene.<sup>[6]</sup> In the course of our program<sup>[7]</sup> directed at the development of cyclization reactions of dianions<sup>[8]</sup> and dianion equivalents with dielectrophiles, we have recently studied nitriles as relais species in reactions of 1,3-dianions<sup>[9a–9c]</sup> and dilithiated allenes.<sup>[9d]</sup> We wish to report full details of our studies related to multiple anion capture reactions of 1,3-dianions with ketones and carboxylic acid dichlorides.<sup>[10]</sup> These reactions provide an efficient access to medium-sized lactones and novel heterospirocyclic isobenzofuranones.<sup>[11–13]</sup>

## Results and Discussion

### Synthesis of Lactones and Silyl Ethers

Chlorosilanes were used in our first experiments aimed at demonstrating the concept of multiple anion capture reactions of dianions with ketone relais species. The dianion<sup>[14]</sup> of 1,1-diphenylacetone **1** was generated by treatment of **1** with potassium hydride and *n*BuLi. The dianion was condensed in situ with one equivalent of benzophenone **2a** to give the dianionic intermediate **A** by regioselective attack of the terminal carbon atom of the dianion at the carbonyl group. Owing to steric and electronic reasons (delocaliz-

ation of the negative charge through the phenyl rings), the carbon attached to the phenyl groups is less nucleophilic than the terminal carbon of the dianion. Subsequent addition of Me<sub>3</sub>SiCl gave the open-chain silyl ethers **3a** and **3b** in high yields (Scheme 1). Reaction of intermediate **A** with dichloro-diphenylsilane afforded the 1,3,2-dioxasilinane **3c** in 76% yield.



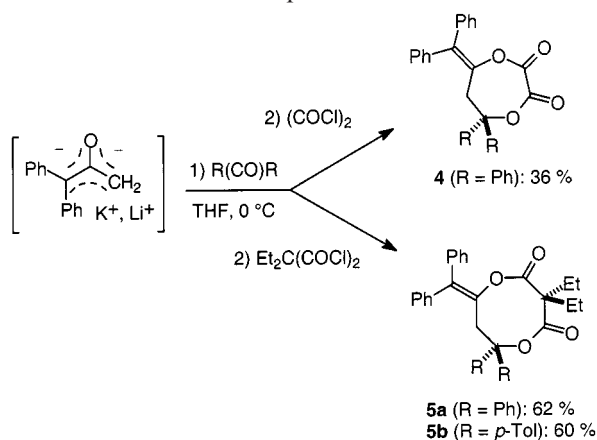
Scheme 1. Reaction of the dianion of 1,1-diphenylacetone with benzophenone and chlorosilanes

Three-component cyclizations of dianions with ketones and dicarboxylic acid dichlorides were studied next. These reactions can, in principle, result in the formation of different regioisomeric cyclization products, as well as macrocyclic or polymeric products. In fact, we have found that they provide an efficient access to medium-sized dilactones. Reaction of the dianion of **1** with benzophenone, and subsequent cyclization with oxalyl chloride gave the 1,4-dioxepane-2,3-dione **4**. Reaction of the dianion of 1,1-diphenylacetone (**1**) with benzophenone (**2a**) or bis(*p*-tolyl) ketone (**2b**) and subsequent addition of diethylmalonic dichloride afforded the eight-membered 1,5-dioxocane-2,4-diones **5a** and **5b**, respectively, in good yields (Scheme 2). Reaction of the dianion of 2-methylbenzimidazole (**6**),<sup>[15]</sup>

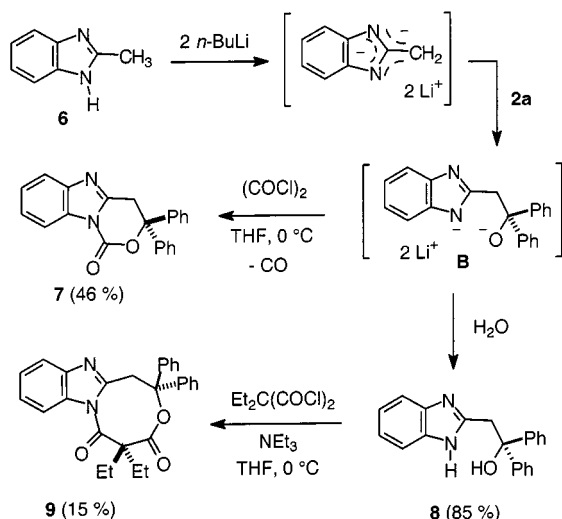
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(an aza analogue of **1**) with benzophenone, and subsequent treatment with oxalyl chloride resulted in the release of CO,<sup>[16]</sup> and in the formation of the 3,4-dihydrobenzo[4,5]-imidazo[1,2-*c*][1,3]oxazin-1-one (**7**) (Scheme 3). Oxazepins are known to undergo decarbonylation reactions at elevated temperatures, and have been used for the synthesis of reserpine alkaloids.<sup>[17]</sup> Reaction of the dianion of **6** with benzophenone and subsequent aqueous quench gave the alcohol **8** (85%) which was reacted with diethylmalonic dichloride to give the eight-membered ring **9**. A direct synthesis of dilactone **9** from **6** was not possible.



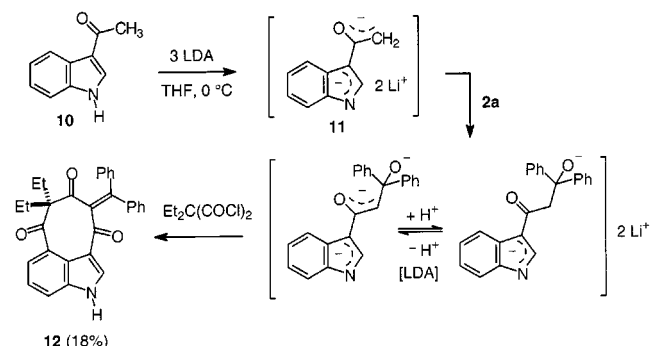
Scheme 2. Synthesis of medium-sized dilactones derived from 1,1-diphenylacetone



Scheme 3. Reaction of the dianion of 2-methylbenzimidazole with benzophenone and dicarboxylic acid dichlorides

Reaction of the dianion **11** of 3-acetylindole (**10**) with benzophenone and subsequent addition of  $\text{Et}_2\text{C}(\text{COCl})_2$  resulted in the formation of a complex mixture, from which the 1,3,5-triketooctene **12** could be isolated (18%) (Scheme 4). Interestingly, **12** contained an eight-membered ring annulated at the 3- and 4-positions of the indole moiety. As an excess of LDA was used, regeneration of an enolate anion appears to be possible after condensation of **11** with benzophenone. The carbon center of the enolate reacts with the dielectrophile, and subsequent ring closure involves

attack at C-4 of the indole system, as an attack at the nitrogen atom would lead to a highly strained product. The exocyclic double bond  $\text{C}=\text{CPh}_2$  is formed by elimination of water during the aqueous workup.<sup>[18]</sup>

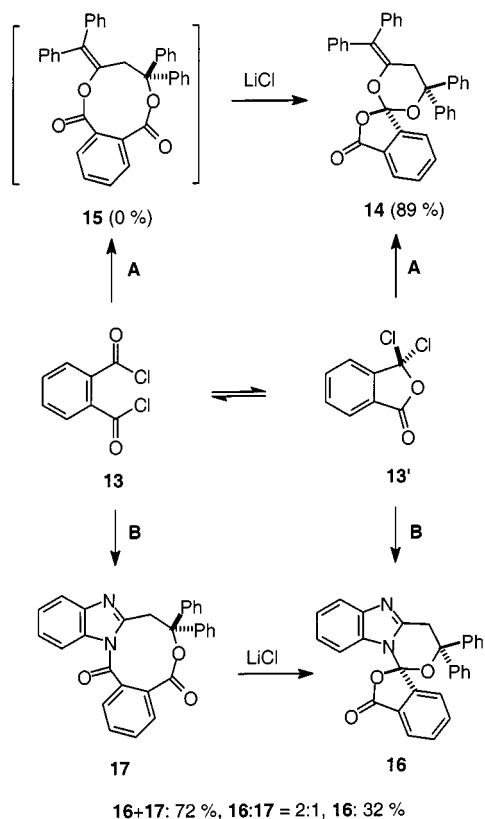


Scheme 4. Reaction of the dianion of 3-acetylindole with benzophenone and diethylmalonic dichloride

### Synthesis of Heterospirocyclic Isobenzofuranones

Reaction of the dianion of 1,1-diphenylacetone with benzophenone, and subsequent addition of phthalic dichloride (**13**) afforded the novel spiro-annulated 1,3-dioxane-2,1'-isobenzofuran-3'-one **14** in 89% yield, rather than the isomeric nine-membered ring **15** (Scheme 5). Similarly, the multiple anion capture reaction of the dianion of 2-methylbenzimidazole with benzophenone and phthalic dichloride afforded a 2:1 mixture (72%) of the spirocyclic amino orthoester **16**, which was isolated in a pure form in 32% yield, and of the nine-membered ring isomer **17**. Unfortunately, complex mixtures were formed when the dianions **A** and **B** were reacted with succinic dichloride. The structures of the isobenzofuranones **14** and **16** were established by means of spectroscopic analysis. For the eight-membered dilactone **5a**, a singlet was observed for the  $\text{CH}_2$  group ( $^1\text{H}$  NMR). In contrast, an AB-system ( $J = 16$  Hz) was observed for the orthoesters **14** and **16**. In contrast to dilactones **5**, only one carbonyl signal was detected for **14** and **16** ( $^{13}\text{C}$  NMR and IR spectroscopy).

The structure of isobenzofuranone **16** was independently confirmed by crystal structure analysis (Figure 1). The geometry in the spiro carbon atom C-4 is only slightly distorted from that of an ideal tetrahedron (the bond angles vary from  $103.3^\circ$  to  $114.6^\circ$ ). The bond length C4–O1 is significantly shorter than C3–O1, presumably due to the anomeric effect within the spiro-orthoester function.<sup>[19]</sup> The C4–O2 bond is relatively long and the C29–O2 bond is short, owing to the electronic influence of the neighboring carbonyl group. Only minor difference in the bond length is observed in the annulated benzene moieties. The N2–C1 bond, which is part of the amidine function, is slightly shorter than the N2–C10 bond. An AB-system ( $^1\text{H}$  NMR) is detected for the diastereotopic  $\text{CH}_2$  hydrogen atoms. Interestingly, deshielding is drastically decreased for the resonance assigned to H9, which is located within the anisotropic cone of the isobenzofuran-3'-one moiety and is shifted upfield by 1.4 ppm relative to the respective signal of 2-methylbenzimidazole.



Scheme 5. Synthesis of heterospirocyclic isobenzofuranones derived from 1,1-diphenylacetone and 2-methylbenzimidazole

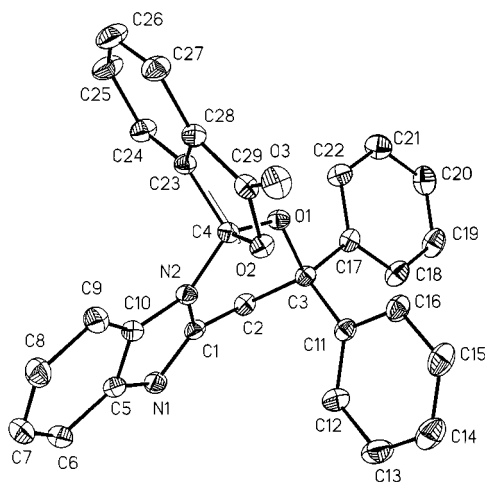
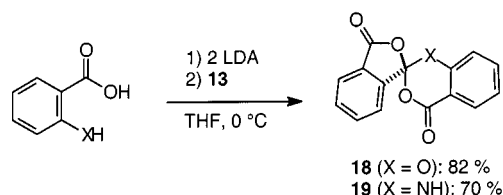


Figure 1. ORTEP plot of **16**. The thermal ellipsoids of 50% probability are shown for the non-hydrogen atoms. Selected bond lengths [Å] and angles [°]: C(1)–C(4) 1.370(3), O(2)–C(29) 1.372(3), O(3)–C(29) 1.200(3), N(1)–C(5) 1.392(3), N(2)–C(10) 1.396(3), N(2)–C(1) 1.381(3), N(2)–C(4) 1.442(3), C(2)–C(3) 1.530(3), C(5)–C(6) 1.390(3), C(6)–C(7) 1.369(5), C(1)–C(2) 1.472(4), C(5)–C(10) 1.399(4), C(7)–C(8) 1.393(5), C(8)–C(9) 1.381(4), C(9)–C(10) 1.385(4), O(1)–C(3) 1.476(3), O(2)–C(4) 1.462(3), N(1)–C(1) 1.299(3); C(4)–O(1)–C(3) 120.5(2), C(1)–N(1)–C(5) 105.2(2), C(1)–N(2)–C(4) 124.8(2), N(1)–C(1)–N(2) 112.9(2), N(2)–C(1)–C(2) 117.8(2), C(10)–N(2)–C(4) 128.2(2), N(1)–C(1)–C(2) 129.3(3), C(1)–C(2)–C(3) 108.6(2), C(29)–O(2)–C(4) 110.6(2), C(1)–N(2)–C(10) 107.0(2).

The formation of the isobenzofuranone rather than of the medium-sized ring isomers can be explained on thermodynamic grounds,<sup>[20]</sup> and presumably proceeds by cycliza-

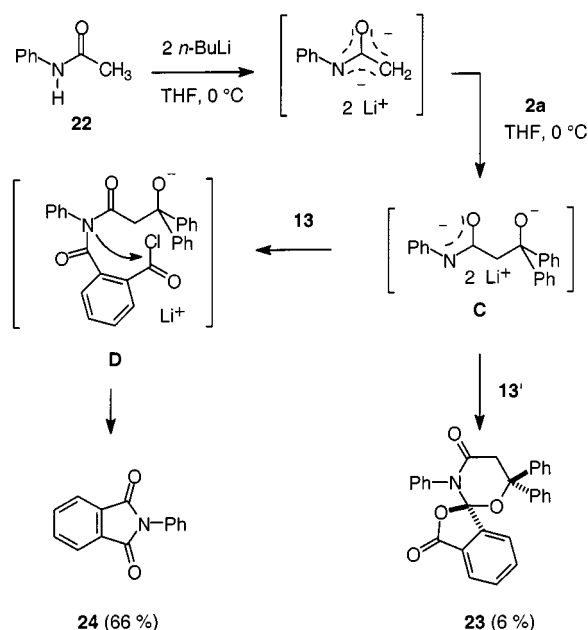
tion of the dianionic intermediates **A** and **B** with the unsymmetric isophthalic dichloride **13'**, which is formed in situ from **13** by Lewis acid catalysis (LiCl) under the reaction conditions.<sup>[21]</sup> Alternatively, initial formation of the medium-sized ring isomers and subsequent base-mediated rearrangement of the latter to form the heterospirocyclic isobenzofuranones represents a possible mechanism.<sup>[22]</sup>

The dianions of salicylic and anthranilic acid,<sup>[23]</sup> which represent analogues of dianions **A** and **B**, respectively, were employed next as starting materials. To our satisfaction, reaction of the lithium salt of salicylic acid with phthalic dichloride afforded the known<sup>[23]</sup> oxaspirocyclic isobenzofuranone **18** (Scheme 6). The base-mediated reaction of anthranilic acid with phthalic dichloride proceeded equally successfully and gave the known<sup>[23]</sup> oxazaspirocyclic product **19**.



Scheme 6. Synthesis of heterospirocyclic isobenzofuranones **18** and **19**

The reaction of the dianion of 1,3-diphenylacetone **20**<sup>[24]</sup> with benzophenone and trimethylchlorosilane afforded the silyl enol ether  $\text{PhCH}=\text{C}(\text{OSiMe}_3)\text{CH}(\text{Ph})-\text{C}(\text{OSiMe}_3)\text{Ph}_2$  (**21**) in 83% yield. In contrast, complex mixtures were obtained when diethylmalonic dichloride and phthalic dichloride were used. Reaction of the dianion of acetanilide (**22**)<sup>[25]</sup> with benzophenone and subsequent reaction with phthalic dichloride resulted in the formation of the oxazaspirocyclic isobenzofuranone **23** in low yield (Scheme 7). The main



Scheme 7. Reaction of the dianion of acetanilide with benzophenone and phthalic dichloride

product (66%) was *N*-phenylphthalimide (**24**), which was presumably formed by a transamination process *via* intermediates **C** and **D**.

In summary, we have reported multiple anion capture reactions of 1,3-dianions with ketones and dielectrophiles. These reactions provide a convenient access to novel medium-sized lactones and heterospirocyclic isobenzofuranones. Medium-sized lactones<sup>[11,12]</sup> and heterospirocyclic systems<sup>[13]</sup> are of pharmacological relevance. Heterospirocyclic systems are also of interest as photochromic materials.<sup>[26]</sup> Our current work is directed towards further exploring the preparative scope of the cyclization reactions presented.

## Experimental Section

**General:** All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. Petroleum ether (PE, bp 40–70 °C), diethyl ether (E) and *tert*-butyl methyl ether (MTBE) were distilled prior to use. – For <sup>1</sup>H NMR, CDCl<sub>3</sub> and CD<sub>2</sub>Cl<sub>2</sub> were used as solvents, with TMS as internal standard, or [D<sub>8</sub>]THF as solvent  $\delta$  = 1.73, 3.58; for <sup>13</sup>C NMR, CDCl<sub>3</sub> was used as solvent, with TMS as internal standard, or [D<sub>8</sub>]THF as solvent,  $\delta$  = 25.5, 67.7. The multiplicity of the C atoms was determined by the DEPT 135 technique and quoted as: CH<sub>3</sub>, CH<sub>2</sub>, CH and C for primary, secondary, tertiary and quaternary carbon atoms. – MS: EI, 70 eV; CI, H<sub>2</sub>O: chemical ionization with water. – Preparative scale chromatography: J. T. Baker silica gel (60–200 mesh). – Melting points are uncorrected and were measured using a Büchi apparatus. – Elemental analyses: Microanalytical laboratory of the Universities of Hannover and Jena.

**General Procedure for Multiple Anion Capture Reactions of the Dianion of 1,1-Diphenylacetone (1):** To a THF suspension (50 mL) of potassium hydride (0.5 g, 12.5 mmol) was added a THF solution (10 mL) of 1,1-diphenylacetone (2.62 g, 12.5 mmol). Evolution of hydrogen was observed. After stirring for 20 min at 20 °C, *n*BuLi (17.5 mL, 28 mmol, 1.6 M solution in hexane) was added by syringe at 0 °C. After stirring for 8 min, a red suspension was formed. A THF solution (30 mL) of benzophenone (2.28 g, 12.5 mmol) was added over 10 min at 0 °C. The color of the solution became deep blue. After stirring for 2 h at 20 °C, a THF solution (20 mL) of the respective dielectrophile (12.5 mmol) was added at 0 °C using a metal cannula. In the case of **14**, the cyclization product precipitated immediately, and was filtered off and washed with water and diethyl ether. For **3a–c**, **4** and **5a–b**, the solution was stirred for 12 h at 20 °C, and the solvent was subsequently removed in vacuo. The residue was extracted with toluene (3 × 50 mL). The extracts were filtered through Celite, the solution was concentrated in vacuo to 50 mL, and the product was precipitated by the addition of hexane (20 mL). The precipitate was filtered off and washed with diethyl ether.

**1,1,4,4-Tetraphenyl-2,4-bis(trimethylsilyloxy)-1-butene (3a):** Starting with 1,1-diphenylacetone (2.62 g, 12.5 mmol) and benzophenone (2.55 g, 14.0 mmol), **3a** was isolated as a colorless solid (5.80 g, 86%), m.p. 68 °C. – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = –0.05, –0.03 (s, 18 H, SiMe<sub>3</sub>), 3.56 (s, 2 H, CH<sub>2</sub>), 7.00–7.60 (m, 20 H, Ph). – <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.27, 2.03 (SiMe<sub>3</sub>), 46.78 (CH<sub>2</sub>), 82.04 (C, OCPh<sub>2</sub>), 125.65 (=CPh<sub>2</sub>), 125.98, 126.66, 127.19, 127.20, 127.28, 127.79, 128.32, 130.87 (CH, Ph), 142.02, 142.38, 146.44 (C, Ph), 147.15 (=COSi). – <sup>29</sup>Si NMR (CDCl<sub>3</sub>):

$\delta$  = 10.20, 16.23. – C<sub>34</sub>H<sub>40</sub>O<sub>2</sub>Si<sub>2</sub>: calcd. C 76.06, H 7.51; found C 75.96, H 7.51.

**2,4-Bis(tert-butyltrimethylsilyloxy)-1,1,4,4-tetraphenyl-1-butene (3b):** Starting with 1,1-diphenylacetone (2.62 g, 12.5 mmol) and benzophenone (2.55 g, 14.0 mmol), **3b** was isolated as a colorless solid (6.51 g, 84%), m.p. 78 °C. – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = –0.43, –0.19 (2 × s, 2 × 6 H, SiMe<sub>3</sub>), 0.68, 0.81 [2 × s, 2 × 9 H, C(CH<sub>3</sub>)<sub>3</sub>], 3.43 (s, 2 H, CH<sub>2</sub>), 6.69 (m, 2 H, Ph), 6.94–7.65 (m, 16 H, Ph), 7.82 (m, 2 H, Ph). – <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  = –3.73, –3.06 (SiMe<sub>3</sub>), 18.16, 18.46 [C(CH<sub>3</sub>)<sub>3</sub>], 26.03, 26.10 [C(CH<sub>3</sub>)<sub>3</sub>], 46.34 (CH<sub>2</sub>), 83.14 (C, OCPh<sub>2</sub>), 126.54 (=CPh<sub>2</sub>), 126.95, 127.30, 127.95, 128.26, 128.59, 130.04, 130.87, 131.10, 132.38 (CH, Ph), 141.69, 142.56, 146.58, 146.71 (C, Ph). – IR (KBr):  $\tilde{\nu}$  = 3058 (w) cm<sup>–1</sup>, 3027 (w), 2956 (w), 2928 (m), 1661 (m), 1599 (m), 1494 (m), 1445 (m), 1278 (m), 1256 (m), 1220 (m), 1056 (m). – MS (CI, H<sub>2</sub>O); *m/z*: 621 (M<sup>+</sup> + 1, 6), 297 (100).

**6-(Diphenylmethylidene)-2,2,4,4-tetraphenyl-1,3-dioxane-2-silacyclohexane (3c):** Starting with 1,1-diphenylacetone (2.62 g, 12.5 mmol), benzophenone (2.55 g, 14.0 mmol) and diphenyldichlorosilane (3.16 g, 12.5 mmol), **3c** was isolated as a colorless solid (5.40 g, 76%), m.p. 70 °C. – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.52 (s, 2 H, CH<sub>2</sub>), 7.00–7.80 (m, 30 H, Ph). – <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  = 43.48 (CH<sub>2</sub>), 82.06 (C, O–CPh<sub>2</sub>), 121.83 (Ph<sub>2</sub>C=), 125.79, 126.65, 127.42, 127.83, 128.23, 129.97, 130.03, 130.72, 130.89 (CH, Ph), 126.08, 127.02, 127.91 (CH, SiPh<sub>2</sub>), 134.77 (C, SiPh<sub>2</sub>), 139.81, 140.78, 145.05 (C, Ph), 145.95 (=COSi). – <sup>29</sup>Si NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  = –27.83. – C<sub>40</sub>H<sub>32</sub>O<sub>2</sub>Si: calcd. C 83.88, H 5.63; found C 84.04, H 5.38.

**7-(Diphenylmethylidene)-5,5-diphenyl-1,4-dioxepan-2,3-dione (4):** Starting with 1,1-diphenylacetone (2.62 g, 12.5 mmol), benzophenone (2.55 g, 14.0 mmol) and oxalyl chloride (1.60 g, 4) was isolated as a colorless solid (2.01 g, 36%), m.p. 162 °C (dec.). – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 3.61 (s, 2 H, CH<sub>2</sub>), 6.90–7.40 (m, 20 H, Ph). – MS (EI); *m/z*: 446 [M<sup>+</sup>], 402 (M<sup>+</sup> – CO<sub>2</sub>), 402 (M<sup>+</sup> – CO<sub>2</sub>, – CO). – C<sub>30</sub>H<sub>22</sub>O<sub>4</sub>: calcd. C 80.70, H 4.97; found C 81.08, H 4.66.

**8-(Diphenylmethylidene)-3,3-diethyl-6,6-diphenyl-1,5-dioxocan-2,4-dione (5a):** Starting with 1,1-diphenylacetone (2.62 g, 12.5 mmol), benzophenone (2.55 g, 14.0 mmol) and diethylmalonic dichloride (2.46 g, 12.5 mmol), **5a** was isolated as colorless crystals (4.02 g, 62%), m.p. 186 °C. – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.86 (t, *J* = 7 Hz, 6 H, CH<sub>3</sub>), 2.01 (q, *J* = 7 Hz, 4 H, CH<sub>2</sub>CH<sub>3</sub>), 3.51 (s, 2 H, CH<sub>2</sub>), 6.17 (d, *J* = 10.5 Hz, 2 H, Ar), 6.95 (t, *J* = 10.5 Hz, 2 H, Ar), 7.00–7.40 (m, 16 H, Ph). – <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>):  $\delta$  = 8.64 (CH<sub>3</sub>), 22.48 (CH<sub>2</sub>CH<sub>3</sub>), 38.87 (CH<sub>2</sub>), 64.60 (C, CEt<sub>2</sub>), 87.02 (C, CPh<sub>2</sub>), 126.24, 126.87, 126.98, 127.45, 127.67, 128.21, 128.87, 129.36, 130.27 (CH, Ph), 136.68 (C, C=CPh<sub>2</sub>), 138.67, 139.35, 142.83, 144.52 (C, C=C–O, Ph), 169.90, 170.34 (CO). – IR (KBr):  $\tilde{\nu}$  = 3058 (m) cm<sup>–1</sup>, 2972 (m), 2879 (s), 1763 (s, CO), 1600 (s), 1494 (m), 1447 (m), 1197 (m), 1116 (s), 1060 (m), 1010 (m). – MS (EI) *m/z*: 516 [M<sup>+</sup>], 374, 194. – C<sub>35</sub>H<sub>32</sub>O<sub>4</sub>: calcd. C 81.37, H 6.24; found C 81.12, H 6.40.

**8-(Diphenylmethylidene)-3,3-diethyl-6,6-di(p-tolyl)-1,5-dioxocan-2,4-dione (5b):** Starting with 1,1-diphenylacetone (2.62 g, 12.5 mmol), bis(p-tolyl) ketone (2.94 g, 14.0 mmol) and diethylmalonic dichloride (2.46 g, 12.5 mmol), **5b** was isolated as colorless crystals (3.87 g, 60%), m.p. 168 °C. – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>):  $\delta$  = 0.82 (t, *J* = 7 Hz, 6 H, CH<sub>3</sub>), 2.05 (q, *J* = 7 Hz, 4 H, CH<sub>2</sub>CH<sub>3</sub>), 2.25 (s, 6 H, CH<sub>3</sub>), 3.50 (s, 2 H, CH<sub>2</sub>), 6.20 (d, *J* = 11 Hz, 2 H, Ar), 6.90 (t, *J* = 11 Hz, 2 H, Ar), 7.00–7.40 (m, 14 H, Ar). – IR (KBr):  $\tilde{\nu}$  = 3060 (m) cm<sup>–1</sup>, 2972 (m), 2881 (s), 1764



(s, CO), 1604 (s), 1496 (m), 1446 (m), 1198 (m), 1112 (s), 1062 (m), 1010 (m). – MS (EI)  $m/z$ : 544 [ $M^+$ ], 374, 194. –  $C_{37}H_{36}O_4$ : calcd. C 81.59, H 6.66; found C 81.30, H 6.50.

**6-Diphenylmethylidene-4,4-diphenylspiro[1,3-dioxan-2,1'(3'H)-isobenzofuran]-3'-one (14):** Starting with 1,1-diphenylacetone (2.62 g, 12.5 mmol), benzophenone (2.55 g, 14.0 mmol) and phthalic dichloride (2.54 g), **14** was isolated as colorless crystals (5.80 g, 89%), m.p. 190 °C. –  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  = 3.45 (d,  $J$  = 16 Hz, 1 H,  $CH_2$ ), 3.91 (d,  $J$  = 16 Hz, 1 H,  $CH_2$ ), 6.90–7.90 (m, 24 H, Ph). –  $^{13}C$  NMR (50 MHz,  $CDCl_3$ ):  $\delta$  = 36.95 ( $CH_2$ ), 83.20 (C,  $OCPH_2$ ), 117.29 (spiro atom), 121.66 ( $Ph_2C=$ ), 123.06, 125.23, 126.30, 126.55, 127.22, 127.55, 127.78, 128.18, 128.44, 129.79, 130.52, 131.61, 134.87 (CH, Ph), 138.05, 139.50, 142.00, 143.04, 144.21 (C, Ar, =CO), 166.21 (CO). – IR (KBr):  $\tilde{\nu}$  = 3058 (w)  $cm^{-1}$ , 3052 (w), 2926 (w), 1781 (s, CO), 1597 (w), 1494 (m), 1449 (m), 1355 (s), 1313 (s), 1281 (s), 1220 (m), 1130 (s), 1108 (s), 1084 (m), 1065 (m). – MS (CI, MeOH);  $m/z$ : 523 [ $M^+$  + 1], 375 ( $M^+$  –  $C_8H_4O_3$ ), 357 ( $M^+$  –  $C_8H_4O_3$ , –  $H_2O$ ), 149 ( $C_8H_4O_3$  +  $H^+$ ). –  $C_{36}H_{26}O_4$ : calcd. C 82.74, H 5.01; found C 82.42, H 5.13.

**General Procedure for the Preparation and Cyclization Reactions of the Dianion of 2-Methylbenzimidazole (6):** To a THF solution (50 mL) of 2-methylbenzimidazole (1.58 g, 12.0 mmol) was added  $nBuLi$  (16.5 mL, 2.2 equiv., 1.6 M solution in hexane) at 0 °C. A yellow suspension was formed. After stirring for 60 min at 0 °C, a THF solution (30 mL) of benzophenone (2.30 g, 12.5 mmol) was added at 0 °C. The color of the solution became deep blue. The solution was stirred at 0 °C for 15 min, and at room temperature for 2 h. Subsequently, a THF solution (30 mL) of the respective dielectrophile (12.5 mmol) was added at 0 °C. The THF was removed in vacuo. The residue was dried and extracted with toluene (3 × 50 mL). The extracts were filtered through Celite, the solution was concentrated in vacuo to 30 mL, and the product was precipitated by the addition of hexane (20 mL). The product was filtered and washed with diethyl ether.

**3,4-Dihydro-4,4-diphenyl-1*H*-[1,3]oxazino[3,4-*a*]benzimidazol-1-one (7):** Starting with 2-methylbenzimidazole (1.58 g, 12.0 mmol), benzophenone (2.54 g, 14.0 mmol) and oxalyl chloride (1.53 g), **7** was isolated as a colorless solid (1.88 g, 46%), m.p. 175 °C. –  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  = 3.87 (s, 2 H,  $CH_2$ ), 7.00–7.90 (m, 14 H, Ar). –  $^{13}C$  NMR (50 MHz,  $CDCl_3$ ):  $\delta$  = 36.69 ( $CH_2$ ), 88.51 (C,  $OCPH_2$ ), 114.36, 119.81, 125.15, 128.71 (CH, Ar), 125.67, 128.91, 129.61 (CH, Ph), 131.23 (C, Ph), 140.80, 142.63 (C, Ar), 145.84 ( $CN_2$ ), 149.10 (C, CO). – IR (Nujol):  $\tilde{\nu}$  = 1767 (s, CO)  $cm^{-1}$ , 1569 (s). – MS (CI, MeOH);  $m/z$ : 369 ( $M^+$  + MeOH), 341 [ $M^+$  + 1], 297 ( $M^+$  –  $CO_2$ ). –  $C_{22}H_{16}O_2N_2$ : calcd. C 77.63, H 4.74; N 8.23; found C 77.96, H 4.64, N 7.88.

**Lactone 9:** The dianion of 2-methylbenzimidazole (1.58 g, 12.0 mmol) was generated and treated with benzophenone (2.28 g, 12.5 mmol) as described in the general procedure. After stirring for 2 h at 20 °C, the solution was poured into an aqueous solution of hydrochloric acid (1 M, 200 mL). The solution was extracted with diethyl ether (3 × 100 mL), and the combined organic layers were dried ( $MgSO_4$ ), filtered and the solvent of the filtrate was removed in vacuo. The product was precipitated by the addition of hexane to the residue to give **8** as a colorless solid (3.20 g, 85%). A THF solution (200 mL) of **8** (1.50 g, 4.8 mmol), diethylmalonic dichloride (1 equiv.), and  $NEt_3$  (2 equiv.) was stirred at 0 °C for 2 h, at 20 °C for 20 h, and at 50 °C for 24 h. The reaction mixture was poured into water and the aqueous layer was repeatedly extracted with diethyl ether. The combined organic layers were dried ( $MgSO_4$ ), filtered and the solvent of the filtrate was removed in vacuo. The

residue was purified by column chromatography (silica gel, ether/petroleum ether = 1:1) to give **9** as a colorless oil (315 mg, 15%). –  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  = 0.85 (t,  $J$  = 7 Hz, 6 H,  $CH_3$ ), 1.95 (q,  $J$  = 7 Hz, 4 H,  $CH_2CH_3$ ), 3.55 (s, 2 H,  $CH_2$ ), 7.00–7.80 (m, 14 H, Ar). – IR (Nujol):  $\tilde{\nu}$  = 3060 (m)  $cm^{-1}$ , 2974 (m), 2880 (s), 1770 (s, CO), 1763 (s, CO), 1604 (s), 1494 (m), 1570 (s). – MS (CI, MeOH);  $m/z$ : 438 (22) [ $M^+$ ].

**3',4'-Dihydro-3',3'-diphenylspiro[isobenzofuran-1(3*H*),1'-[1*H*][1,3]-oxazino[3,4-*a*]benzimidazol-3-one (16):** Starting with 2-methylbenzimidazole (1.58 g, 12.0 mmol), benzophenone (2.55 g, 14.0 mmol) and phthalic dichloride (2.43 g, 12.0 mmol), **16** was isolated as colorless crystals (from MTBE, 1.71 g, 32%), m.p. 176 °C. –  $^1H$  NMR (200 MHz,  $CDCl_3$ ):  $\delta$  = 3.95 (d,  $J$  = 16 Hz, 1 H,  $CH_2$ ), 4.40 (d,  $J$  = 16 Hz, 1 H,  $CH_2$ ), 6.10 (d,  $J$  = 12 Hz, 1 H, Ar), 6.95 (t,  $J$  = 12 Hz, 1 H, Ar), 7.25 (t,  $J$  = 12 Hz, 1 H, Ar), 7.30–8.20 (m, 15 H, Ar). –  $^{13}C$  NMR (50 MHz,  $CDCl_3$ ):  $\delta$  = 36.55 ( $CH_2$ ), 83.83 (C,  $OCPH_2$ ), 108.20 (spiro atom), 110.59, 119.83, 123.34, 125.66, 125.75, 127.19 (CH, Ar), 127.94, 128.32, 128.51 (CH, Ph), 128.57 (C, Ar–C to CO), 131.06 (C, Ph), 132.32, 135.44 (CH, Ar), 143.06, 144.58, 144.69 (C, Ar), 148.46 ( $CN_2$ ), 165.51 (CO). – IR (Nujol):  $\tilde{\nu}$  = 1770 (s, CO)  $cm^{-1}$ , 1465 (s), 1453 (s), 1355 (s), 1380 (s), 1269 (s), 1220 (m), 1103 (s). – MS (CI, MeOH);  $m/z$ : 473 [ $M^+$  + MeOH], 445 [ $M^+$  + 1], 297 [ $M^+$  –  $C_8H_4O_3$ ], 149 [ $C_8H_4O_3$  +  $H^+$ ]. –  $C_{29}H_{20}O_3N_2$ : calcd. C 78.37, H 4.54, N 6.30; found C 78.12, H 4.65, N 6.59.

**X-ray Crystal Structure Analysis of (16):** The structure determination was carried out on an Enraf–Nonius CAD4 diffractometer using graphite-monochromated  $Mo-K_{\alpha}$  radiation. The crystals were mounted in a cold nitrogen stream at –90 °C. Data were corrected for Lorentz and polarization effects, but not for absorption.<sup>[27]</sup> The structures were solved by direct methods (SHELXS)<sup>[28]</sup> and refined by full-matrix least-squares techniques against  $F^2$  (SHELXL-93). The hydrogen atoms were included at calculated positions with fixed thermal parameters; all non-hydrogen atoms were refined anisotropically. XP (SIEMENS Analytical X-ray Instruments, Inc.) was used for structure representations. Crystal Data:<sup>[30]</sup>  $C_{29}H_{20}N_2O_3$ ,  $M_r$  = 444.5  $gmol^{-1}$ , colorless, size  $0.40 \times 0.3 \times 0.10$  mm<sup>3</sup>, monoclinic, space group  $P2_1/c$  No. 14,  $a$  = 17.888(4),  $b$  = 9.951(2),  $c$  = 13.623(3) Å,  $\alpha$  = 90.0,  $\beta$  = 111.29(3),  $\gamma$  = 90.0°,  $V$  = 2259.4(8) Å<sup>3</sup>,  $Z$  = 4,  $\rho_{calcd}$  = 1.31  $gcm^{-3}$ ,  $\mu$  ( $Mo-K_{\alpha}$ ) = 0.85  $cm^{-1}$ ,  $F(000)$  = 928, 8094 reflections in  $\pm h$ ,  $\pm k$ ,  $\pm l$ , measured in the range  $2.75^\circ \leq \Theta \leq 23.71^\circ$ , 7804 independent reflections,  $R_{int}$  = 0.028, 4566 reflections with  $F_o > 4\sigma(F_o)$ , 387 parameters,  $R$  = 0.063,  $wR_2$  = 0.128, GOF = 1.23, largest difference peak: 0.23  $e\text{-}\text{\AA}^{-3}$ .

**1,3,4,4-Tetraphenyl-2,4-bis(trimethylsilyloxy)-1-butene (21):** The preparation of **21** follows the procedure for the preparation of **3a**. Starting with 1,3-diphenylacetone (2.62 g, 12.5 mmol) and benzophenone (2.55 g, 14.0 mmol), **21** was isolated as colorless crystals (5.61 g, 83%) from hexane, m.p. 68 °C. –  $^1H$  NMR (300 MHz,  $CDCl_3$ ):  $\delta$  = –0.04, 0.20 (s, 18 H,  $SiMe_3$ ), 4.17 (s, 1 H, CH), 6.47 (s, 1 H, =CHPh), 7.00–7.80 (m, 20 H, Ph). –  $^{13}C$  NMR (75 MHz,  $CDCl_3$ ):  $\delta$  = 0.67, 2.44 ( $SiMe_3$ ), 63.26 (CH), 85.67 (C,  $OCPH_2$ ), 112.18 (CH, =CHPh), 125.42, 126.32, 126.43, 126.80, 127.06, 127.31, 127.61, 127.87, 128.14, 128.61, 129.35, 131.68 (CH, Ph), 137.31, 138.61, 145.54, 146.76 (C, Ph), 152.12 (=COSi). – IR (Nujol):  $\tilde{\nu}$  = 3061 (m)  $cm^{-1}$ , 3024 (m), 1601 (m), 1455 (s), 1377 (s), 1251 (s), 1132 (s), 1072 (s), 1009 (s). –  $C_{34}H_{40}O_2Si_2$ : calcd. C 76.06, H 7.51; found C 75.84, H 7.62.

**Synthesis of Heterospirocyclic Isobenzofuranones 18 and 19:** To a THF solution (30 mL) of LDA (2.2 equiv.) was added a THF solu-

tion (10 mL) of salicylic or anthranilic acid (2.0 mmol). The solution was stirred for 1 h at 0 °C, and subsequently phthalic dichloride (1.0 mmol) was added by syringe. After stirring for 12 h at 20 °C, the solution was concentrated to 10 mL and hexane (20 mL) was added. The precipitated solid was filtered off and washed with water and diethyl ether to give the products as colorless solids. The synthesis of **18** and **19** has been previously reported in the literature.<sup>[23]</sup>

**Isobenzofuranone 18:** Yield 82%, colorless crystals, m.p. 172 °C. – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.00–7.80 (m, 8 H, Ar). – IR (KBr):  $\tilde{\nu}$  = 3060 (w) cm<sup>-1</sup>, 3052 (w), 2925 (w), 1780 (s, CO), 1595 (w), 1492 (m), 1449 (m), 1354 (s), 1284 (s), 1220 (m), 1132 (s), 1108 (s), 1085 (m), 1063 (m). – MS (CI); *m/z*: 269 (100) [M<sup>+</sup> + 1]. – C<sub>15</sub>H<sub>8</sub>O<sub>5</sub>: calcd. C 67.17, H 3.01; found C 67.32, H 3.22. Owing to the low solubility of **18**, no <sup>13</sup>C NMR spectrum could be recorded. Similar to the cases of **14** and **16**, only one carbonyl absorption was observed in the IR spectrum.

**Isobenzofuranone 19:** Yield 70%, colorless crystals, m.p. 160 °C. – <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 7.00–7.80 (m, 8 H, Ar). – IR (KBr):  $\tilde{\nu}$  = 3062 (w) cm<sup>-1</sup>, 3048 (w), 2926 (w), 1778 (s, CO), 1596 (w), 1490 (m), 1450 (m), 1355 (s), 1285 (s), 1220 (m), 1130 (s), 1110 (s), 1085 (m), 1065 (m). – MS (CI); *m/z*: 268 (100) [M<sup>+</sup> + 1]. – C<sub>15</sub>H<sub>9</sub>O<sub>4</sub>N: calcd. C 67.42, H 3.39; found C 67.30, H 3.52. Owing to the low solubility of **19**, no <sup>13</sup>C NMR spectrum could be recorded. Similar to the case of **18**, only one carbonyl absorption was observed in the IR spectrum.

**Reaction of the Dianion of Acetanilide with Benzophenone and Phthaloyl Dichloride:** To a THF solution (30 mL) of acetanilide (810 mg, 6.0 mmol) was added *n*BuLi (8.25 mL, 2.2 equiv., 1.6 M solution in hexane) at 0 °C. The color of the solution became yellow. After stirring for 45 min at 0 °C, a THF solution (10 mL) of benzophenone (1.15 g, 6.3 mmol) was added at 0 °C. The color of the solution changed to green. After stirring for 2 h at 20 °C, a THF solution (30 mL) of phthalic dichloride (1.27 g, 6.3 mmol) was added within 10 min at 0 °C. The solution was stirred at 0 °C for 15 min, and at room temperature for 12 h. The solution was then extracted with a saturated aqueous solution of NaHCO<sub>3</sub>. The combined organic layers were dried (MgSO<sub>4</sub>), filtered and concentrated in vacuo. Addition of hexane to a diethyl ether solution of the crude product resulted in the precipitation of *N*-phenylphthalimide (**24**) (722 mg, 54%) as a colorless solid. The product was identified by <sup>1</sup>H NMR spectroscopy and MS spectrometry, and by its melting point (202–204 °C).<sup>[31]</sup> The filtrate was purified by chromatography (silica gel, ether, petroleum ether) to give **23** (160 mg, 6%) and an additional amount of **24** (161 mg, 12%). – **23**: <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>): δ = 3.40 (d, *J* = 15 Hz, 1 H, CH<sub>2</sub>), 3.80 (d, *J* = 15 Hz, 1 H, CH<sub>2</sub>), 6.80–7.85 (m, 19 H, Ar). – IR (KBr):  $\tilde{\nu}$  = 3062 (w) cm<sup>-1</sup>, 3050 (w), 2925 (w), 1780 (s, CO), 1690 (s, CO), 1595 (w), 1490 (m), 1449 (m), 1351 (s), 1312 (s), 1280 (s), 1221 (m), 1130 (s), 1106 (s), 1064 (m). – MS (CI, MeOH); *m/z*: 448 [M<sup>+</sup> + 1], 149 [C<sub>8</sub>H<sub>4</sub>O<sub>3</sub> + H<sup>+</sup>].

**1,3,5-Tricarbonyloctene (12):** To a THF solution (80 mL) of 3-acetylindole (2.50 g, 15.5 mmol) was added a THF solution of LDA, prepared by the addition of *n*BuLi (37.5 mL, 58.0 mmol, 1.6 M solution in hexane) to a THF solution (30 mL) of diisopropylamine (7.65 mL, 58.0 mmol), at 0 °C. After stirring for 6 h at 20 °C, a THF solution (20 mL) of benzophenone (3.70 g, 20.15 mmol) was added at 0 °C. The solution was stirred at 0 °C for 15 min, and at room temperature for 7 h, during which time the color changed to deep green. Diethylmalonyl dichloride (3.4 g, 16.0 mmol) was subsequently added at 0 °C. After stirring for 12 h,

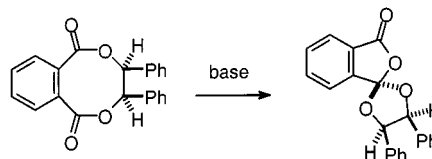
water (20 mL) and diethyl ether (80 mL) were added, and the solution was extracted with a saturated aqueous solution of NaHCO<sub>3</sub>. The combined organic layers were dried (MgSO<sub>4</sub>), filtered and the solvent of the filtrate was concentrated in vacuo to give a deep red oil. Storage of a diethyl ether solution of the crude product at 0 °C for 12 h resulted in the precipitation of **12** as a yellow solid (1.25 g, 18%). – <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ = 0.83 (t, *J* = 7 Hz, 6 H, CH<sub>3</sub>), 1.96 (q, *J* = 7 Hz, 4 H, CH<sub>2</sub>CH<sub>3</sub>), 7.10–7.60 (m, 12 H, Ph), 7.97 (s, 1 H, NH), 8.19, 8.44 (d, 2 H, *J* = 12 Hz, Ar). – <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 9.23 (CH<sub>3</sub>), 28.45 (CH<sub>2</sub>CH<sub>3</sub>), 38.87 (CH<sub>2</sub>), 63.15 (C, C=O), 77.20 (C, C=CPh<sub>2</sub>), 114.17 (CH, Ar), 120.00 (C, Ar), 125.18, 125.76, 126.63, 127.94, 128.13, 128.45, 128.99, 129.38, 129.66 (CH, Ar), 131.73, 132.81, 134.78 (C, Ar), 139.46, 141.18 (C, Ar–C to N), 156.56 (C, C=CPh<sub>2</sub>), 171.79, 186.22, 193.16 (CO). – IR (KBr):  $\tilde{\nu}$  = 3420 (br) cm<sup>-1</sup>, 2978 (m), 1718 (s), 1720 (s), 1650 (m), 1582 (m), 1571 (m), 1531 (m), 1341 (m), 1318 (s), 1137 (s), 1086 (s). – MS (FAB); *m/z*: 448 (100) [M<sup>+</sup> + 1].

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