

A Useful and Convenient Synthetic Protocol for Iodination of Organic Substrates Using a Combination of Vanadyl Acetylacetonate, Hydrogen Peroxide, and Sodium Iodide

Abu T. Khan* and Shahzad Ali

Department of Chemistry, Indian Institute of Technology Guwahati, Guwahati 781039, India

Received May 31, 2012; E-mail: atk@iitg.ernet.in

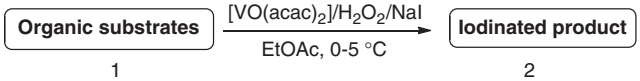
A wide variety of organic substrates can be iodinated selectively in good yields by employing a combination of vanadyl acetylacetonate, hydrogen peroxide, and sodium iodide at ice-bath temperature. Good yield, selectivity, use of cost effective reagents, and mild and environmentally benign reaction conditions are some of the major advantages of this protocol.

Organohalogen compounds are distributed in nature[1] and serve as useful synthetic precursors for Sonogashira and Suzuki coupling reactions[2] as well as for preparation of organolithium, Grignard reagents,[3] and Wittig reagents,[4] which are extensively used in C–C bond forming reactions. Due to poor the electrophilicity of molecular iodine, it cannot be used alone for iodination reaction. Iodinated compounds are extensively also used for C–N and C–S cross-coupling reaction[5] and in medical diagnosis as radioactivity labeled markers.[6]

Taking cues from the discovery of vanadium bromoperoxidase (VBrPO),[7,8] a vanadium enzyme which catalyzes the oxidation of bromide by hydrogen peroxide, we have developed numerous synthetic methodologies such as cleavage of dithioacetals and oxathioacetals, hydrolysis of 1-thioglycosides, synthesis of bromoflavones and α-monobrominated 1,3-dicarbonyl compounds using a combination of $V_2O_5/H_2O_2/NH_4Br$.[9] Biomimicking studies of iodoperoxidases like bromoperoxidases[10–12] have not yet been investigated by employing a vanadium complex. Therefore, vanadyl acetylacetonate was chosen as it can form selectively vanadium(V) monoperoxo complex, which may change the course of the reaction pathway. Though numerous reagents have been developed for iodination reaction of organic substrates over the years,[13] still there is a further scope to develop a new methodology, which might work under mild reaction conditions.

The usefulness of vanadyl acetylacetonate was demonstrated by West et al. recently for the olefination of α,α'-divinyl ketones through catalytic Meyer–Schuster rearrangement[14a] and synthesis of benzimidazoles.[14b] It was well known in the literature that it can also be used for asymmetric oxidation of sulfides[15a] and oxidation of cyclohexane into cyclohexanol,[15b] epoxidation of allylic alcohols[15c] in the presence of either hydrogen peroxide or *tert*-butylhydroperoxide (TBHP) as well as conversion of *bis*-homoallylic alcohols into functionalized *cis*-THFs by catalytic olefin epoxidation followed by epoxide ring opening,[15d] and cleavage of dithioacetals of sugars into aldehyde sugars.[15e]

Our present aim is to investigate whether selective iodination can be achieved using in situ generated iodonium ion or not.



Scheme 1. Iodination of organic substrates.

Literature survey reveals that the following reagents have been used for α-iodination of 1,3-dicarbonyl compounds such as periodic acid in glacial acetic acid,[16] iodine in presence of cooxidants,[17] NIS with other additive,[18] Koser's reagent (HTIB) along with MgI_2,[19] and $KI/NaNO_2/O_2/H_2SO_4$.[20] Most of the above methods have some demerits such as they are not applicable for a wide range of substrates, provide low yield and poor selectivity,[16] high cost of the reagents[18] and longer reaction time.[20] In fact, it is difficult to obtain selectively α-iodinated 1,3-dicarbonyl compounds. In this paper, we would like to report the iodination of various organic substrates using a combination of $[VO(acac)_2]/H_2O_2/NaI$ as shown in Scheme 1.

Results and Discussion

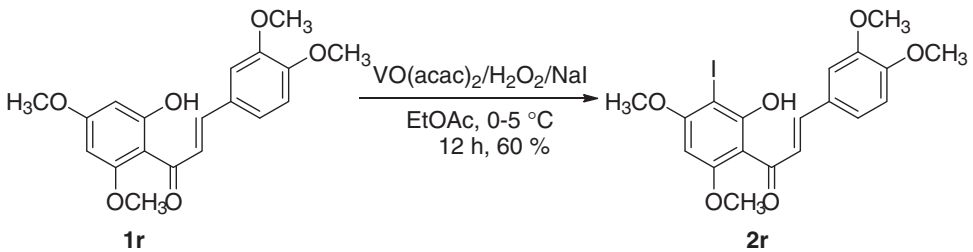
In this study, the catalyst vanadyl acetylacetonate was prepared according to a literature procedure.[21] To find suitable reaction conditions, benzoyl acetone (**1a**) was chosen as a model substrate for optimization of the reaction conditions. Several reactions were examined using different amounts of $[VO(acac)_2]$ and NaI. The best yield of iodinated product **2a** was obtained using the combination of substrate:$[VO(acac)_2]$:H_2O_2:NaI (1.0:0.2:4.4:2.0 equiv), respectively (Table 1, Entry 5). After screening of various solvent systems such as CH_2Cl_2, CH_3CN, CH_3OH, and CH_3COCH_3 (Table 1, Entries 7–10), it was noted that ethyl acetate was the best solvent for obtaining mono-iodinated product in terms of yield and reaction time. To compare the effectiveness of $[VO(acac)_2]$ as compared to other vanadium compounds, we have conducted the reaction with V_2O_5 and NH_4VO_3 as well as without $[VO(acac)_2]$, respectively and the results are summarized in Table 1 (Entries 11–13). In the absence of $[VO(acac)_2]$ only trace quantities (<5%) of the desired mono iodinated product **2a** was produced and unreacted starting material was recovered in high yield. From these observations, it is quite clear that vanadyl acetylacetonate

Published on the web October 27, 2012; doi:10.1246/bcsj.20120155

Table 1. Optimization of the Reaction Conditions for the Selective α-Iodination of Benzoyl Acetone[a)]

Entry	Catalyst used	mol %	NaI/equiv	Solvent	Time/min	Yield[b)]/%
1	$[VO(acac)_2]$	10	2.0	EtOAc	30	59
2	$[VO(acac)_2]$	15	2.0	EtOAc	25	75
3	$[VO(acac)_2]$	20	1.5	EtOAc	25	73
4	$[VO(acac)_2]$	20	1.7	EtOAc	25	81
5	**$[VO(acac)_2]$**	**20**	**2.0**	**EtOAc**	**25**	**91**
6	$[VO(acac)_2]$	20	2.2	EtOAc	25	90
7	$[VO(acac)_2]$	20	2.0	CH_2Cl_2	25	66
8	$[VO(acac)_2]$	20	2.0	CH_3CN	25	69
9	$[VO(acac)_2]$	20	2.0	CH_3OH	10	65
10	$[VO(acac)_2]$	20	2.0	CH_3COCH_3	35	72
11	V_2O_5	20	2.0	EtOAc	25	38
12	NH_4VO_3	20	2.0	EtOAc	15	20
13	Without $[VO(acac)_2]$	00	2.0	EtOAc	35	05

a) All the reactions were carried out with 1 mmol of benzoyl acetone. b) Isolated yield.



1r **2r**

Scheme 2.

plays a crucial role for the formation of product. To prove the usefulness of the present protocol, similar reactions were carried out with molecular iodine (1 equiv) and hydrogen peroxide (4.4 equiv) in ethyl acetate as well as with molecular iodine (1 equiv) and $[VO(acac)_2]$ (0.2 equiv) under identical conditions. We have obtained 56% and 38% yield respectively based on starting material recovery. From these results we may conclude that a combination of $[VO(acac)_2]$, NaI and H_2O_2 is essential for effective conversion of the starting material into products. The product **2a** was characterized by recording ^1H and ^{13}C NMR spectra and elemental analysis. Next, dibenzoylmethane (**1b**) was subjected to iodination under similar reaction conditions and the product **2b** was isolated in 90% yield.

These successful results further motivated us to investigate the iodination reaction with cyclic 1,3-diketones such as dimedone (**1c**) and 1,3-cyclohexanedione (**1d**) using the same combination under identical reaction conditions. The iodinated products **2c** and **2d** were obtained in fairly good yields.

To examine the efficacy of the present protocol, various β-esters **1e**–**1k** were subjected to iodination reactions with the same combination by following the same experimental procedure. The mono α-iodinated β-ketoesters **2e**–**2k** were obtained in good yields (Entries 5–11), which is shown in Table 2.

Very recently, many new reagents have been developed by various groups for aromatic iodination such as 18-crown-6-supported ICl_2^-,[22] NIS/In(OTf)$_3$,[23] ICl/In(OTf)$_3$,[24] I_2/H_5IO_6,[25] TMADCI,[26] and benzyltriethylammonium dichloroiodate/$NaHCO_3$.[27] The only demerits of these reagents are they have to be prepared prior to use and are expensive.

To verify further the scope of the present protocol, the iodination reactions of electron-rich aromatic substrates such as aniline, *N*-methylaniline, 4-ethylaniline, and phenol were also examined under similar reaction conditions. We have obtained only monoiodinated products **2l**–**2n** regioselectively in good yields as shown in Table 2. It was observed that 10 mol % $[VO(acac)_2]$ is required for complete conversion of aniline into 4-iodoaniline in 90% yield when the reaction was carried out with 10 mmol scale. From this observation, we may conclude iodination can be performed with lesser amounts of $[VO(acac)_2]$. Unfortunately, we obtained a mixture of products in the case of phenol under similar reaction conditions.

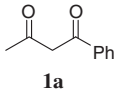
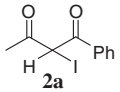
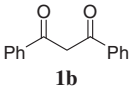
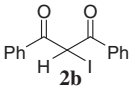
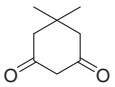
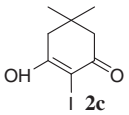
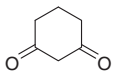
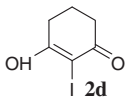
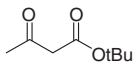
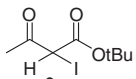
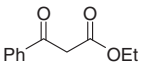
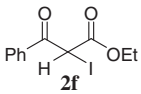
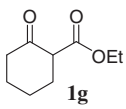
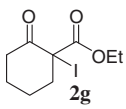
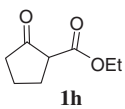
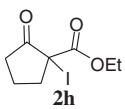
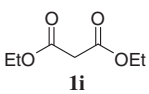
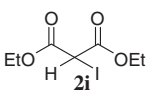
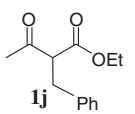
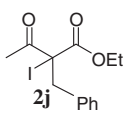
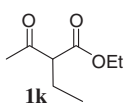
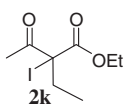
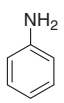
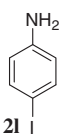
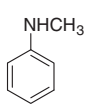
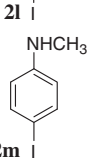
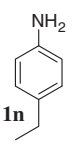
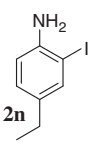
To extend the scope and general applicability of this protocol, pyrazole derivatives **1p** and **1q** were also iodinated easily and provided the desired products **2p** and **2q**, respectively in very good yields as shown in the Table 2.

To verify competitive iodination reaction between aromatic rings and electron-deficient double bonds, we have carried out an iodination reaction with (*E*)-1-(2-hydroxy-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (**1r**) under similar reaction conditions, which are shown in Scheme 2. From the observation, it reveals iodination at the aromatic ring is preferred over conjugated double bonds.

All these products were characterized by recording ^1H and ^{13}C NMR spectra and elemental analysis. Compounds **2a**,[17c] **2b**,[20] **2c**,[17c] **2e**,[17c] **2f**,[20] **2h**,[20] **2j**,[18a] **2k**,[18a] **2l**,[25] **2m**,[25] **2p**,[28b] and **2q**[28b] have previously been reported and NMR data are in good agreement with the literature data.

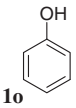
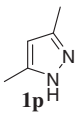
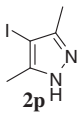
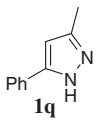
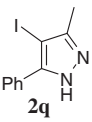
We put forward a proposed mechanism that the interaction of vanadyl acetylacetonate with hydrogen peroxide can generate mono peroxo complex of vanadium(V) (Scheme 3),[15b] which can oxidize iodide ion to iodonium ion, which may exist in solution as HOI or I_2 or I_3^-. Then in situ generated iodonium

Table 2. Iodination of Various Organic Compounds Using $[VO(acac)_2]/H_2O_2/NaI$[a)]

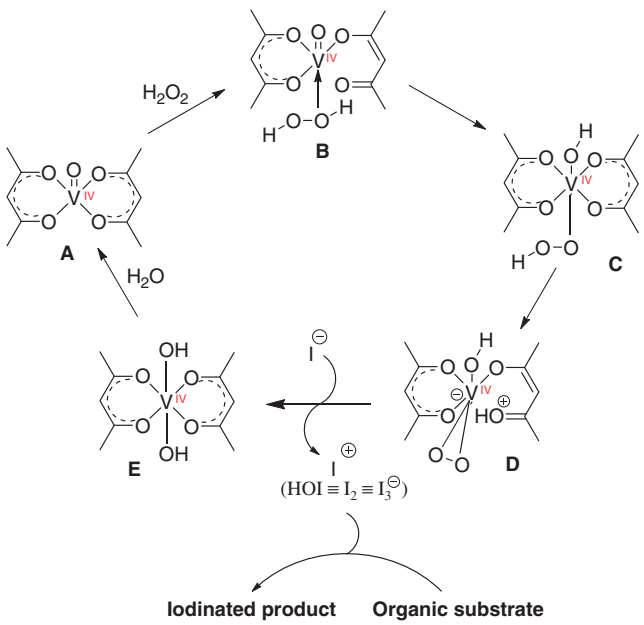
Entry	Substrate (a)	Products (b)	NaI /equiv	Time /h	Yield[a)] /%
1	 **1a**	 **2a**	2.0	0.5	91
2	 **1b**	 **2b**	2.0	3.5	90
3	 **1c**	 **2c**	2.0	instant	67
4	 **1d**	 **2d**	2.0	instant	62
5	 **1e**	 **2e**	2.0	11.5	87
6	 **1f**	 **2f**	2.5	24	92
7	 **1g**	 **2g**	2.0	1	73
8	 **1h**	 **2h**	2.0	1	90
9	 **1i**	 **2i**	2.5	26	80
10	 **1j**	 **2j**	2.0	16	75
11	 **1k**	 **2k**	2.0	13	79
12	 **1l**	 **2l**	2.0	8.0	85
13	 **1m**	 **2m**	2.0	8.0	87
14	 **1n**	 **2n**	2.0	8.0	84

Continued on next Column.

Continued.

Entry	Substrate (a)	Products (b)	NaI /equiv	Time /h	Yield[a)] /%
15	 **1o**	Mixture of products	2.0	1.0	—
16	 **1p**	 **2p**	2.0	1.0	90
17	 **1q**	 **2q**	2.0	6.5	92

a) The reactions were performed with 1 mmol of substrates. b) Isolated yield.



Scheme 3. Probable mechanism for the formation of iodinated product.

ion was successfully trapped by the organic substrates to afford iodinated compounds. The cycle continues by further regeneration of the peroxo complex by the action of the intermediate with H_2O_2. However, the correct oxidized species is not known yet, which we are trying to determine.

Conclusion

In conclusion, we have demonstrated an important and efficient method for the mono-iodination of 1,3-dicarbonyl compounds, anilines and pyrazoles by using a combination of $[VO(acac)_2]/H_2O_2/NaI$ in ethyl acetate. It was observed that most of the halogenation reactions are carried out in halogenated solvents such as dichloromethane, chloroform, and carbon tetrachloride, which is replaceable with non-halogented less expensive solvent such as ethyl acetate. In addition, the reaction can be done in the presence of lower amounts of $[VO(acac)_2]$ if the reaction is performed in large scale. More-

over, these reagents are environmentally acceptable. Notably, the ester functionality does not undergo hydrolysis under the reaction conditions although the medium is acidic. Good yield, high selectivity, use of cost effective reagents, and mild and environmentally benign reaction conditions are some major advantages of this protocol.

Experimental

Typical Procedure for Iodination. Vanadyl acetylacetonate (0.053 g, 0.2 mmol) was taken in 2 mL of water at ice-bath temperature (0–5 °C). Then, 0.5 mL of H_2O_2 (4.4 mmol) was added slowly to it and kept stirring at the same temperature. The solution becomes yellow after 10 min and subsequently the substrate was added to it by dissolving in 3 mL of ethyl acetate followed by NaI (0.3 g, 2.0 mmol) solution by taking into 1.5 mL of water. The solution becomes dark brown instantly. After completion of the reaction, it was extracted with ethyl acetate (3 × 25 mL) and the organic layer was washed with 10% sodium thiosulfate solution to remove unreacted iodine. Finally, the organic layer was washed with water and dried over sodium sulfate. The solvent was evaporated under vacuum and pure product was obtained **2a** as yellow oil in 91% yield.

2-Iodo-1-phenylbutane-1,3-dione (2a): Yellow oil. IR (KBr): 3388, 3066, 1687, 1599, 1448, 1355, 1221, 1185, 1124, 1018 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.56 (s, 3H), 5.97 (s, 1H), 7.51 (t, $J = 7.6$ Hz, 2H), 7.64 (t, $J = 7.6$ Hz, 1H), 7.98 (d, $J = 7.6$ Hz, 2H). ^{13}C NMR (100 Hz, $CDCl_3$): δ 27.3, 33.0, 129.3, 129.4, 133.9, 134.6, 191.2, 198.9. Anal. Calcd for $C_{10}H_9IO_2$ (288.08): requires C, 41.69; H, 3.15%. Found C, 41.51; H, 3.06%.

2-Iodo-1,3-diphenylpropane-1,3-dione (2b): White solid; mp 107–108 °C. (Lit.[17a] 108–109 °C). IR (KBr): 2957, 1688, 1662, 1594, 1446, 1289, 1240, 1182, 994, 979 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.95 (s, 1H), 7.48 (t, $J = 8.0$ Hz, 4H), 7.61 (t, $J = 7.6$ Hz, 2H), 8.00 (d, $J = 7.6$ Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.1, 129.3, 129.5, 133.4, 134.4, 190.3. Anal. Calcd for $C_{15}H_{11}IO_2$ (350.15): requires C, 51.45; H, 3.17%. Found C, 51.32; H, 3.09%.

3-Hydroxy-2-iodo-5,5-dimethylcyclohex-2-enone (2c): White solid; mp 154–155 °C. (Lit.[17c] 166–167 °C). IR (KBr): 3448, 1624, 1574, 1317, 1000 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.15 (s, 6H), 2.48 (s, 4H). ^{13}C NMR (100 MHz, DMSO): δ 27.5, 32.3, 46.6, 76.7, 184.5. Anal. Calcd for $C_8H_{11}IO_2$ (266.08): requires C, 36.11; H, 4.17%. Found C, 36.01; H, 4.06%.

3-Hydroxy-2-iodocyclohex-2-enone (2d): White solid; mp 138–139 °C. IR (KBr): 3105, 1645, 1580, 1368, 1315, 1190, 1144, 1066, 956 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$ + DMSO): δ 1.97 (quint, $J = 6.0$ Hz, 2H), 2.61 (t, $J = 6.0$ Hz, 4H). ^{13}C NMR (100 MHz, DMSO): δ 20.9, 33.3, 78.6, 185.6. Anal. Calcd for $C_6H_7IO_2$ (238.02): requires C, 30.28; H, 2.96%. Found C, 30.16; H, 2.88%.

***tert*-Butyl 2-Iodo-3-oxobutanoate (2e):** Yellow oil. IR (KBr): 2981, 1731, 1639, 1371, 1251, 1154 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.48 (s, 9H), 2.51 (s, 3H), 4.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.3, 27.8, 28.2, 84.3, 165.7, 197.9. Anal. Calcd for $C_8H_{13}IO_3$ (284.09): requires C, 33.82; H, 4.61%. Found C, 33.74; H, 4.53%.

Ethyl 2-Iodo-3-oxo-3-phenylpropanoate (2f): Yellow oil. IR (KBr): 2931, 1675, 1272, 1002 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.22 (t, $J = 7.2$ Hz, 3H), 4.24 (q, $J = 7.2$ Hz, 2H), 5.92 (s, 1H), 7.46 (t, $J = 7.6$ Hz, 2H), 7.57 (t, $J = 7.6$, 1H), 7.96 (d, $J = 7.6$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 24.2, 63.5, 129.1, 129.3, 133.1, 134.3, 166.7, 189.4. Anal. Calcd for $C_{11}H_{11}IO_3$ (318.10): requires C, 41.53; H, 3.49%. Found C, 41.42; H, 3.39%.

Ethyl 1-Iodo-2-oxocyclohexanecarboxylate (2g): Yellow oil. IR (KBr): 2941, 2868, 1722, 1449, 1235, 1122, 1092, 1018 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.28 (t, $J = 7.2$ Hz, 3H), 1.67–1.74 (m, 2H), 1.75–1.80 (m, 1H), 1.94–1.98 (m, 1H), 2.25–2.32 (m, 1H), 2.47–2.54 (m, 1H), 2.91–2.96 (m, 2H), 4.27 (q, $J = 7.2$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 24.8, 27.3, 38.3, 43.3, 53.3, 63.1, 169.5, 200.0. Anal. Calcd for $C_9H_{13}IO_3$ (296.10): requires C, 36.51; H, 4.43%. Found C, 36.38; H, 4.33%.

Ethyl 1-Iodo-2-oxocyclopentanecarboxylate (2h): Yellow oil. IR (KBr): 2973, 1745, 1256, 1180, 1132, 1020 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.29 (t, $J = 7.2$ Hz, 3H), 2.07–2.14 (m, 2H), 2.35–2.53 (m, 4H), 4.26 (dq, $J = 7.2$, 0.6 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 20.0, 35.1, 40.3, 43.6, 63.3, 168.1, 207.1.

Diethyl 2-Iodomalonate (2i): Yellow oil. IR (KBr): 2984, 1745, 1630, 1372, 1300, 1236, 1136, 1099, 1024 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.30 (t, $J = 7.2$ Hz, 3H), 4.32 (q, $J = 7.2$ Hz, 2H), 4.80 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 14.0, 63.5, 90.4, 168.4. Anal. Calcd for $C_7H_{11}IO_4$ (286.06): requires C, 29.39; H, 3.88%. Found C, 29.23; H, 3.71%.

Ethyl 2-Benzyl-2-iodo-3-oxobutanoate (2j): Yellow oil. IR (KBr): 2978, 1711, 1356, 1309, 1236, 1187, 1083, 1015 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 1.20 (t, $J = 7.6$ Hz, 3H), 2.47 (s, 3H), 3.54 (d, $J = 14.4$ Hz, 1H), 3.67 (d, $J = 14.4$ Hz, 1H), 4.17 (q, $J = 7.2$ Hz, 2H), 7.17–7.26 (m, 5H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.9, 26.9, 44.4, 54.5, 63.4, 127.6, 128.4, 130.4, 136.4, 168.4, 198.2. Anal. Calcd for $C_{13}H_{15}IO_3$ (346.16): requires C, 45.11; H, 4.37%. Found C, 45.01; H, 4.26%.

Ethyl 2-Ethyl-2-iodo-3-oxobutanoate (2k): Yellow oil. IR (KBr): 3418, 2979, 2044, 1714, 1457, 1358, 1229, 1122, 1022 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 0.96 (t, $J = 7.2$ Hz, 3H), 1.28 (t, $J = 7.6$ Hz, 3H), 2.17 (q, $J = 7.2$ Hz, 2H), 2.45 (s, 3H), 4.25 (q, $J = 7.2$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.3, 14.0, 26.0, 32.5, 56.5, 63.3, 168.8, 198.2. Anal. Calcd for $C_8H_{13}IO_3$ (284.09): requires C, 33.82; H, 4.61%. Found C, 33.69; H, 4.53%.

4-Iodoaniline (2l): White solid; mp 60–62 °C (Lit.[25] 62–63 °C). IR (KBr, cm^{-1}): 3405 (–NH_2), 3297 (–NH_2). ^1H NMR (400 MHz, $CDCl_3$): δ 3.68 (brs, 2H), 6.47 (d, $J = 8.4$ Hz, 2H), 7.41 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 79.5, 117.5 (2C), 138.1 (2C), 146.2. Anal. Calcd for C_6H_6NI (219.02): requires C, 32.90; H, 2.76; N, 6.40%. Found C, 32.71; H, 2.55; N, 6.26%.

4-Iodo-*N*-methylaniline (2m): Colorless Liquid. IR (KBr, cm^{-1}): 3422 (–NH_2); ^1H NMR (400 MHz, $CDCl_3$): δ 2.72 (s, 3H), 3.67 (brs, 1H), 6.31 (d, $J = 8.4$ Hz, 2H), 7.35 (d, $J = 8.8$ Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.7, 77.9, 114.8 (2C), 137.9 (2C), 149.0. Anal. Calcd for C_7H_8NI (233.05): requires C, 36.08; H, 3.46; N, 6.01%. Found C, 36.26; H, 3.54; N, 6.14%.

4-Ethyl-2-iodoaniline (2n): Colorless Liquid. IR (KBr, cm^{-1}): 3398 (–NH_2), 3299 (–NH_2). ^1H NMR (400 MHz, $CDCl_3$): δ 1.17 (t, $J = 7.6$ Hz, 3H), 2.50 (q, $J = 7.6$ Hz, 2H), 3.96 (brs, 2H), 6.69 (d, $J = 8.4$ Hz, 1H), 6.98 (dd, $J_1 = 2.0$, $J_2 = 8.0$ Hz, 1H), 7.48 (d, $J = 1.6$ Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 16.0, 27.6, 84.5, 114.9, 129.0, 136.2, 138.1, 144.6. Anal. Calcd for $C_8H_{10}NI$ (247.08): requires C, 38.89; H, 4.08; N, 5.67%. Found C, 38.71; H, 3.99; N, 5.54%.

4-Iodo-3,5-dimethyl-1*H*-pyrazole (2p): White solid, mp 138–140 °C (Lit.[28b] 134–136 °C). IR (KBr): 3165, 3067, 3030, 2917, 2830, 1577, 1412, 1305, 1164, 1077, 1034 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.24 (s, 6H), 4.27 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.1, 62.7, 146.5. Anal. Calcd for $C_5H_7IN_2$ (222.02): requires C, 27.05; H, 3.18; N, 12.62%. Found C, 26.92; H, 3.11; N, 12.46%.

4-Iodo-3-methyl-5-phenyl-1*H*-pyrazole (2q): White solid, mp 117–120 °C (Lit.[28b] 113–115 °C). IR (KBr): 3173, 3067, 2929, 1567, 1448, 1291, 1269, 1179, 1116, 1045, 967, 915 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 2.26 (s, 3H), 7.39–7.46 (m, 3H), 7.70–7.73 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 12.7, 60.6, 128.4, 128.6, 128.7, 131.9, 146.4, 149.8. Anal. Calcd for $C_{10}H_9IN_2$ (284.10): requires C, 42.28; H, 3.19; N, 9.86%. Found C, 42.17; H, 3.08, N, 9.69%.

(*E*)-1-(2-Hydroxy-3-iodo-4,6-dimethoxyphenyl)-3-(3,4-dimethoxyphenyl)prop-2-en-1-one (2r): Yellow solid, mp 152 °C. IR (KBr, cm^{-1}): 3445 (–OH), 1624 (–C=O). ^1H NMR (400 MHz, $CDCl_3$): δ 3.94 (s, 3H), 3.95 (s, 3H), 3.98 (s, 3H), 4.00 (s, 3H), 6.05 (s, 1H), 6.90 (d, $J = 8.0$ Hz, 1H), 7.12 (s, 1H), 7.22 (d, $J = 8.4$ Hz, 1H), 7.75 (d, $J = 15.2$ Hz, 1H), 7.81 (d, $J = 15.6$, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 56.1, 56.2, 56.3, 56.6, 87.2, 91.4, 106.9, 110.7, 111.4, 123.0, 124.8, 128.5, 143.8, 149.3, 151.5, 163.8, 164.3, 165.8, 192.4. Anal. Calcd for $C_{19}H_{19}IO_6$ (470.26): requires C, 48.53; H, 4.07%. Found C, 48.71; H, 4.18%.

SA is thankful to UGC, New Delhi, India for their Senior Research Fellowship. The authors are also grateful to the Director, IIT Guwahati for providing general facilities to carry out our research work. We are also thankful to the referees for their valuable comments and suggestions.

References

1 G. W. Gribble, *Naturally Occurring Organohalogen Compounds—A Comprehensive Update* in *Progress in the Chemistry of Organic Natural Products*, Springer, New York, **2010**, Vol. 91. doi:10.1007/978-3-211-99323-1.

2 J. J. Li, G. W. Gribble, *Palladium in Heterocyclic Chemistry: A Guide for the Synthetic Chemist*, 2nd ed., Elsevier, Oxford, UK, **2007**, Vol. 26. doi:10.1016/S1460-1567(07)80047-X.

3 L. Kürti, B. Czakó, *Strategic Applications of Named Reactions in Organic Synthesis*, Elsevier, Amsterdam, **2005**.

4 O. I. Kolodiazhnyi, *Phosphorus Ylides*, Wiley-VCH, Weinheim, **1999**.

5 a) F. Diederich, P. J. Stang, *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH, Weinheim, **1998**. doi:10.1002/9783527612222. b) J. Hassan, M. Sévignon, C. Gozzi, E. Schulz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359. c) F. Bellina, A. Carpita, R. Rossi, *Synthesis* **2004**, 2419.

6 *Handbook of Radiopharmaceuticals: Radiochemistry and Applications*, ed. by M. J. Welch, C. S. Redvanly, Wiley, Chichester, **2003**. doi:10.1002/0470846380.

7 A. Butler, J. V. Walker, *Chem. Rev.* **1993**, *93*, 1937.

8 H. Vilter, *Phytochemistry* **1984**, *23*, 1387.

9 a) E. Mondal, G. Bose, P. R. Sahu, A. T. Khan, *Chem. Lett.* **2001**, 1158. b) E. Mondal, P. R. Sahu, G. Bose, A. T. Khan, *J. Chem. Soc., Perkin Trans. 1* **2002**, 1026. c) P. M. B. Barua, P. R. Sahu, E. Mondal, G. Bose, A. T. Khan, *Synlett* **2002**, 81. d) A. T. Khan, P. Goswami, *Tetrahedron Lett.* **2005**, *46*, 4937. e) A. T. Khan, P. Goswami, L. H. Choudhury, *Tetrahedron Lett.* **2006**, *47*, 2751.

10 A. Butler, J. N. Carter-Franklin, *Nat. Prod. Rep.* **2004**, *21*, 180.

11 J. N. Carter-Franklin, A. Butler, *J. Am. Chem. Soc.* **2004**, *126*, 15060.

12 a) V. Conte, F. Di Furia, S. Moro, *Tetrahedron Lett.* **1994**, *35*, 7429. b) V. Conte, F. Di Furia, S. Moro, S. Rabbolini, *J. Mol. Catal. A: Chem.* **1996**, *113*, 175. c) M. Andersson, V. Conte, F. Di Furia, S. Moro, *Tetrahedron Lett.* **1995**, *36*, 2675.

13 S. Stavber, M. Jereb, M. Zupan, *Synthesis* **2008**, 1487.

14 a) C. J. Rieder, K. J. Winberg, F. G. West, *J. Org. Chem.* **2011**, *76*, 50. b) M. Dey, K. Deb, S. S. Dhar, *Chin. Chem. Lett.* **2011**, *22*, 296.

15 a) H. Liu, M. Wang, Y. Wang, Y. Wang, H. Sun, L. Sun, *Catal. Commun.* **2009**, *11*, 294. b) A. Pokutsa, J. Kubaj, A. Zaborovskyi, D. Maksym, J. Muzart, A. Sobkowiak, *Appl. Catal., A* **2010**, *390*, 190. c) J. B. Shotwell, E. S. Krygowski, J. Hines, B. Koh, E. W. D. Huntsman, H. W. Choi, J. S. Schneekloth, Jr., J. L. Wood, C. M. Crews, *Org. Lett.* **2002**, *4*, 3087. d) A. Blanc, F. D. Toste, *Angew. Chem., Int. Ed.* **2006**, *45*, 2096. e) A. T. Khan, S. Ali, R. Sidick Basha, Md. M. Khan, M. Lal, *Carbohydr. Res.* **2011**, *346*, 2629.

16 A. J. Fatiadi, *J. Chem. Soc. D* **1970**, 11.

17 a) I. Urasaki, Y. Ogata, *J. Chem. Soc., Perkin Trans. 1* **1975**, 1285. b) M. Jereb, M. Zupan, S. Stavber, *Chem. Commun.* **2004**, 2614. c) P. Goswami, S. Ali, Md. M. Khan, A. T. Khan, *ARKIVOC* **2007**, Part xv, 82.

18 a) D. Yang, Y.-L. Yan, B. Lui, *J. Org. Chem.* **2002**, *67*, 7429. b) H. M. Meshram, P. N. Reddy, P. Vishnu, K. Sadashiv, J. S. Yadav, *Tetrahedron Lett.* **2006**, *47*, 991, and references therein.

19 J. C. Lee, J. Y. Park, S. Y. Yoon, Y. H. Bae, S. J. Lee, *Tetrahedron Lett.* **2004**, *45*, 191.

20 G. Stavber, J. Iskra, M. Zupan, S. Stavber, *Adv. Synth. Catal.* **2008**, *350*, 2921.

21 M. L. Kantam, B. Neelima, Ch. V. Reddy, M. K. Chaudhuri, S. K. Dehury, *Catal. Lett.* **2004**, *95*, 19.

22 H. W. Mbatia, O. A. Ulloa, D. P. Kennedy, C. D. Incarvito, S. C. Burdette, *Org. Biomol. Chem.* **2011**, *9*, 2987.

23 C.-Y. Zhou, J. Li, S. Peddibhotla, D. Romo, *Org. Lett.* **2010**, *12*, 2104.

24 R. Johnsson, A. Meijer, U. Ellervik, *Tetrahedron* **2005**, *61*, 11657.

25 M. Sosnowski, L. Skulski, K. Wolowik, *Molecules* **2004**, *9*, 617.

26 A. R. Hajipour, M. Arbabian, A. E. Ruoho, *J. Org. Chem.* **2002**, *67*, 8622.

27 D. V. Kosynkin, J. M. Tour, *Org. Lett.* **2001**, *3*, 991.

28 a) H. A. Stefani, C. M. P. Pereira, R. B. Almeida, R. C. Braga, K. P. Guzen, R. Cella, *Tetrahedron Lett.* **2005**, *46*, 6833. b) D.-P. Cheng, Z.-C. Chen, Q.-G. Zheng, *Synth. Commun.* **2003**, *33*, 2671. c) M. I. Rodríguez-Franco, I. Dorronsoro, A. I. Hernández-Higueras, G. Antequera, *Tetrahedron Lett.* **2001**, *42*, 863.