Carbonylation of Doubly Lithiated *N′*-Aryl-*N*,*N*-Dimethylureas: A Novel Approach to Isatins *via* Intramolecular Trapping of Acyllithiums

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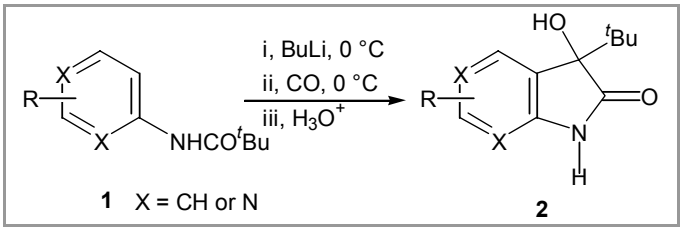
Abstract: Lithiation of *N′*-(2-bromoaryl)-*N*,*N*-dimethylureas with methyllithium and *tert*-butyllithium under nitrogen in dry THF at 0 °C gave doubly lithiated arylurea derivatives, which react with carbon monoxide at 0 °C to give isatins in good yields.

Key words: carbonylation, *N*,*N*-dimethylureas, isatins, intramolecular trapping, positron emission tomography

The carbonylation of organometallics has been reviewed.[2] The nature of the reactions depends on the nature of the organometallics. Although organolithium reagents are frequently reacted with carbon dioxide for the formation of carboxylic acids, reactions with carbon monoxide are much more limited due to the extreme reactivity of the acyllithium intermediates. This reactivity leads to dimerisation, decomposition, reaction with further carbon monoxide or other reactions, giving rise to a range of compounds other than those expected for simple electrophilic trapping.[2] A range of acyl anion equivalents has been developed to overcome this problem,[3] but such reagents are not without drawbacks. In particular, they require additional steps to unmask the carbonyl functionality and they cannot be used for introducing isotopically labelled carbon monoxide. It has been shown that it is possible to trap acyllithiums derived from carbonylation of alkyllithium reagents *in situ*, given that the reaction is carried out at very low temperature with a highly reactive electrophile.[4] The conditions are, however, rather restrictive and the method has only rarely been used with aryllithiums.[5] Therefore, it appeared that intramolecular trapping of acyllithiums might provide a more generally useful synthetic approach for carbonylation reactions of organolithium reagents.[6]

As part of our continuing interest in lithiation reactions,[7] we have also made use of intramolecular trapping of acyllithiums formed *via* carbonylation reactions. For example, we have shown that carbonylation of doubly lithiated *N*-pivaloylanilines and *N*-pivaloylaminopyridines affords 3-*tert*-butyl-3-hydroxy-2,3-dihydroindol-2-ones and aza-3-*tert*-butyl-3-hydroxy-2,3-dihydroindol-2-ones (**2**), respectively, in good yields (Scheme 1).[8]



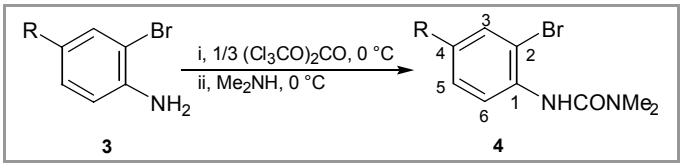
Scheme 1

Unfortunately, the presence of a *tert*-butyl group in compounds **2** greatly restricts the utility of those compounds. Recently we have also obtained unexpected products from the carbonylation of 3-pivaloylaminoquinazolin-4(3*H*)-one.[9] We have therefore sought to replace the

pivaloylamino group in the starting material with another group that would provide products of greater utility.

We tried the reaction of carbon monoxide and doubly lithiated *N*-*tert*-butoxycarbonylaniline, but although the reaction mixture turned a deep colour on introduction of carbon monoxide, as had been the case with doubly lithiated compounds of type **1**, we were unable to isolate indole derivatives in more than trace amounts after work-up of the reaction mixture. We had more success with doubly lithiated *N*′-aryl-*N,N*-dimethylthioureas, which on carbonylation led to indigotins,[10] but these products are also not very amenable to further modification. We therefore turned our attention to doubly lithiated *N*′-aryl-*N,N*-dimethylureas. We attempted direct lithiation of various *N*′-aryl-*N,N*-dimethylureas but could not routinely achieve selective *ortho*-lithiation under standard conditions.[11] Fortunately, this difficulty was easily overcome by the use of *N*′-(2-bromoaryl)-*N,N*-dimethylureas. In a preliminary communication we reported that the carbonylation reaction of *N*′-(2-bromoaryl)-*N,N*-dimethylureas was useful for the production of isatins.[12] We now report the full details of this work.

N′-(2-Bromoaryl)-*N,N*-dimethylureas (**4**) were prepared in a one-pot reaction involving 4-substituted 2-bromoanilines (**3**), triphosgene and dimethylamine. Triphogene is an alternative to phosgene, with the advantages that it is a solid, gives three equivalents of phosgene per mole *in situ*, is easy to handle and is much more pleasant to use than phosgene.[13] The slow addition of a solution of **3** in THF to a stirred solution of triphosgene in THF at 0 °C produced the corresponding arylisocyanate *in situ*. Reaction of the arylisocyanate with dimethylamine at 0 °C gave the corresponding *N*′-aryl-*N,N*-dimethylureas (**4**) (Scheme 2) in good yield (Table 1). It was found that the corresponding bis(2-bromo-aryl)urea was formed as a by-product in a yield of 4-8% as a result of reaction between 2-bromoaniline (**3**) and an arylisocyanate generated *in situ*.



Scheme 2

Table 1 Synthesis of *N*′-(2-bromoaryl)-*N,N*-dimethylureas (**4a-e**) according to Scheme 2

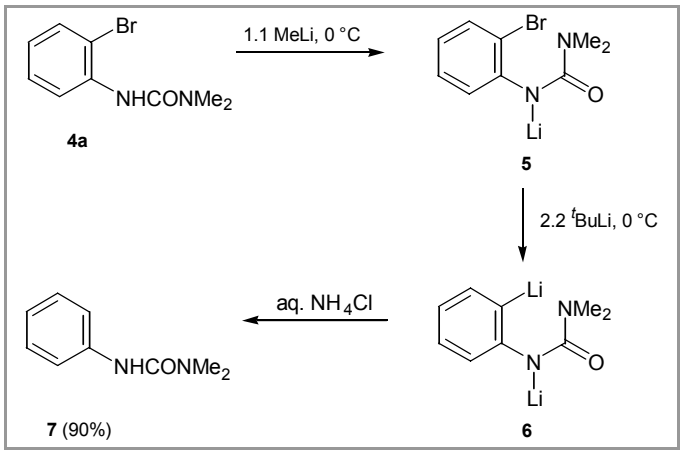
Product	R	Yield (%)[a]	Mp (°C)
4a	H	72	85-86
4b	Me	65	68-69
4c	^{i}Pr	70	92-93
4d	Cl	76	71-72
4e	F	71	80-81

[a] Yield of isolated, purified product.

As can be seen from Table 1, the yields of compounds **4** are good, proving that the procedure is general for a range of substituents, and this overcomes the poor availability and stability of appropriately substituted bromoaryl isocyanates. Therefore, it represents a useful one-pot procedure for the synthesis of *N*′-(2-bromoaryl)-*N,N*-dimethylureas (**4**).

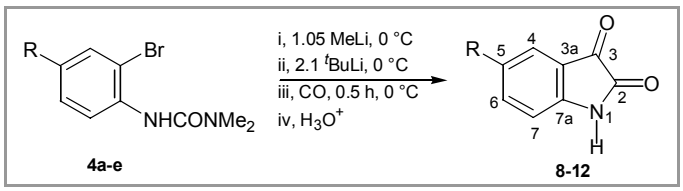
N′-(2-Bromophenyl)-*N,N*-dimethylurea (**4a**) underwent successful lithiation on nitrogen to form the monolithio reagent **5** using methyllithium (1.1 equiv.), followed by bromine-lithium exchange using *tert*-butyllithium (2.2

equiv.) to give the dilithio reagent **6** at 0 °C (Scheme 3). In order to verify the formation **6**, the mixture was treated with aqueous ammonium chloride solution to give *N,N*-dimethyl-*N′*-phenylurea (**7**), Mp 135-136 °C (lit.,[14] 131-133 °C), which was isolated in 90% yield.



Scheme 3

Another sample of the dilithio reagent **6** was then exposed to carbon monoxide (Scheme 4). The mixture turned a blue colour and after work-up isatin (**8**) was obtained in 66% yield. A series of experiments was conducted in which the reaction conditions were varied in an attempt to optimise the yield of **8** (Table 2). It was found that on treatment of a solution of **4a** in THF at 0 °C with MeLi (1.05 equiv.) and *t*-BuLi (2.1 equiv.), followed by reaction of dilithio reagent **6** thus formed with carbon monoxide for 30 minutes, isatin (**8**) was obtained in 76% isolated yield.



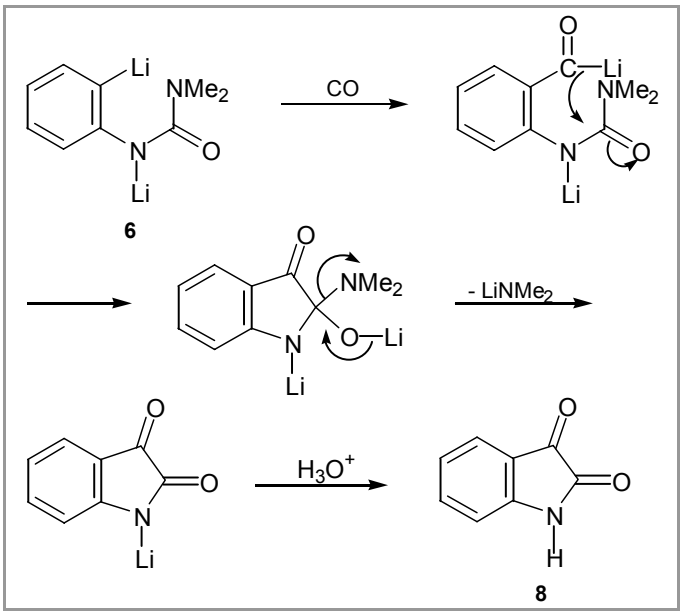
Scheme 4

Table 2 Synthesis of isatin (**8**) under various reaction conditions

Lithium reagent (mmol)		T (°C)[a]	t (h)[b]	Yield (%)[c]
MeLi	*t*-BuLi			
—	3.3	-78	1	38
1.2	2.4	-78	1	54
1.2	2.4	0	1	59
1.1	2.2	-78	1	62
1.1	2.2	0	1	66
1.1	2.2	-78	0.5	65
1.1	2.2	0	0.5	70
1.05	2.1	-78	0.5	69
1.05	2.1	0	0.5	76

[a] Temperature of the cooling bath at which lithiation and carbonylation reactions were carried out.
[b] Reaction time under carbon monoxide atmosphere.
[c] Yield of isolated, purified product.

The likely mechanism, involving carbonylation followed by cyclisation, is shown in Scheme 5.



Scheme 5

Isatin is a useful synthetic intermediate. It reacts with carbanions to give 3-substituted dioxindoles.[15] Therefore, the reaction was applied to a range of *N′*-(2-bromoaryl)-*N,N*-dimethylureas (**4b-e**) under identical reactions conditions, without optimisation of the individual cases. Indeed, these reactions afforded the corresponding substituted isatins **9-12** (Scheme 4) in good yields (Table 3).

Table 3 Synthesis of substituted isatins (**8-12**) according to Scheme 4

Product	R	Yield (%)[a]	Mp (°C)
8	H	76	201-202, decomp. (lit.,[16] 200-202)
9	Me	72	186-187 (lit.,[16] 185-187)
10	^{i}Pr	71	140
11	Cl	77	250-252 (lit.,[16] 249-251)
12	F	79	223 (lit.,[17] 223)

[a] Yield of isolated, purified product.

As can be seen from Table 3, the yields are quite good and the reaction accommodates a range of substituents in the isatin moiety. Therefore, it represents a useful new procedure for the formation of isatins.

In conclusion, the procedure applied represents a useful new method for the synthesis of isatins. This work extends the applicability of our work on the tandem carbonylation-intramolecular trapping of acyllithiums and is more generally useful than the reactions of doubly lithiated *N*-pivaloylanilines and *N*-pivaloylamino-pyridines, isatins having no bulky *tert*-butyl group and being much more amenable to modification. It should prove more attractive for synthesis of compounds of interest for positron emission tomography.[18]

Melting points were determined on an electrothermal digital melting point apparatus and are reported uncorrected. IR spectra were recorded on a Perkin-Elmer 1725X spectrometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker spectrometer operating at 400 MHz for ^{1}H and 100 MHz for ^{13}C measurement. Chemical shifts are reported in parts per million relative to tetramethylsilane. Assignments of signals are based on coupling patterns and expected chemical shift values and have not been rigorously confirmed. Signals with similar characteristics might be interchanged. For fluoro compounds, C-F doublets in the ^{13}C NMR spectra are recorded as two lines, identified by the two apparent δ values at 100 MHz, as they appear in the spectral printout. Low-resolution mass spectra were recorded on a VG 12-253 spectrometer, electron impact (E1) at 70 eV and chemical ionisation (CI) by use of ammonia as ionising gas. Accurate mass data were obtained on a VG ZAB-E instrument. Elemental analyses were obtained from the laboratories of the University of Wales Cardiff. Column chromatography was carried out using Merck Kieselgel 60 (230-400 mesh). *tert*-Butyllithium and methyllithium were obtained from Aldrich Chemical Company and were estimated prior to use by the method of Watson and Eastham.[19] THF was distilled from sodium benzophenone ketyl. Other chemicals were obtained from Aldrich Chemical Company and used without further purification. Solvents were purified by standard procedures.[20,21]

Synthesis of *N′*-(2-bromoaryl)-*N,N*-dimethylureas (4)

To a cooled (0 °C) stirred solution of triphosgene (2.36 g, 8.0 mmol) in dichloromethane or THF (30 mL) a solution of the appropriate 4-substituted 2-bromoaniline (**3**) (20.0 mmol) and triethylamine (4.44 g, 44.0 mmol) in THF (30 mL) was slowly added in a dropwise manner over 30 min. The reaction mixture was stirred at 0 °C for 2 h, after which a solution of dimethylamine in THF (12.0 ml, 2.0 M, 24.0 mmol) was added. The reaction mixture was stirred at 0 °C for an extra 1 h. The mixture was poured onto water (50 mL) and the organic layer was separated, washed with water (2 x 15 mL), dried ($MgSO_4$) and the solvent was removed under reduced pressure. The crude product obtained was purified by column chromatography on silica gel (hexane-Et_2O, 1;2) give **4**. The yields obtained are reported in Table 1.

***N′*-(2-Bromophenyl)-*N,N*-dimethylurea (4a)**

IR (KBr): 3300, 2910, 1670, 1550, 1510, 1450, 1320, 1255, 1190, 880, 820, 790, 620 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 8.22 (dd, *J* = 8.2, 1.3 Hz, 1 H, H6), 7.47 (dd, *J* = 8.2, 1.3 Hz, 1 H, H3), 7.28 (apparent dt, *J* = 8.2, 1.3 Hz, 1 H, H5), 7.00 (s, exch., 1 H, NH), 6.86 (apparent dt, *J* = 8.2, 1.3 Hz, 1 H, 4-H), 3.07 [s, 6 H, $N(CH_3)_2$].

^{13}C NMR ($CDCl_3$): δ = 155.0 (s, C=O), 137.1 (s, C1), 131.8 (d, C3), 128.3 (d, C5), 123.4 (d, C4), 120.9 (d, C6), 113.0 (s, C2), 36.4 [q, $N(CH_3)_2$].

EI-MS: *m/z* (%) = 244 (M^{+81}Br, 22), 242 (M^{+79}Br, 23), 199 (26), 197 (27), 172 (94), 170 (100).

CI-MS: *m/z* (%) = 262 (M^{+81}Br + NH_4, 54), 260 (M^{+79}Br + NH_4, 55), 245 (MH^{+81}Br, 99), 263 (MH^{+79}Br, 100).

HRMS: *m/z* calcd for $C_9H_{11}{}^{79}BrN_2O$ (M^+), 242.0054; found, 242.0055.

Anal. Calcd for $C_9H_{11}BrN_2O$: C, 44.47; H, 4.56; N, 11.52. Found: C, 44.6; H, 4.6; N, 11.6.

***N′*-(2-Bromo-4-methylphenyl)-*N,N*-dimethylurea (4b)**

IR (KBr): 3290, 2985, 2495, 1690, 1575, 1520, 1480, 1415, 1370, 1290, 1245, 1185, 1050, 1020, 920, 855, 707, 662, 610 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 8.07 (d, *J* = 8.4 Hz, 1 H, H6), 7.31 (d, *J* = 1.3 Hz, 1 H, H3), 7.09 (dd, *J* = 8.4, 1.3 Hz, 1

H, H5), 6.89 (s, exch., 1 H, NH), 3.06 [s, 6 H, $N(CH_3)_2$], 2.27 (s, CH_3).

^{13}C NMR ($CDCl_3$): δ = 155.1 (s, C=O), 134.5 (s, C1), 133.4 (s, C4), 132.1 (d, C3), 129.0 (d, C5), 120.9 (d, C6), 112.9 (s, C2), 36.4 [q, $N(CH_3)_2$], 20.4 (q, CH_3).

EI-MS: *m/z* (%) = 258 ($M^{+81}Br$, 2), 256 ($M^{+79}Br$, 2), 177 (40), 132 (8), 104 (16), 77 (81), 72 (100), 42 (36).

CI-MS: *m/z* (%) = 259 ($MH^{+81}Br$, 78), 257 ($MH^{+79}Br$, 76), 179 (100), 133 (16), 108 (14), 72 (24), 46 (35), 44 (38).

HRMS: *m/z* calcd for $C_{10}H_{13}{}^{79}BrN_2O$ (M^+), 256.0211; found, 256.0205.

Anal. Calcd for $C_{10}H_{13}BrN_2O$: C, 46.71; H, 5.10; 12.77; N, 10.89. Found: C, 46.9; H, 5.1; N, 10.7.

N'-(2-Bromo-4-*iso*-propylphenyl)-*N,N*-dimethylurea (4c)

IR (KBr): 3247, 2930, 1640, 1583, 1520, 1473, 1427, 1375, 1290, 1248, 1190, 1050, 1025, 905, 850, 705, 662, 610 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.08 (d, = *J* 8.5 Hz, 1 H, H6), 7.34 (d, *J* = 2.0 Hz, 1 H, H3), 7.14 (dd, *J* = 8.5, 2.0 Hz, 1 H, H5), 6.89 (s, exch., 1 H, NH), 3.06 [s, 6 H, $N(CH_3)_2$], 2.82 [septet, *J* = 7.0 Hz, 1 H, $CH(CH_3)_2$], 1.21 [d, *J* = 7.0 Hz, 6 H, $CH(CH_3)_2$].

^{13}C NMR ($CDCl_3$): δ = 155.1 (s, C=O), 144.5 (s, C4), 134.7 (s, C1), 129.6 (d, C3), 126.4 (d, C5), 121.1 (d, C6), 113.1 (s, C2), 36.4 [q, $N(CH_3)_2$], 33.3 [d, $CH(CH_3)_2$], 23.9 [q, $CH(CH_3)_2$].

EI-MS: *m/z* (%) = 286 ($M^{+81}Br$, 4), 284 ($M^{+79}Br$, 4), 226 (6), 224 (6), 206 (20), 205 (100), 190 (6), 91 (15), 72 (80), 44 (16).

CI-MS: *m/z* (%) = 287 ($MH^{+81}Br$, 50), 285 ($MH^{+79}Br$, 51), 207 (100), 205 (28), 136 (8), 72 (95).

HRMS: *m/z* calcd for $C_{12}H_{17}{}^{79}BrN_2O$ (M^+), 284.0466; found, 284.0468.

Anal. Calcd for $C_{12}H_{17}BrN_2O$: C, 50.54; H, 6.01; N, 9.82. Found: C, 50.4; H, 5.8; N, 10.0.

N'-(2-Bromo-4-chlorophenyl)-*N,N*-dimethylurea (4d)

IR (KBr): 3290, 2985, 2495, 1690, 1575, 1520, 1480, 1415, 1370, 1290, 1245, 1185, 1050, 920, 855, 707, 662, 610 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.20 (d, *J* = 8.0 Hz, 1 H, H6), 7.49 (d, *J* = 2.4 Hz, 1 H, H3), 7.25 (dd, *J* = 8.0, 2.4 Hz, 1 H, H5), 6.96 (s, exch., 1 H, NH), 3.07 [s, 6 H, $N(CH_3)_2$].

^{13}C NMR ($CDCl_3$): δ = 154.7 (s, C=O), 135.9 (s, C1), 131.2 (d, C3), 128.3 (d, C5), 127.5 (s, C4), 121.4 (d, C6), 112.9 (s, C2), 36.4 [q, $N(CH_3)_2$].

EI-MS: *m/z* (%) = 280 ($M^{+\,81}Br^{37}Cl$, 2), 278 ($M^{+81}Br^{35}Cl$ and $M^{+79}Br^{37}Cl$, 6), 276 ($M^{+79}Br^{35}Cl$, 4), 233 (4), 231 (3), 199 (11), 197 (32), 72 (100), 44 (18).

CI-MS: *m/z* (%) = 281 ($MH^{+81}Br^{37}Cl$, 12), 279 ($MH^{+81}Br^{35}Cl$ and $M^{+79}Br^{37}Cl$, 44), 277 ($MH^{+79}Br^{35}Cl$, 33), 201 (30), 199 (100), 197 (18), 165 (17), 72 (86).

HRMS: *m/z* calcd for $C_9H_{10}{}^{79}Br^{35}ClN_2O$ (M^+), 275.9665; found, 275.9668.

Anal. Calcd for C_9H_{10} $BrClN_2O$: C, 38.95; H, 3.63; N, 10.09. Found: C, 38.8; H, 3.8; N, 10.3.

N'-(2-Bromo-4-fluorophenyl)-*N,N*-dimethylurea (4e)

IR (KBr): 3280, 2970, 1670, 1580, 1520, 1480, 1420, 1375, 1290, 1250, 1185, 1050, 1020, 915, 860, 705, 660, 610 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 8.16 (dd, *J* = 9.2, 5.9 Hz, 1 H, H6), 7.25 (dd, *J* = 7.9, 2.9 Hz, 1 H, H3), 7.03 (ddd, *J* = 9.2, 8.0, 2.9 Hz, 1 H, H5), 6.84 (s, exch., 1 H, NH), 3.07 [s, 6 H, $N(CH_3)_2$].

^{13}C NMR ($CDCl_3$): δ = 158.80, 156.36 (C4), 155.0 (s, C=O), 133.58, 133.55 (C1), 122.14, 122.06 (C6), 118.90, 118.64 (C3), 115.23, 115.01 (C5), 112.93, 112.83 (C2), 36.4 [q, $N(CH_3)_2$].

EI-MS: *m/z* (%) = 262 ($M^{+81}Br$, 9), 260 ($M^{+79}Br$, 9), 181 (78), 109 (18), 108 (18), 82 (14), 72 (100), 56 (19), 44 (22).

CI-MS: *m/z* (%) 280 = ($M^{+81}Br + NH_4$, 9), 278 ($M^{+79}Br + NH_4$, 9), 263 ($MH^{+81}Br$, 100), 261 ($MH^{+79}Br$, 94), 183 (8), 181 (9), 72 (85), 44 (22).

HRMS: *m/z* calcd for $C_9H_{10}{}^{79}BrFN_2O$ (M^+), 259.9961; found, 259.9960.

Anal. Calcd for $C_9H_{10}BrFN_2O$: C, 41.40; H, 3.86; N, 10.73. Found: C, 41.6; H, 3.9; N, 10.6.

Typical experimental procedure: formation of isatins (8-12) from *N'*-(2-bromoaryl)-*N,N*-dimethylureas (4)

To a cooled solution (0 °C) of the appropriate *N'*-(2-bromoaryl)-*N,N*-dimethylurea (**4**) (2.0 mmol) in dry THF (15 mL) under a nitrogen atmosphere was added a solution of methyllithum in ether (2.1 mL, 1.0 M, 2.1 mmol), in order to deprotonate the nitrogen. Bromine-lithium exchange was then effected by the addition of *tert*-butyllithium in heptane (2.47 mL, 1.7 M, 4.2 mmol). The mixture was stirred at 0 °C for 1 h then exposed to carbon monoxide, which was introduced to the reaction vessel from a balloon fitted with a needle, *via* a septum. The dilithio reagent thus obtained was stirred under carbon monoxide for 30 min, after which, the mixture was diluted with ethyl acetate (10 mL) and then quenched with aqueous saturated ammonium chloride solution (10 mL). The organic layer was separated, dried ($MgSO_4$), and evaporated under reduced pressure. The crude product obtained was purified by flash column chromatography on silica gel (hexane-Et_2O, 1:1) to give the pure isatins (**8-12**). The yields obtained are recorded in Table 3.

Isatin (8)

IR (KBr): 3210, 1710, 1610, 1450, 1310, 1200, 1120, 950, 780, 620 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 11.02 (s, exch., 1 H, NH), 7.58 (apparent dt, *J* = 7.8, 1.3 Hz, 1 H, H6), 7.50 (dd, *J* = 7.8, 1.3 Hz, 1 H, H7), 7.06 (apparent dt, *J* = 7.8, 1.3 Hz, 1 H, H5), 6.91 (d, *J* = 7.8 Hz, 1 H, 4-H).

^{13}C NMR (DMSO-d_6): δ = 184.4 (s, C3), 159.4 (s, C2), 150.7 (s, C7a), 138.4 (d, C6), 124.7 (d, C4), 122.8 (d, C5), 117.8 (s, C3a), 112.2 (d, C7).

EI-MS: *m/z* (%) = 147 (M^+, 22), 119 (84), 92 (100), 64 (47).

CI-MS: *m/z* (%) = 165 ($M^+ + NH_4$, 100), 148 (MH^+, 13), 134 (43), 118 (50), 94 (22).

HRMS: *m/z* calcd for $C_8H_5NO_2$ (M^+), 147.0321; found, 147.0320.

Anal. Calcd for $C_8H_5NO_2$: C, 65.31; H, 3.43; N, 9.52. Found: C, 65.2; H, 3.3; N, 9.7.

5-Methylisatin (9)

IR (KBr): 3322, 1750, 1622, 1527, 1433, 1226, 1151, 1150, 1044, 839, 752 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 10.93 (s, exch., 1 H, NH), 7.37 (d, *J* = 8.0 Hz, 1 H, H6), 7.29 (s, 1 H, 4-H), 6.76 (d, *J* = 8.0 Hz, 1 H, H7), 2.24 (s, 3 H, CH_3).

^{13}C NMR (DMSO-d_6): δ = 184.6 (s, C3), 159.5 (s, C2), 148.5 (s, C7a), 138.8 (d, C6), 132.0 (s, C5), 124.8 (d, C4), 117.8 (s, C3a), 112.0 (d, C7), 20.1 (q, CH_3).

EI-MS: *m/z* (%) = 161 (M^+, 21), 133 (21), 104 (41), 78 (43), 51 (72), 43 (100).

CI-MS: *m/z* (%) = 179 ($M^+ + NH_4$, 100), 162 (MH^+, 10), 150 (20), 148 (33), 132 (30), 108 (15).

HRMS: *m/z* calcd for $C_9H_7NO_2$ (M^+), 161.0478; found, 161.0477.

Anal. Calcd for $C_9H_7NO_2$: C, 67.07; H, 4.38; N, 8.69. Found: C, 67.2; H, 4.5; N, 8.6.

5-*iso*-Propylisatin (10)

IR (KBr): 3351, 1752, 1620, 1522, 1431, 1149, 1046, 1041, 848, 770, 706 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 10.95 (s, exch., 1 H, NH), 7.47 (dd, *J* = 8.0, 1.4 Hz, 1 H, H6), 7.37 (d, *J* = 1.4 Hz, 1 H, H4), 6.83 (d, *J* = 8.0 Hz, 1 H, H7), 2.86 [septet, *J* = 6.9 Hz, 1 H, C*H*(CH_3)$_2$], 1.16 [d, *J* = 6.9 Hz, 6 H, CH(C*H*$_3$)$_2$].

^{13}C NMR (DMSO-d_6): δ = 184.6 (s, C3), 159.6 (s, C2), 148.9 (s, C7a), 143.2 (d, C6), 136.6 (s, C5), 122.3 (d, C4), 117.8 (s, C3a), 112.1 (d, C7), 32.7 [d, *C*H(CH_3)$_2$], 23.7 [q, CH(*C*H_3)$_2$].

EI-MS: *m/z* (%) = 189 (M^+, 25), 161 (53), 146 (100), 91 (76), 63 (50), 41 (53), 39 (78).

CI-MS: *m/z* (%) = 207 ($M^+ + NH_4$, 100), 190 (MH^+, 8), 176 (37), 160 (57), 136 (17), 77 (12).

HRMS: *m/z* calcd for $C_{11}H_{11}NO_2$ (M^+), 189.0789; found, 189.0790.

Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 70.0; H, 5.7; N, 7.5.

5-Chloroisatin (11)

IR (KBr): 3190, 2950, 2390, 1780, 1710, 1610, 1430, 1240, 1205, 1132, 1041, 842, 770 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 11.15 (s, exch., 1 H, NH), 7.60 (dd, *J* = 8.3, 1.3 Hz, 1 H, H6), 7.54 (d, *J* = 1.3 Hz, 1 H, H4), 6.91 (d, *J* = 8.3 Hz, 1 H, H7).

^{13}C NMR (DMSO-d_6): δ = 183.4 (s, C3), 159.2 (s, C2), 149.2 (s, C7a), 137.3 (d, C6), 126.8 (s, C5), 124.2 (d, C4), 119.2 (s, C3a), 113.9 (d, C7).

EI-MS: *m/z* (%) = 183 ($M^{+37}Cl$, 5), 181 ($M^{+35}Cl$, 14), 155 (21), 153 (33), 125 (13), 91 (34), 84 (33), 49 (95), 43 (100).

CI-MS: *m/z* (%) = 199 ($M^{+35}Cl + NH_4$, 100), 182 ($MH^{+35}Cl$, 10), 178 (18), 165 (22), 152 (50), 151 (65), 118 (53), 77 (79).

HRMS: *m/z* calcd for $C_8H_4{}^{37}ClNO_2$ (M^+), 182.9904; found, 182.9901.

Anal. Calcd for $C_8H_4ClNO_2$: C, 52.92; H, 2.22; N, 7.71. Found: C, 52.9; H, 2.3; N, 7.9.

5-Fluoroisatin (12)

IR (KBr): 3341, 1750, 1625, 1521, 1434, 1156, 1041, 845, 771 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 11.02 (s, exch., 1 H, NH), 7.44 (m, 1 H, 6-H), 7.38 (dd, *J* = 7.2, 2.7 Hz, 1 H, H4), 6.91 (dd, *J* = 8.5, 4.0 Hz, 1 H, H7).

^{13}C NMR (DMSO-d_6): δ = 183.9 (s, C3), 159.53, 159.31 (C5), 156.9 (s, C2), 147.0 (s, C7a), 124.66, 124.43 (C6), 118.56, 118.49 (C3a), 113.54, 113.47 (C7), 111.54, 111.30 (C4).

EI-MS: *m/z* (%) = 165 (M^+, 40), 137 (100), 109 (53), 82 (42).

CI-MS: *m/z* (%): 183 ($M^+ + NH_4$, 100), 166 (MH^+, 4), 151 (24), 136 (21), 76 (10).

HRMS: *m/z* calcd for $C_8H_4FNO_2$ (M^+), 165.0226; found, 165.0226.

Anal. Calcd for $C_8H_4FNO_2$: C, 58.19; H, 2.44; N, 8.48. Found: C, 58.3; H, 2.5; N, 8.3.

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Carbonylation of Doubly Lithiated *N'*-Aryl-*N,N*-Dimethylureas: A Novel Approach to Isatins *via* Intramolecular Trapping of Acyllithiums

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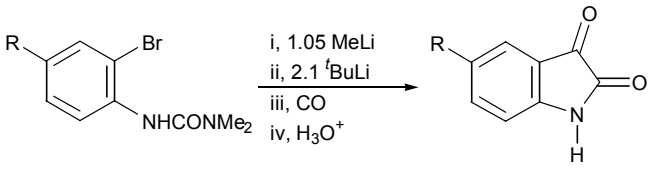

A Novel Approach to Isatins