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Mild and efficient iodination of aromatic and heterocyclic compounds with the $NaClO_2$/NaI/HCl system

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Abstract

$NaClO_2$/NaI in the presence of HCl is a mild, cheap, and non-toxic reagent for the iodination of phenols, including estradiol and naphthol, aromatic amines, and heterocyclic substrates, e.g., indoles, 8-hydroxyquinoline, imidazole, in fair to excellent yields by a very simple isolation protocol. The scope of the procedure is exemplified by the first iodination of 5-nitroindole to 3-iodo-5-nitroindole in 75% yield.

Keywords: Activated aromatic; Nitrogenous heterocycles; Sodium chlorite; Mild iodination

1. Introduction

The iodination of phenols and other aromatic compounds is the subject of continuing interest in organic chemistry due to the extensive use of iodinated derivatives as versatile intermediates or building blocks in a variety of synthetic transformations, in medicinal chemistry, and in the biomedical sciences, e.g., as imaging agents in non-invasive medical diagnostic techniques.[1] The biological importance of iodophenols is illustrated by the thyroid hormones which derive biogenetically from the phenolic amino acid tyrosine via repeated iodination steps.[2] The methodologies currently available to organic chemists for the preparation of iodophenols and iodinated aromatic amines and heteroarenes are based on a broad range of iodinating agents such as iodine/HgO,[3a] iodine/tetrabutylammonium peroxydisulphate,[3b] *n*-BuLi/CF_3CH_2I,[3c] NIS/CF_3SO_3H,[3d] NIS,[3e] ICl,[3f] $KBrO_3$/KI,[3g] $IPyBF_4$[3h] or iodide coupled with oxone,[4a] polymethylhydrosiloxane,[4b] diiodine pentoxide,[4c] Ag_2SO_4,[4d] $NaIO_4$,[4e] HIO_4,[4f] NaOCl,[4g] urea/H_2O_2,[4h] HIO_3,[4i] catalytic ceric ammonium nitrate.[4j] These iodinating systems rely for their activity on the presence of Lewis acids or strong oxidizing agents to overcome the problems relating to the low electrophilicity of molecular iodine that renders direct iodination difficult compared to chlorination or bromination.

Despite the broad choice of options, however, many iodination methodologies are cumbersome, costly, harsh, involve use of toxic heavy metals, or do not perform equally well on sensitive aromatic substrates. The development of quick, inexpensive, widely applicable, and environmentally benign iodinating agents is therefore still an active area of research.

In connection with a program aimed at preparing new steroidal scaffolds for application in medicinal chemistry and as precursors for innovative materials, we required access to the iodoestradiols, comprising the 2-, 4-iodo and 2,4-diiodoestradiol, which have been used in protein binding studies[5] and as starting materials for the preparation of several estrogen derivatives, including methoxy,[6a] alkynyl, alkenyl, and alkyl derivatives.[6b] Previous routes to iodoestradiols comprise (a) direct iodination of estradiol with KI/KIO_3,[7a] I_2, and $Hg(OAc)_2$ in AcOH at 50 °C,[7b] yielding 36% 2-iodoestradiol and 21% 4-iodoestradiol, or NaI and chloramine T;[7c] reaction of estradiol 17-acetate with iodine/copper(II) acetate in acetic acid,[7d,e] and (b) indirect methodologies, such as transformation of trimethylsilyl derivatives,[8a] phenylselenenylation of estradiol followed by reaction with ICl or I_2,[8b] reaction of

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estrone or estradiol diacetate with $(CF_3CO_2)_3Tl$ in CF_3CO_2H and subsequent reaction with KI[8c] giving the 2-iodoestrogens as the major products.

Our entry to iodoestradiol was guided by the observation that $NaClO_2$ in acidic media is an effective chlorinating agent for estradiol leading to 10-chloro-substituted derivatives.[9] Upon addition of NaI the reaction was diverted toward iodination of the A-ring to give iodoestradiols in good yields. On this basis the $NaClO_2$/NaI system in the presence of HCl was probed on a variety of substrates and we report here its application for the iodination of phenols, aromatic amines, and heterocyclic substrates, including nitrated derivatives, in fair to excellent yields.

2. Results and discussion

Iodination of estradiol was typically carried out by reacting the substrate (9 mM) with 4 equiv $NaClO_2$ and 8 equiv NaI in 0.01 M HCl/MeOH 1:1 v/v for 30 min followed by extraction with EtOAc and reductive washings with $Na_2S_2O_3$. By this method, 2,4-diiodoestradiol and 4-iodoestradiol were obtained in 35 and 40% yield, respectively, following fractionation on a silica gel column. Interestingly, under the same conditions but using only 0.5 equiv $NaClO_2$/NaI, the reaction gave 2-iodoestradiol in 40% yield after 18 h, the remainder being mainly unreacted substrate with little or no detectable 4-iodoestradiol or diiodo derivative. These results can be explained in the light of the greater ease of formation and reactivity of 2-iodoestradiol compared to 4-iodoestradiol, which is well documented in previous reports.[7] Thus, when the iodinating system is the limiting reactant, 2-iodoestradiol is formed as the main product, as a result of selective iodination at the less hindered 2-position. When an excess of iodinating agent is used, on the other hand, 2-iodoestradiol undergoes further iodination to give 2,4-diiodoestradiol, and 4-iodoestradiol is also formed. The iodoestradiols proved to be stable on standing in the reaction medium in the absence of reagents and did not interconvert. Because of the low reagent costs, operational simplicity, and environmental impact, the present methodologies may offer a convenient alternative to previous ones for the preparation of iodoestradiols.[7,8]

In order to probe the scope of the proposed reagent system, we then investigated its efficiency with a series of representative phenols, aromatic amines, and heterocyclic compounds (Table 1). Reported yields refer to isolated compounds as obtained after ethyl acetate extraction of the crude reaction mixtures, with the exception of reactions under entries 1 and 2, where two products were obtained and separated by column chromatography. In all cases reactions were stopped when the starting materials were consumed and tarry materials and other side products were removed by extraction.

Good-to-excellent yields were obtained with all aromatic compounds examined (entries 1–12). Reported yields refer to carefully optimized reaction conditions and time. Remarkably high isolated yields were also obtained with 4-nitrophenol (**3a**) (entry 4), and with acid-sensitive substrates like aromatic amines (entries 7 and 8) including notably *p*-nitroaniline (**7a**). Among heterocyclic compounds, worthy of note is the preparation of 5,6-diacetoxy-2,3-diiodoindole (**8b**), a novel derivative of the eumelanin precursor 5,6-dihydroxyindole. We required this compound for studies of indole-quinone chemistry[10] and despite several efforts, none of the known procedures for the direct iodination of *O*-protected 5,6-dihydroxyindole[11] proved effective. Eventually,[12] we succeeded in obtaining 5,6-diacetoxy-3-iodoindole (**8a**) by iodination of 5,6-diacetoxyindole with a slight modification of the NH_4I/oxone procedure.[13] However, all attempts to obtain the desired 2,3-diiodo derivative by that procedure were unsuccessful. It should be noted that 2,3-diiodoindoles are not extensively documented in the literature and the recent recourse to a non-classical access route[14] to these compounds illustrates the difficulties of the direct iodination approach. The result in entry 9 supports the value of the present procedure. As expected, all attempts to extend the protocol to the parent heterocycle, indole, were unsuccessful due to the intrinsic instability of 3-iodoindole.[12] To the best of our knowledge, the preparation of 3-iodo-5-nitroindole (**9b**) by iodination of 5-nitroindole (**9a**) is also unprecedented, and represents a significant achievement in the light of the deactivated nature of the substrate. Alternative procedures for the iodination of deactivated aromatics require harsh reaction conditions (e.g., 95% sulfuric acid,[4e] CF_3SO_3H[3d]) which can not clearly be extended to indole and other heterocyclic aromatics. The effective iodination of 8-hydroxyquinoline (**10a**) to give the 5,7-diiodo derivative (iodoquinol, **10b**) in a very good yield (entry 11) further underscores the potential of the reported protocol. Previous procedures for the iodination of **10a** were more costly and cumbersome, relying, e.g., on the use of crosslinked poly(styrene-[4-vinylpyridinium dichloroiodate(I)])[15a] or $MeOCONCl_2$ and NaI.[15b] The reagent proved also useful for the preparation of triiodoimidazole (**11b**), a well known iodinating agent, which was previously obtained in better yields but with the more expensive bis(trifluoroacetoxy)iodobenzene/iodine reagent.[16]

A plausible mechanism for the iodination of aromatic substrates with the $NaClO_2$/NaI system is given in the following equations. The reaction of ClO_2^- with I^- has been extensively investigated as a remarkable example of oscillating chemical reaction, and has been a focal point of nonlinear chemical dynamics in the past decade.[17a,b] Substantial evidence supports the oxidation of I^- by ClO_2^- according to the following equation:

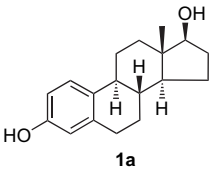
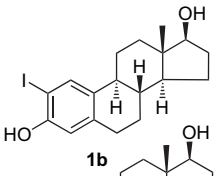
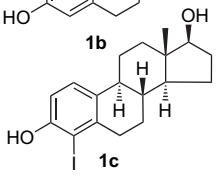
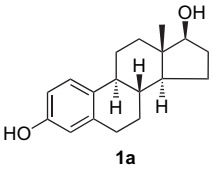
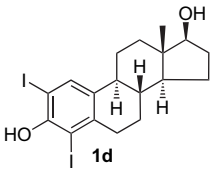
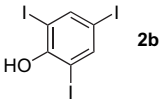
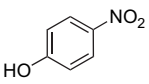
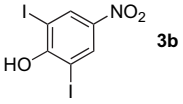
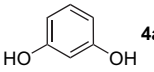
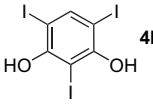
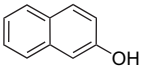
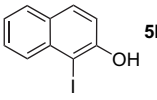
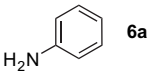
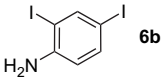
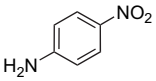
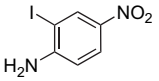
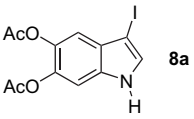
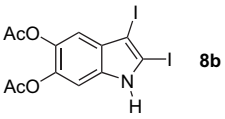
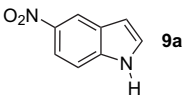
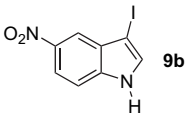
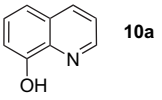
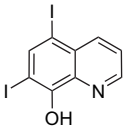
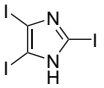
$$4I^- + ClO_2^- + 4H^+ = 2I_2 + Cl^- + 2H_2O \quad (1)$$

Fast oxidation of I_2 by ClO_2^- would then result in the generation of ICl, according to Eq. 2:

$$2I_2 + 3ClO_2^- = 2ICl + 2IO_3^- + Cl^- \quad (2)$$

The reaction requires the addition of acids, which are critical in the initial step, and leads to the formation of both I_2 and ICl as possible iodinating agents. The latter has been implicated in related iodination procedures involving $NaIO_4$/KI/NaCl[17c] or NaI/$FeCl_3$,[17d] which have been reported to effectively iodinate phenolic and indole substrates.

Table 1
Isolation yields of the iodinated products obtained by the $NaClO_2$/NaI/HCl system

Entry	Substrate	$NaClO_2$/NaI mol equiv	Reaction time	Product	Yield (%)	Ref.
1	 **1a**	0.5/0.5	18 h	 **1b**  **1c**	40	18
2	 **1a**	4/8	30 min	 **1d**	Monoiodo (40)+diiodo (35)	18
3	 **2a**	2/4	1 h	 **2b**	80	4g
4	 **3a**	2/4	30 min	 **3b**	95	19
5	 **4a**	2/4	30 min	 **4b**	73	20
6	 **5a**	1/2	18 h	 **5b**	87	4g
7	 **6a**	2/4	1.5 h	 **6b**	98	24
8	 **7a**	4/8	10 min	 **7b**	95	20
9	 **8a**	2/4	2 h	 **8b**	47	—[a]
10	 **9a**	1/2	30 min	 **9b**	75	—[a]
11	 **10a**	1/2	40 min	 **10b**	98	21
12	 **11a**	2/4	3 h	 **11b**	45	22

[a] Not reported in literature to our knowledge.

3. Conclusion

We have highlighted the potential of $NaClO_2$/NaI/HCl as a cheap, non-toxic system for the facile iodination of a range of aromatic compounds under mild conditions. The protocol is effective with common phenols and aromatic amines, but seems to be of special interest for the mild iodination of heterocyclic compounds, including deactivated indoles and 8-hydroxyquinoline. Iodinated products are obtained in good isolated yields and with satisfactory purity by a simple extraction procedure.

4. Experimental

4.1. General

All solvents were reagent grade. All chemicals were purchased from Aldrich and Acros Chemical Co. Merck silica gel 60 (particle size 0.04–0.063 mm) was employed for column chromatography. (HR) ESI^+/MS and ESI^-/MS spectra were obtained in 2% formic acid/methanol 1:1 v/v and water/methanol 1:1 v/v, respectively. ^1H and ^{13}C NMR spectra were obtained on a Bruker WM 400 instrument at 400 and 100 MHz, respectively. IR spectra were recorded with a Nicolet IR100 FT-IR Spectrometer. UV spectra were recorded with an HP 8452A UV/vis spectrophotometer. Mass spectral and ^1H and ^{13}C NMR data are reported for all compounds synthesized. Melting points were determined on a Gallenkamp melting point apparatus with digital thermometer.

4.2. General iodination procedure

A solution of the appropriate starting compound (2 mmol) in methanol (100 mL) was added to $NaClO_2$ and NaI (mol equiv as indicated in Table 1) in water (100 mL) followed by 12 M HCl (6 mmol) and the mixture was stirred at room temperature. At completion of the reaction as determined by TLC analysis, the mixture was diluted with water (100 mL) and extracted with ethyl acetate. The combined organic layers were washed with a saturated solution of sodium chloride containing sodium thiosulfate (10 g/L), to remove excess iodine, dried over anhydrous sodium sulfate and taken to dryness under reduced pressure to give in most cases a single product (TLC evidence) as amorphous powder. In the case of reaction entries 2 and 10 methanol was used as the reaction medium, with substrate at 60 and 150 mM, respectively. In the case of entries 1 and 2 the reaction mixture was purified by column chromatography using a 40–60% cyclohexane/ethyl acetate gradient.

4.2.1. 2-Iodo-17β-estradiol[18] (**1b**)

R_f 0.50 (eluant cyclohexane/AcOEt 60:40). Pale yellow oil; ESI(−) MS *m/z* 397 $[M-H]^-$; ESI-HRMS calculated for $C_{18}H_{22}O_2I$ $[M-H]^-$: 397.0664, found 397.0668; UV λ_{max} (MeOH) 286, 295 (s) nm; IR ν_{max} ($CHCl_3$) 3479, 2942, 2867, 1620, 1465, 1385, 1186 cm^{-1}; ^1H NMR (CD_3OD) δ (ppm) 0.76 (3H, s), 1.20 (1H, m), 1.22–1.34 (4H, m), 1.4–1.5 (2H, m), 1.61 (1H, m), 1.82 (1H, m), 1.94 (1H, m), 2.0–2.1 (2H, m), 2.22 (1H, m), 2.71 (2H, m), 3.63 (1H, t), 6.53 (1H, s), 7.49 (1H, s); ^{13}C NMR (CD_3OD) δ (ppm) 12.5 (CH_3), 24.9 (CH_2), 28.8 (CH_2), 29.1 (CH_2), 31.2 (CH_2), 31.6 (CH_2), 38.8 (CH_2), 41.1 (CH), 45.2 (C), 45.7 (CH), 52.1 (CH), 82.4 (C), 83.3 (CH), 116.8 (CH), 136.1 (C), 137.9 (CH), 140.4 (C), 156.4 (C).

4.2.2. 4-Iodo-17β-estradiol[18] (**1c**)

R_f 0.55 (eluant cyclohexane/AcOEt 60:40). Pale yellow oil; ESI(−) MS *m/z* 397 $[M-H]^-$; ESI-HRMS calculated for $C_{18}H_{22}O_2I$ $[M-H]^-$: 397.0664, found 397.0660; UV λ_{max} (MeOH) 288 nm; IR ν_{max} ($CHCl_3$) 3480, 2951, 2866, 1615, 1461, 1389, 1179 cm^{-1}; ^1H NMR (CD_3OD) δ (ppm) (selected data) 0.72 (3H, s), 1.11 (1H, m), 1.14–1.40 (4H, m), 1.4–1.75 (2H, m), 1.75–2.1 (5H, m), 2.23 (1H, m), 2.82 (1H, m), 2.95 (1H, m), 3.55 (1H, t), 6.60 (1H, d, *J* 8.8 Hz), 7.08 (1H, d, *J* 8.8 Hz); ^{13}C NMR (CD_3OD) δ (ppm) 12.7 (CH_3), 25.3 (CH_2), 27.9 (CH_2), 30.5 (CH_2), 32.2 (CH_2), 33.0 (CH_2), 39.6 (CH_2), 40.5 (CH), 44.6 (C), 46.8 (CH), 53.2 (CH), 83.3 (CH), 85.0 (C), 114.8 (CH), 132.9 (CH), 136.8 (C), 141.0 (C), 156.1 (C).

4.2.3. 2,4-Diiodo-17β-estradiol[18] (**1d**)

R_f 0.44 (eluant cyclohexane/AcOEt 60:40). Pale yellow oil; ESI(−) MS *m/z* 523 $[M-H]^-$; ESI-HRMS calculated for $C_{18}H_{21}O_2I_2$ $[M-H]^-$: 522.9631, found 522.9638; UV λ_{max} (MeOH) 289 nm; IR ν_{max} ($CHCl_3$) 3474, 2937, 2872, 1613, 1452, 1393, 1188 cm^{-1}; ^1H NMR ($CDCl_3$) δ (ppm) 0.72 (3H, s), 1.07 (1H, m), 1.1–1.3 (4H, m), 1.4–1.5 (2H, m), 1.62 (1H, m), 1.8–1.9 (2H, m), 2.0–2.1 (2H, m), 2.21 (1H, m), 2.58 (1H, m), 2.74 (1H, m), 3.68 (1H, t), 7.57 (1H, s); ^{13}C NMR ($CDCl_3$) δ (ppm) 10.9 (CH_3), 23.0 (CH_2), 26.6 (CH_2), 27.9 (CH_2), 30.5 (CH_2), 36.5 (CH_2), 37.2 (CH_2), 37.8 (CH), 43.1 (C), 43.8 (CH), 49.8 (CH), 78.0 (C), 81.7 (CH), 92.1 (C), 135.8 (CH), 136.6 (C), 140.8 (C), 151.2 (C).

4.2.4. 2,4,6-Triiodophenol[4g] (**2b**)

Light brown solid; mp 156–159 °C (lit.[4g] mp 158.5–159.5 °C); ESI(−) MS *m/z* 471 $[M-H]^-$; ESI-HRMS calculated for $C_6H_2OI_3$ $[M-H]^-$: 470.7240, found 470.7198; UV λ_{max} (MeOH) 290 (s), 300, 310 (s) nm; IR ν_{max} ($CHCl_3$) 3440, 2970, 1430, 1080 cm^{-1}; ^1H NMR ($CDCl_3$) δ (ppm) 7.95 (2H, s); ^{13}C NMR ($CDCl_3$) δ (ppm) 83.3 (C), 146.4 (CH), 153.7 (C).

4.2.5. 2,6-Diiodo-4-nitrophenol[19] (**3b**)

Yellow crystals (ethanol); mp 154–157 °C (lit.[23] mp 155 °C); ESI(−) MS *m/z* 390 $[M-H]^-$; ESI-HRMS calculated for $C_6H_2NO_3I_2$ $[M-H]^-$: 389.8124, found 389.8128; UV λ_{max} (MeOH) 290, 320, 397 nm; IR ν_{max} 3460, 3085, 1595, 1525, 1446, 1341, 1327 cm^{-1}; ^1H NMR (acetone-d_6) δ (ppm) 8.62 (2H, s); ^{13}C NMR (acetone-d_6) δ (ppm) 81.9 (C), 130.4 (C), 135.1 (CH), 161.4 (C).

4.2.6. 2,4,6-Triiodoresorcine[20] (**4b**)

Light brown solid; mp 142–145 °C (lit.[20] mp 154–157 °C); ESI(−) MS *m/z* 487 $[M-H]^-$; ESI-HRMS calculated for $C_6H_2O_2I_3$ $[M-H]^-$: 486.7189, found 486.7107; UV λ_{max}

(MeOH) 302 nm; IR ν_{max} ($CHCl_3$) 3474, 1554, 1440, 1427, 1327, 1296 cm^{-1}; ^1H NMR ($CDCl_3$) δ (ppm) 7.93 (1H, s); ^{13}C NMR ($CDCl_3$) δ (ppm) 71.7 (C), 145.2 (CH), 155.0 (C).

4.2.7. 1-Iodo-2-naphthol[4g] (**5b**)

Brown oil; ESI(−) MS *m/z* 269 $[M-H]^-$; ESI-HRMS calculated for $C_{10}H_6OI$ $[M-H]^-$: 268.9463, found 268.9428; UV λ_{max} (MeOH) 280, 320, 330, 360 (s) nm; IR ν_{max} ($CHCl_3$) 3500, 3380, 2940, 1620, 1600, 1470, 1380, 1220, 1170, 1150 cm^{-1}; ^1H NMR (acetone-d_6) δ (ppm) 7.29 (1H, d, *J* 9.0 Hz), 7.37 (1H, t, *J* 7.2 Hz), 7.56 (1H, t, *J* 7.2 Hz), 7.81 (1H, d, *J* 8.1 Hz), 7.82 (1H, d, *J* 9.0 Hz), 8.06 (1H, d, *J* 8.1 Hz), 9.52 (1H, s); ^{13}C NMR (acetone-d_6) δ (ppm) 94.3 (C), 117.4 (CH), 123.0 (CH), 124.9 (CH), 128.2 (CH), 128.6 (CH), 129.9 (C), 130.5 (CH), 137.7 (C), 152.36 (C).

4.2.8. 2,4-Diiodoaniline[24] (**6b**)

Dark powder; mp 94–96 °C (lit.[24] mp 93 °C); ESI(+) MS *m/z* 346 $[M+H]^+$; ESI-HRMS calculated for $C_6H_6NI_2$ $[M+H]^+$: 345.8590, found 345.8596; UV λ_{max} (MeOH) 250, 305 nm; IR ν_{max} ($CHCl_3$) 3480, 3393, 1610, 1470, 1380 cm^{-1}; ^1H NMR (CD_3OD) δ (ppm) 6.57 (1H, d, *J* 8.2 Hz), 7.33 (1H, dd, *J* 8.2, 2.0 Hz), 7.80 (1H, d, *J* 2.0 Hz); ^{13}C NMR (CD_3OD) δ (ppm) 78.6 (C), 85.2 (C), 117.9 (CH), 139.3 (CH), 147.2 (CH), 149.8 (C).

4.2.9. 2-Iodo-4-nitroaniline[20] (**7b**)

Orange powder; mp 96–98 °C (lit.[25] mp 106–107 °C); ESI(+) MS *m/z* 265 $[M+H]^+$, 287 $[M+Na]^+$; ESI-HRMS calculated for $C_6H_6N_2O_2I$ $[M+H]^+$: 264.9474, found 264.9470; UV λ_{max} (MeOH) 270, 360 nm; IR ν_{max} ($CHCl_3$) 3390, 2940, 1640, 1600, 1515, 1470, 1330 cm^{-1}; ^1H NMR (CD_3OD) δ (ppm) 6.70 (1H, d, *J* 8.7 Hz), 8.04 (1H, dd, *J* 8.7, 2.4 Hz), 8.54 (1H, d, *J* 2.4 Hz); ^{13}C NMR (CD_3OD) δ (ppm) 80.2 (C), 113.5 (CH), 127.0 (CH), 137.1 (CH), 139.6 (C), 156.5 (C).

4.2.10. 5,6-Diacetoxy-2,3-diiodoindole (**8b**)

Needles from ethanol; mp dec >80 °C; ESI(+) MS *m/z* 486 $[M+H]^+$; ESI-HRMS calculated for $C_{12}H_{10}NO_4I_2$ $[M+H]^+$: 485.8699, found 485.8705; UV λ_{max} (MeOH) 304 nm; IR ν_{max} 1769, 1602, 1444, 1371, 1319 cm^{-1}; ^1H NMR (CD_3OD) δ (ppm) 2.29 (6H, s, 2×$OCOCH_3$), 7.15 (1H, s, H-7), 7.31 (1H, s, H-4), 11.29 (1H, s, NH); ^{13}C NMR (acetone-d_6) δ (ppm) 21.2 (2×$COCH_3$), 71.2 (C), 90.0 (C), 106.1 (CH), 114.4 (CH), 129.4 (C), 136.6 (C), 138.4 (C), 139.9 (C), 168.8 ($OCOCH_3$), 168.9 ($OCOCH_3$).

4.2.11. 3-Iodo-5-nitroindole (**9b**)

Light yellow crystals (ethanol); mp 167–170 °C; ESI(+) MS *m/z* 289 $[M+H]^+$, 311 $[M+Na]^+$; ESI-HRMS calculated for $C_8H_6N_2O_2I$ $[M+H]^+$: 288.9474, found 288.9479; UV λ_{max} (MeOH) 269, 319 nm; IR ν_{max} 1622, 1525, 1472, 1341 cm^{-1}; ^1H NMR (CD_3OD) δ (ppm) 7.51 (1H, d, *J* 9.0 Hz), 7.56 (1H, d, *J* 2.2 Hz), 8.05 (1H, dd, *J* 9.0, 2.2 Hz), 8.24 (1H, d, *J* 2.1 Hz); ^{13}C NMR (CD_3OD) δ (ppm) 58.9 (C), 113.7 (CH), 118.8 (CH), 119.2 (CH), 131.4 (C), 134.9 (CH), 141.4 (C), 143.9 (C).

4.2.12. 8-Hydroxy-5,7-diiodoquinoline[21] (**10b**)

Greenish powder; mp 206–210 °C (lit.[15a] mp 214–215 °C); ESI(+) MS *m/z* 398 $[M+H]^+$; ESI-HRMS calculated for $C_9H_6NOI_2$ $[M+H]^+$: 397.8539, found 397.8544; UV λ_{max} (MeOH) 260, 335 nm; IR ν_{max} ($CHCl_3$) 2940, 1480, 1450, 1380, 1330, 1200 cm^{-1}; ^1H NMR (CD_3OD) δ (ppm) 7.53 (1H, dd, *J* 8.4, 8.7 Hz), 8.25 (1H, dd, *J* 8.4, 1.5 Hz), 8.32 (1H, s), 8.80 (1H, dd, *J* 8.7, 1.5 Hz); ^{13}C NMR (DMSO-d_6) δ (ppm) 80.8 (C), 85.2 (C), 124.2 (CH), 129.6 (C), 138.0 (C), 140.0 (CH), 144.6 (CH), 149.6 (CH), 154.8 (C).

4.2.13. 2,4,5-Triiodoimidazole[22] (**11b**)

Yellowish oil; ESI(−) MS *m/z* 445 $[M-H]^-$; ESI-HRMS calculated for $C_3N_2I_3$ $[M-H]^-$: 444.7196, found 444.7195; ^{13}C NMR (CD_3OD) δ (ppm) 89.0 (C).

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