Metal hydride mediated reduction of 1,3-dimethyl-3(methylthio)oxindole

Terrence J. Connolly and Tony Durst

Abstract: The metal hydride mediated reduction of 4-carboethoxy-1,3-dimethyl-3-(methylthio)oxindole with lithium aluminum hydride and lithium triethylborohydride was studied. The results show that reduction of the oxindole carbonyl group is competitive with reduction of the pendant ester. The hemi-aminal that results from initial addition of hydride to the oxindole carbonyl may follow a number of reaction pathways, one of which is an unprecedented rearrangement. A mechanism is proposed that accounts for all observed products.

Key words: oxindole, reduction, rearrangement.

Résumé : On a étudié la réduction du 4-carboéthoxy-1,3-diméthyl-3-(méthylthio)oxindole par $LiAlH_4$ et par le triéthylborohydrure de lithium. Les résultats montrent que la réduction du groupe carbonyle de l'oxindole est en compétition avec la réduction du groupe ester exocyclique. L'hémi-aminal qui résulte de l'addition initiale d'hydrure sur le groupe carbonyle de l'oxindole peut donner lieu à un certain nombre de réactions subséquentes; l'une d'elle est une transposition sans précédent. On propose un mécanisme pour expliquer la formation de tous les produits observés.

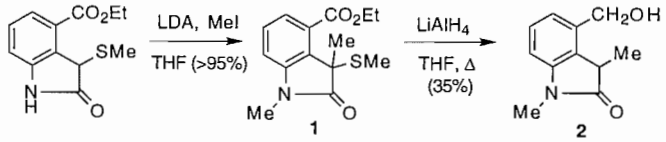
Mots clés : oxindole, réduction, transposition.

[Traduit par la rédaction]

Introduction

The biological activity of some compounds possessing the oxindole nucleus and their structural relationship to indoles continue to make these compounds attractive targets in synthetic organic chemistry (1). In particular, the chemistry of 3-(alkylthio)oxindoles is of great interest. Much of this interest may be traced to the reliable yields and ease of preparation of this class of compounds, primarily due to the pioneering works of Gassman and van Bergen (2, 3). A number of notable variations of the original Gassman methodology have been published recently (4, 5). The fact that these advances and improvements have come primarily from industrial pharmaceutical laboratories lends credence to the importance of these compounds. In addition to the improvements in preparative methods, Karp has recently described conditions that allow for the selective alkylation of this nucleus, thus providing a method for the preparation of 1-, 3-, and 1,3-substituted oxindoles (6), a notable achievement given the difficulty associated with oxindole alkylation. Our contribution to this field has focused on a new, mild, and general nonreductive desulfenylation protocol allowing for the selective removal of the 3-alkylthio group always present if the Gassman approach is utilized (7). In the preceding paper, we described the results of a study dealing with the metal hydride mediated reduction of 3-(alkylthio)oxindoles bearing pendant ester groups on the aromatic ring (8). This study concluded that in this series of compounds the presence of a proton α to the oxindole carbonyl group protects it from reduction, presumably via deprotonation by the metal hydride. We also noted the complications involved in the reduction of ester groups attached at various positions on the benzene ring and ascribed these to the formation of a C3 anion. In continuing our studies in this area, we were interested in seeing what effect blocking both of the positions α to the oxindole carbonyl would have on the course of the reaction. The results of this chemistry, and a postulated mechanism regarding the unusual rearrangement we observed, are the focus of this publication.

Scheme 1.



Results

The required 1,3-(dimethylated)oxindole **1** was prepared by treating 4-carboethoxy-3-(methylthio)oxindole (8) with 2 equivalents of LDA at −78°C followed by the addition of excess MeI and allowing the reaction mixture to warm to room temperature. The product oxindole **1**, prepared in a yield of >95%, was readily identified based on the appearance of three equally intense singlets in the ^1H NMR spectrum, accounting for the three methyl groups. Reduction of oxindole **1** with excess $LiAlH_4$ in refluxing THF led to the formation of oxindole **2** as the major polar material in a yield of 35% after column chromatography (Scheme 1).

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To gain insight into the reaction mechanism, the reaction was repeated with a controlled amount of $LiAlD_4$ at room temperature. Quenching the reaction mixture with a saturated solution of potassium sodium tartrate followed by careful chromatography led to the isolation of three products (Scheme 2). The most polar compound (**2-*d***), isolated as a pale yellow solid (mp 100–101°C) in 41% yield, was identical to **2** except that two atoms of deuterium had been incorporated at the benzylic alcohol position. The second compound, also obtained as a pale yellow solid (mp 81–82°C) in 30% yield, proved to be indole **3-*d***. Key spectral evidence included the absence of carbonyl and presence of alcohol functional groups (3391 cm^{-1}) and an aromatic region in the ^1H NMR spectrum that failed to show the fine structure associated with an oxindole. Additionally, ^2H NMR showed that two deuterium atoms had been incorporated into the molecule at chemical shifts of 4.68 and 6.78 ppm in a ratio of 2:1. These chemical shifts correspond to deuterium incorporation at the C4 benzylic and the C2 position of the indole, respectively. The third compound, isolated as a yellow solid (mp 106–107°C) in 25% yield, was confirmed as being **4-*d*** by converting it to **3** via desulfurization with Ni_2B (9–11).

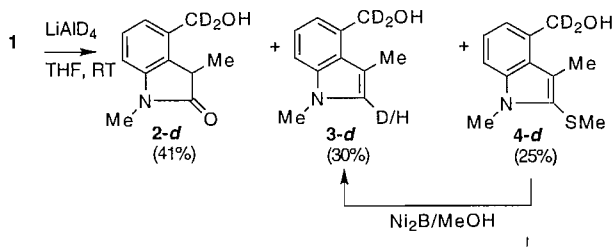
Reduction with $LiEt_3BH$ in THF at room temperature followed by careful chromatography afforded *four* products (Scheme 3). The isolation of **4** and **5** indicates that reduction of the oxindole carbonyl is competitive with reduction of the C4 ester group.

Discussion

The ease of reduction of the oxindole carbonyl group in **1** as compared to oxindoles lacking the 1,3-dimethyl groups (8) proves that an adjacent proton indeed protects it from reduction. In the case of **1**, reduction of the oxindole carbonyl group occurs and leads to either dethiomethylation or an interesting rearrangement. A proposed mechanism to account for all of the isolated products is shown in Scheme 4.

Although it was not possible to determine which carbonyl group was reduced first, it is apparent that reduction of the oxindole carbonyl is facile. Addition of one equivalent of hydride to the oxindole carbonyl results in the formation of hemi-aminal **7**. Further addition of hydride to **7** in a manner reminiscent of amide to amine reduction may occur through **8** to give indoline **9**. We have found that these 3-methylthioindolines are extremely susceptible to dethiomethylation, and readily afford indoles.[2] An analogous transformation on substrate **9** would account for **10**. Reduction of the ester group of **1** prior to or following oxindole reduction accounts for **3**.

Scheme 2.



To account for indole **4**, C3 to C2 migration of the methylthio group of **8** via an episulfonium salt **11** has been invoked. Migrations of alkylthio groups from the 3 to 2 position are known to occur for indoles. Ottenheijm and co-workers first proposed the intermediacy of episulfonium salts to account for this transformation (12). Hamel, Girard, and Atkinson (13, 14) have since shown that a complex intermolecular process can occur, although a concomitant intramolecular rearrangement via an episulfonium species remains a distinct possibility (15). The similarities between intermediate **8** and the intermediates formed in the acid catalyzed rearrangement of 3-alkylthioindoles is striking.

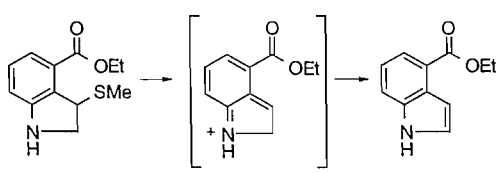
Finally, hemi-aminal **7** may lose MeS, possibly via a nitrogen-assisted 1,4-elimination giving **12**, which may re-aromatize to give enol **13**, which could then re-enolize, accounting for **7**. In this case, ester reduction *must* precede reduction of the oxindole. We have previously shown that C4 esters are difficult to reduce when a C3 anion is formed (8), which is the case for **13a**, and could be the case for **7**, which has a highly acidic C3 proton. We have also shown that reduction of **7** does not lead to the formation of **2**.

Alternatively, **12** may undergo a 1,2-hydride shift that would afford **7** or **2** directly. This latter 1,2-shift is not favored, since we could not detect any deuterium incorporation at this center when conducting the reductions with $LiAlD_4$. However, the high acidity of this C3 proton may cause exchange on work-up, thereby causing scrambling and facilitating against deuterium incorporation in the product.

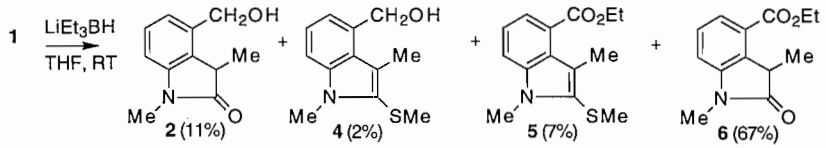
In an extension of this work, oxygen analogs of the thioethers were prepared. Reduction of oxindole **15**, prepared in three steps from isatin, did not lead to **17**. This, indirectly, lends support to the intermediacy of the episulfonium salt **11** since the longer C—S bond may allow the formation of compounds like **11**, whereas oxonium salt **16** is not accessible due to the shorter C—O bond (Scheme 5).

In related work, the reactive carbonyl group of isatin was transformed into a dithiane and a dithiolane as in **18**. Reaction of **18** with $LiEt_3BH$ or $LiAlH_4$ did not result in the formation of **20** (Scheme 6). The failure to form **20** is probably the result of the rather unlikely nature of forming intermediate **19**, an idea which again supports the intermediary of an episulfonium salt in the migration of SMe from the 3 to 2 position reported earlier. It is also worth noting that this also supports the intermediacy of episulfonium salts in the acid-catalyzed isomerization of indole-3-sulfides to indole-2-sulfides.

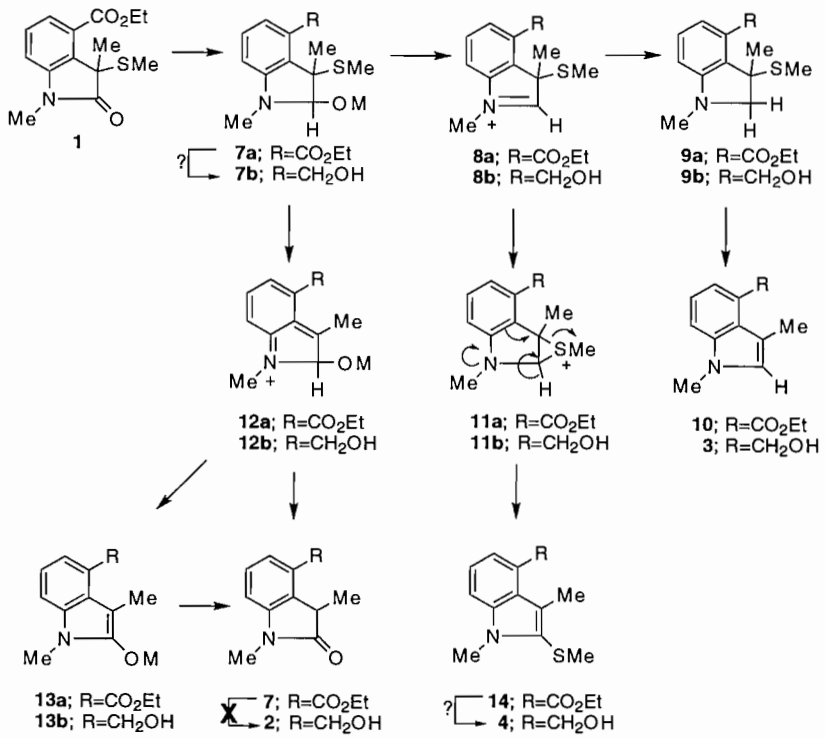
[2] We found that 3-methylthio-4-carboethoxyindolines readily dethioalkylate to afford 4-carboethoxyindole. Although this transformation readily occurs by treatment with reducing agents, including $NaBH_4$, a sample of the pure indoline is slowly converted to the indole, in the absence of other reagents. This observation has led us to propose a nitrogen-assisted 1,4-elimination, followed by re-aromatization as shown below.



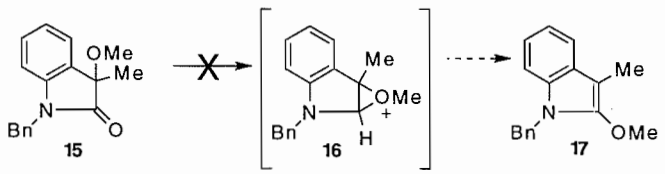
Scheme 3.



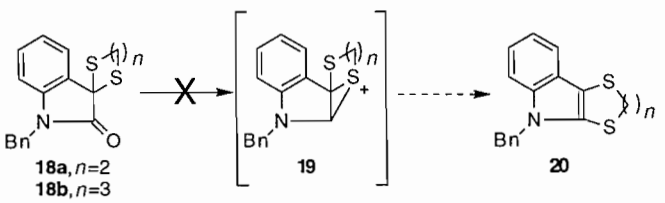
Scheme 4.



Scheme 5.



Scheme 6.



Conclusion

We have shown that the reduction of substituted 3-(methylthio)oxindoles with metal hydrides is a complicated reaction. In the case of 1,3-dialkyl derivatives, oxindole carbonyl reduction is facile, and competitive with the reduction of remote ester groups. The hemi-aminal that results from the first addition of hydride to the oxindole carbonyl affords a number of products. Two dethiomethylation routes compete for oxindole and indole formation. The other observed products, 1,3-dimethyl-2-(methylthio)indoles, seem to be the result of an unusual rearrangement. To the best of our knowledge, this is the first example of such a rearrangement from oxindoles under reductive conditions.

Experimental

General experimental procedures have been described previously (8). In addition to this, ^2H NMR spectra were recorded in CH_2Cl_2 solutions on a Varian XL-300 spectrometer, operating at a frequency of 46.06 MHz, and are referenced to the natural abundance of CD_2Cl_2 at 5.20 ppm.

1,3-Dimethyl-3-(methylthio)oxindole (1)

A solution of freshly prepared LDA (2.1 equiv.) in THF was added dropwise to a cooled (0°C) solution of oxindole 7 (500 mg, 1.99 mmol) in THF (20 mL). Stirring was continued for 1 h, after which time a solution of MeI (631 mg, 4.38 mmol) in THF (5 mL) was added dropwise. The ice bath was removed and the temperature of the resulting solution was allowed to slowly rise to room temperature (RT) over 12 h; the solution was then poured into H_2O (50 mL) and extracted with Et_2O (4 × 20 mL). The combined organic extracts were worked up in the usual manner, affording, after chromatography (2:1

hex:EtOAc), the title compound **14** as a pale yellow oil (540 mg, <95%); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.40 (t, 3H, J = 7.5 Hz), 1.80 (s, 3H), 2.02 (s, 3H), 3.21 (s, 3H), 4.40 (q, 2H, J = 7.5 Hz), 6.98 (dd, 1H, J = 7.0, 1.0 Hz), 7.38 (t, 1H, J = 7.0 Hz), 7.59 (dd, 1H, J = 7.0, 1.0 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.29, 14.20, 21.32, 26.55, 51.59, 61.40, 111.28, 124.61, 128.70, 129.09, 130.93, 143.62, 165.99, 177.25 ppm; EI-MS *m/z* (%): 279 (12.2, M^+), 233 (100); HRMS calcd. for $C_{14}H_{17}NO_3S$: 279.09292; found: 279.09141.

Reduction of oxindole 1 with $LiAlD_4$ (2-*d*, 3-*d*, 4-*d*)

A solution of oxindole **1** (200 mg, 0.72 mmol) was added dropwise to a suspension of $LiAlD_4$ (50 mg, 1.19 mmol) in THF (10 mL) at RT. After stirring at RT for 7 h, the resulting gray cloudy solution was poured into a solution (50 mL) of saturated potassium sodium tartrate and EtOAc (20 mL). After stirring for 4 h, the organic phase was separated and subjected to normal work-up, affording 180 mg of a pale yellow oil. Chromatography with a gradient of 2:1 to 1:1 hex:EtOAc provided three compounds.

Indole ***4*-d**: 40.3 mg (25.0%), R_f = 0.5 (1:1 hex:EtOAc), pale yellow solid; mp 106–107°C; IR (CH_2Cl_2): 3392 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.12 (s, 3H), 2.58 (s, 3H), 3.75 (s, 3H), 6.95 (d, 1H, J = 7.5 Hz), 7.10 (m, 2H) ppm; ^{2}H NMR (46 MHz, CH_2Cl_2) δ: 4.87 (s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 12.03, 19.61, 29.89, 63.80 (quintet), 109.45, 116.38, 119.24, 122.11, 124.65, 130.10, 132.91, 137.88 ppm; EI-MS *m/z* (%): 223 (100) (M^+), 205 (15.0), 190 (48.5), 175 (28.5); HRMS calcd. for $C_{12}H_{13}NOSD_2$: 223.10309; found: 223.09989.

Indole ***3*-d**: 38.4 mg (30.1%), R_f = 0.40 (1:1 hex:EtOAc), pale yellow solid; mp 80–81°C; IR (CH_2Cl_2): 3391 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 2.41 (s, 3H), 3.62 (s, 3H), 6.90 (d, 1H, J = 7.5 Hz), 7.15 (t, 1H, J = 7.5 Hz), 7.23 (d, 1H, J = 7.5 Hz); ^{2}H NMR (46 MHz, CH_2Cl_2) δ: 4.86 (s, 2D), 6.78 (s, 1D); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 12.14, 32.54, 63.80 (quintet), 109.42, 109.75, 119.42, 121.36, 122.86, 128.72, 132.48, 138.62 (doublet); EI-MS *m/z* (%): 178 (96.3) (M^+), 160 (100).

Oxindole ***2*-d**: 56.0 mg (40.5%), R_f = 0.1 (1:1 hex:EtOAc), pale yellow solid; mp 99–101.3°C; IR (CH_2Cl_2): 3603, 1710 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.38 (d, 3H, J = 7.5 Hz), 3.08 (s, 3H), 3.42 (q, 1H, J = 7.5 Hz), 6.65 (d, 1H, J = 7.5 Hz), 6.98 (d, 1H, J = 7.5 Hz), 7.18 (t, 1H, J = 7.5 Hz); ^{2}H NMR (46 MHz CH_2Cl_2) δ: 4.56 (s, 1D), 4.63 (s, 1D); EI-MS m/z (%): 193 (45.6, M^+), 175 (32.9), 160 (23.9), 43 (100); HRMS calcd. for $C_{11}H_{11}NO_2D_2$: 193.11028; found: 193.10784.

Reduction of oxindole 1 with $LiEt_3BH$ (2, 4, 5, 6)

A solution of $LiEt_3BH$ (2.80 mL, 2.80 mmol, 1.0 M in THF) was added dropwise via syringe to a solution of oxindole **3** (156.3 mg, 0.56 mmol) in THF (15 mL) at RT. The resulting bright yellow solution was stirred at RT for 3 h, after which time the yellow solution was poured into H_2O (20 mL), adjusted to pH 3 by the dropwise addition of HCl (10%), and extracted with EtOAc (4 × 20 mL). The combined organic extracts were worked up as usual, affording a pale yellow oil (120 mg) that was chromatographed with a gradient of 2:1 to 1:1 hex:EtOAc and afforded four compounds.

Indole ***5***: yellow oil, 9.8 mg (6.6%), R_f = 0.9 (1:1 hex:EtOAc); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.40 (t, 3H, J = 7.5 Hz), 2.25 (s, 3H), 2.51 (s, 3H), 3.88 (s, 3H), 4.42 (q, 2H, J = 7.5 Hz), 7.20 (t, 1H, J = 7.5 Hz), 7.41 (d, 1H, J = 7.5 Hz), 7.52 (d, 1H, J = 7.5 Hz); EI-MS *m/z* (%): 263 (57.3, M^+), 248 (12.6), 234 (14.0), 219 (24.3), 205 (53.3), 57.0 (100); HRMS calcd. for $C_{14}H_{17}NO_2S$: 263.09800; found: 263.09847.

Indole ***4***: white solid, 2.4 mg (1.9%), R_f = 0.75 (1:1 hex:EtOAc); mp 115–116°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.21 (s, 3H), 2.68 (s, 3H), 3.85 (s, 3H), 5.05 (s, 2H), 7.04 (d, 1H, J = 7.5 Hz), 7.20 (m, 2H); EI-MS *m/z* (%): 221 (100, M^+), 188 (43.3), 173 (32.2), 145 (36.5); HRMS calcd. for $C_{12}H_{15}NOS$: 221.08744; found: 221.08616.

Oxindole ***6***: pale yellow solid, 88.2 mg (67.6%), R_f = 0.50 (1:1 hex:EtOAc); mp 70–70.5°C; IR (CH_2Cl_2): 1714 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.38 (t, 3H, J = 7.5 Hz), 1.48 (d, 3H, J = 7.5 Hz), 3.22 (s, 3H), 3.86 (q, 1H, J = 7.5 Hz), 4.38 (q, 2H, J = 7.5 Hz), 6.98 (d, 1H, J = 7.5 Hz), 7.32 (t, 1H, J = 7.5 Hz), 7.68 (d, 1H, J = 7.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 13.89, 15.93, 26.00, 41.65, 60.86, 111.36, 123.46, 126.58, 127.59, 132.41, 144.66, 165.55, 178.66; EI-MS *m/z* (%): 233 (100, M^+), 204 (40.3), 188 (29.7), 160 (83.7); HRMS calcd. for $C_{13}H_{15}NO_3$: 233.10519; found: 233.10495.

Oxindole ***2***: pale yellow solid, 11.8 mg (11.0 %), R_f = 0.10 (1:1 hex:EtOAc); mp 99–100°C; IR (CH_2Cl_2): 3603, 1710 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 1.44 (d, 3H, J = 7.6 Hz), 2.70 (br, 1H), 3.14 (s, 3H), 3.44 (q, 1H, J = 7.6 Hz), 4.65 (d, 1H, J = 13.0 Hz), 4.73 (d, 1H, J = 13.0 Hz), 6.72 (d, 1H, J = 8.0 Hz), 7.05 (d, 1H, J = 8.0 Hz), 7.24 (t, 1H, J = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 15.43, 26.29, 40.11, 62.26, 107.42, 121.62, 127.93, 128.12, 137.15, 144.10, 178.81; HRMS calcd. for $C_{11}H_{13}NO_2$: 191.09463; found: 191.09650.

N-(Benzyl)isatin

To a solution of isatin (5.00 g, 33.98 mmol) in CH_2Cl_2 (25 mL) was added benzyl bromide (5.81 g, 33.98 mmol), an aqueous solution of NaOH (10 mL, 20%), and benzyl triethylammonium bromide (100 mg). The dark-red solution was stirred at RT for 4 h, after which time the organic phase was separated and worked up in the usual manner, affording the title compound as an orange solid (6.85 g, 85%); mp 124–125°C; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 4.82 (s, 2H), 6.68 (d, 1H, J = 8.0 Hz), 6.98 (t, 1H, J = 8.0 Hz), 7.20 (s, 1H), 7.35 (td, 1H, J = 8.0, 1.0 Hz), 7.50 (dd, 1H, J = 8.0 1.0 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ: 50.62, 110.68, 117.39, 123.54, 125.11, 127.11, 127.86, 128.74, 134.19, 137.98, 150.43, 157.96, 182.91 ppm; EI-MS *m/z* (%): 237 (62.2, M^+), 180 (38.4), 146 (100); HRMS calcd. for $C_{15}H_{11}NO_2$: 237.07898; found: 237.07912.

1-Benzyl-3-methyl-3-(hydroxy)oxindole

A solution of MeMgBr (0.85 mL, 3.0 M in Et_2O, 2.55 mmol) was added dropwise to a cooled (0°C) solution of *N*-benzylisatin (500 mg, 2.11 mmol) in THF (20 mL). The resulting yellow solution was allowed to warm to RT over 12 h, and the red solution that resulted was poured into a solution of NH_4Cl (10%, 20 mL) and extracted with EtOAc (4 × 10 mL). Usual work-up afforded a reddish oil that was subjected to column

chromatography (2:1 hex:EtOAc), providing the title compound as a yellow solid (346.2 mg, 65%); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.63 (s, 3H), 4.80 (d, 1H, J = 15.0 Hz), 4.95 (d, 1H, J = 15.0 Hz), 6.70 (d, 1H, J = 8.0 Hz), 7.05 (t, 1H, J = 8.0 Hz), 7.18 (dd, 1H, J = 8.0, 1.0 Hz), 7.30 (s, 5H), 7.42 (dd, 1H, J = 8.0, 1.0 Hz) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 24.78, 43.44, 73.41, 109.28, 122.96, 123.21, 126.90, 127.43, 128.56, 129.26, 131.01, 135.16, 141.63, 178.30 ppm; EI-MS *m/z* (%): 253 (24.7, M^+), 235 (20.5), 149 (38.3), 91 (100); HRMS calcd. for $C_{16}H_{15}NO_2$: 253.11078; found: 253.11042.

1-Benzyl-3-methyl-3-(methoxy)oxindole (15)

A THF solution (10 mL) of *N*-benzyl-3-methyl-3-(hydroxy)oxindole (150 mg, 0.59 mmol) was added dropwise to a suspension of NaH (20 mg, 0.83 mmol) in THF (5 mL). The pale yellow solution was stirred at RT for 1 h, excess MeI was added, and the still pale yellow solution was stirred at RT for 18 h, after which time it was evaporated to dryness, leaving a pale yellow solid that was recrystallized from CH_2Cl_2–hexanes, affording the title compound as a bright yellow solid (81.2 mg, 51%); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 1.60 (s, 3H), 3.06 (s, 3H), 4.91 (d, 1H, J = 16.0 Hz), 4.92 (d, 1H, J = 16.0 Hz), 6.70 (d, 1H, J = 8.0 Hz), 7.05 (t, 1H, J = 8.0 Hz), 7.20–7.40 (m, 7H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 23.83, 43.44, 52.87, 79.33, 109.21, 122.82, 123.51, 126.93, 127.44, 128.29, 128.55, 129.31, 135.37, 142.23, 176.31 ppm; EI-MS *m/z* (%): 267 (23.4, M^+), 237 (25.3), 176 (14.5), 144 (28.6), 91 (100); HRMS calcd. for $C_{17}H_{17}NO_2$: 267.12593; found: 267.12731.

1-Benzyl-3,3-(ethylenedithio)oxindole (18a)

A solution of *N*-benzylisatin (250 mg, 1.05 mmol) in CH_2Cl_2 (15 mL) containing ethane-1,2-dithiol (119 mg, 1.27 mmol) was stirred at RT while $BF_3{\cdot}OEt_2$ (1 mL) was added dropwise. The resulting solution was stirred at RT for 2 h, then quenched by the addition of H_2O (20 mL), washed with sodium carbonate (10%, 3 × 20 mL), and worked up in the usual manner. Chromatography (5:1 hex:EtOAc) afforded the title compound as a pale yellow solid (222 mg, 67%); mp 107–108°C; IR (CH_2Cl_2): 1717 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.65 (m, 2H), 3.95 (m, 2H), 4.90 (s, 2H), 6.65 (d, 1H, J = 8.0 Hz), 7.10 (t, 1H, J = 8.0 Hz), 7.15 (t, 1H, J = 8.0 Hz), 7.30 (s, 5H), 7.55 (d, 1H, J = 8.0 Hz) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 40.34, 43.82, 109.22, 123.13, 125.34, 125.94, 126.99, 127.54, 128.54, 128.69, 129.73, 135.31, 142.22, 177.96 ppm; EI-MS *m/z* (%): 313 (33.1, M^+), 254 (54.2), 222 (53.2), 162 (51.0), 91 (100); HRMS calcd. for $C_{17}H_{15}NOS_2$: 313.05951; found: 313.06144.

1-Benzyl-3,3-(propylenedithio)oxindole (18b)

The title compound was prepared as above, except that propane-1,3–dithiol was used in the place of ethane-1,2-dithiol. Chromatography (6:1 hex:EtOAc) afforded the title compound as a pale yellow solid (241.8 mg, 70.1%); mp 148–149°C; IR (CH_2Cl_2): 1708 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.0–2.3 (m, 2H), 2.65 (dt, 2H, J = 14.0, 2.0 Hz), 4.09 (td, 2H, J = 14.0, 2.0 Hz), 4.85 (s, 2H), 6.63 (d, 1H, J = 7.6 Hz), 7.00 (t, 1H, J = 7.6 Hz), 7.15 (t, 1H, J = 7.6 Hz), 7.30 (s, 5H), 7.45 (d, 1H, J = 7.6 Hz) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ: 24.18, 25.88, 43.16, 109.17, 122.94, 124.99, 126.80, 127.48, 128.71, 129.90, 135.39, 141.43, 175.67 ppm; EI-MS *m/z* (%): 327 (M^+, 23.2), 294 (22.0), 254 (39.5), 162 (61.5), 91 (100); HRMS calcd. for $C_{18}H_{17}NOS_2$: 327.07516; found: 327.07519.

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