Iodination of Methylated Anisoles: Unusual Aryl Methyl Replacements and Oxidations

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The treatment of methylated anisoles with iodine, periodic acid, sulfuric acid, and aqueous acetic acid has resulted in iododemethylations and/or aryl methyl oxidations in addition to the expected mono- and diiodinations of the aromatic ring. Four dimethylanisoles and *o*-methylanisole were treated under identical conditions. Iododemethylations were observed in three of the four dimethylanisoles and aryl methyl oxidations to benzaldehydes occurred with *o*-methylanisole and two of the dimethylanisoles. No precedence could be found for either of these reactions under the experimental conditions employed. Several possible mechanisms are discussed for these transformations. Some experimental evidence suggests that methyl oxidation to a benzaldehyde could be a prerequisite for an iododemethylation via an iodonium ion-assisted reverse Gatterman-Koch reaction; single-electron-transfer or classical electrophilic mechanisms are also consistent with the iododemethylations.

For the last several years, our laboratory has been involved in the syntheses of novel organic products that may be used as electron acceptors in molecular electronic devices. Some of the required intermediates, in recent work, were certain iodinated and methylated anisoles. It was during the investigation of the monoiodination of 2,5-dimethylanisole (**1**) that we uncovered a unique replacement of an aryl methyl group by an iodine atom. When **1** was heated with iodine, periodic acid, and sulfuric acid in aqueous acetic acid at 85 °C for 12 h, two products, formed in approximately equal amounts, were isolated and identified: 2,4-diiodo-3,6-dimethylanisole (**3**) and the unforeseen 2,4-diiodo-5-methylanisole (**4**). The structure of **4** was readily established by analyses of its ^{13}C and ^{1}H NMR spectra and by comparing its melting point with that reported in the literature.[1] No monoiodinated products or recovered 2,5-dimethylanisole were obtained, and the remainder of the product mixture appeared to be higher-molecular-weight materials which were slower moving on TLC plates. Later, the desired 4-iodo-2,5-dimethylanisole (**2**) was found to be the major product after the reaction mixture was stirred at room temperature for 12 h.

The result precipitated a search to find a literature precedent. The Jacobsen Reaction[2] has been long known as the inter- or intramolecular migration of an alkyl group or a halogen atom in a sulfonic acid derived from a halogenated and/or alkylated benzene. There are numerous examples[3–5] which involve the rearrangement of iodine atoms, but the no examples could be found where the iodine migrated to a position formerly occupied by an alkyl group. Some reports show bromine atoms displacing secondary and tertiary alkyls[6,7] and chlorines replacing ethyl and isopropyl groups.[8] The acid-catalyzed iodination of **1**, apparently, is a unique reaction, and we attempted to determine its scope next.

Several other methylated anisoles were subjected to the same iodination conditions described above. The results of these experiments are summarized in Scheme 1. [Yields in Scheme 1 are based on the anisole starting material. However, due to multiple iodinations, iodine species turned out to be the limiting reagents even though the I/ArH ratio was 1.6/1 (assuming 9 mmol of I_2 and 11 mmol of H_5IO_6 can both contribute to the formation of I^+, then there are 29 mmol of iodonium ion for 18 mmol of methylated anisole). Yields based on iodine would be somewhat higher for diiodinated products and somewhat lower for monoiodinated products.] All of the dimethylanisoles tested, except for the 2,6-isomer **17**, showed replacements of a methyl group by iodine in significant amounts. Perhaps of equal interest was the isolation of oxidized products **15**, **16**, **21**, **22**, **23**, and **27** from the iodination of 2,4- and 2,6-dimethylanisoles (**11** and **17**, respectively) and 2-methylanisole (**24**).

Structural assignments for Scheme 1 were made primarily through spectroscopic analysis. Aldehydes were detected by characteristic infrared and proton magnetic resonance peaks. Proton coupling constants could distinguish whether tetrasubstituted products had their two aromatic protons meta or para. ^{13}C NMR data also helped in determining substitution patterns, as iodine deshields ipso carbons by about 32 ppm while shielding ortho carbons by about 10 ppm. Compounds **22** and **23** were only isolated as a mixture in low yield, and their assignments are tentative. Compound **20** was isolated as a mixture with **14** and a small amount of **25**, but could be identified because pure **14** was available from a separate sequence for comparison. Some of these experiments showed products by TLC in addition to those that were identified.

The structure of **15** was, at first, ambiguous because an alternate structure (with interchanged formyl and methyl groups) was also consistent with the spectral data. However, iodination of **15** under standard conditions gave a small amount of **14**, as identified by its R_f

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(1) Kajigaeshi, S.; Kakinami, T.; Moriwaki, M.; Watanabe, M.; Fujisaki, S.; Okamoto, T. *Chem. Lett.* **1988**, 795–8.

(2) Smith, L. I. The Jacobsen Reaction. *Organic Reactions*; Wiley: New York, 1942; Vol. 1, pp 370–384.

(3) Suzuki, H.; Sugiyama, T.; Goto, R. *Bull. Chem. Soc. Jpn.* **1964**, *37*, 1858.

(4) Suzuki, H. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 1642.

(5) Suzuki, H.; Goto, R. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 389.

(6) Muller, E.; Ley, K.; Kiedaisch, W. *Chem. Ber.* **1954**, *87*, 1605.

(7) Hennion, G. F.; Anderson, J. G. *J. Am. Chem. Soc.* **1946**, *68*, 424.

(8) Ross, S. D.; Nazzewski, M. *J. Am. Chem. Soc.* **1947**, *69*, 3146.

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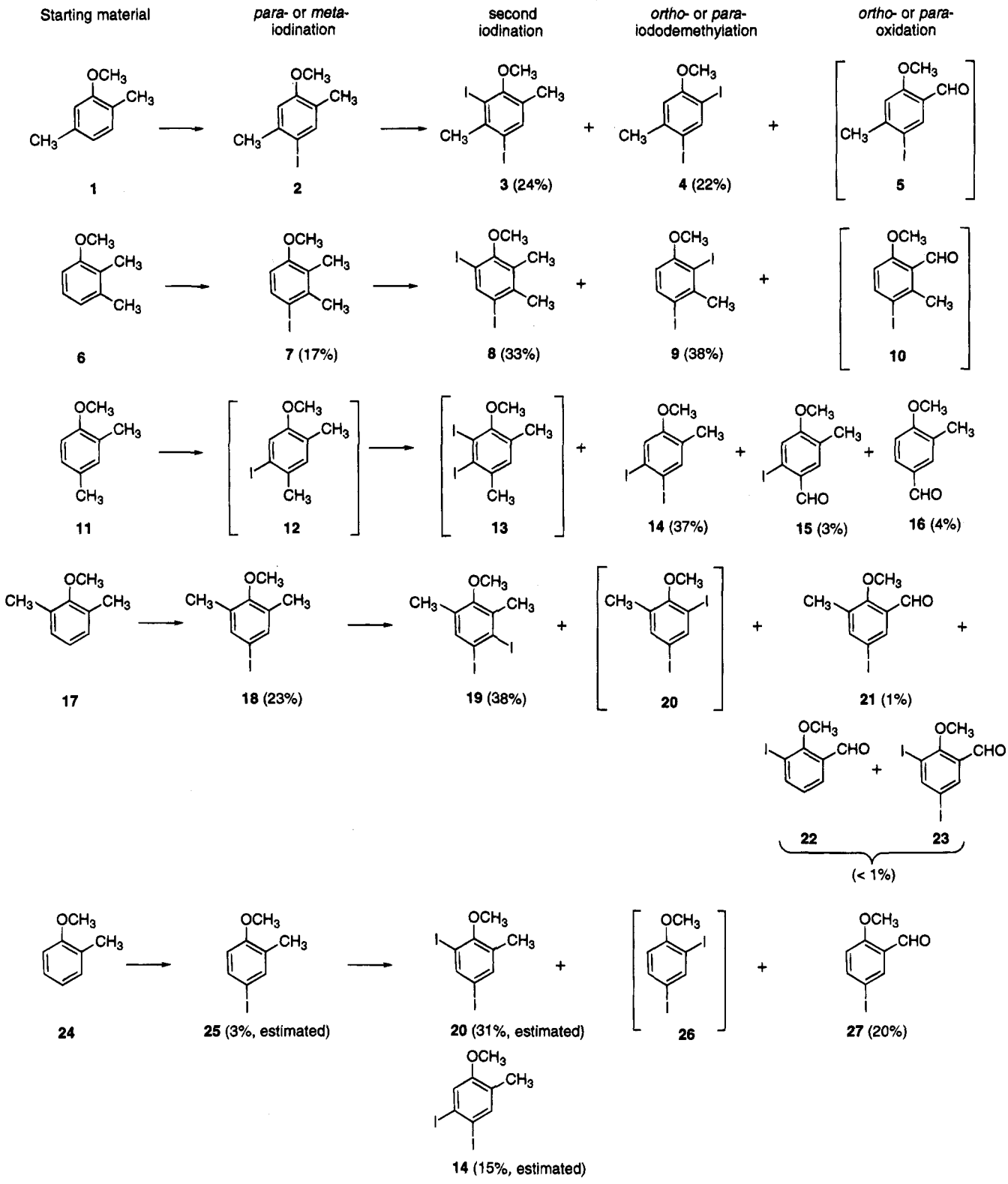
Scheme 1. Iodinations of *o*-Methylanisoles. Structures in Brackets Are Proposed as Likely Intermediates or Products but Have Not Been Isolated or Detected

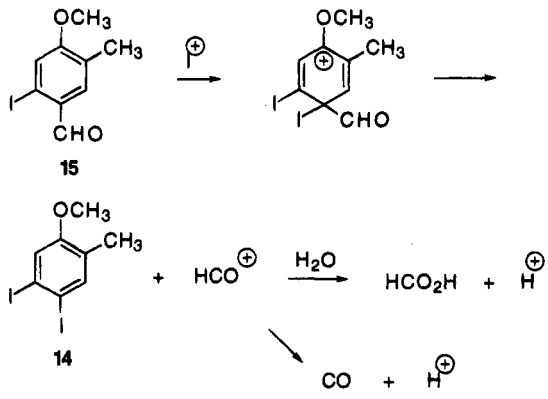


value in thin-layer chromatography and its ^{1}H NMR spectrum in the product mixture. This supported the structure assignment shown. An I^+-assisted reverse Gatterman–Koch mechanism, which can rationalize this iododeformylation, is shown in Scheme 2, although we have no direct evidence for the formation of formic acid. In addition, the known 4-methoxy-3-methylbenzaldehyde (**16**) was isolated and identified from the same reaction mixture with **14** and **15**.

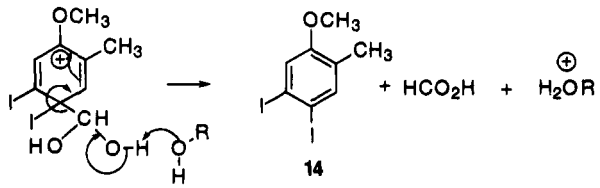
Discussion

The first step in the reaction pathway (see Scheme 1) appears to be conventional iodination para to the methoxy group (except in the case of **11**, in which the para position is blocked and meta attack occurs instead). In the cases of **6** and **17**, these monoiodination products are isolated, as is **2** from **1** when mild conditions are used; **25**, the monoiodination product of **24**, is detected as a minor component of the product mixture; and initial

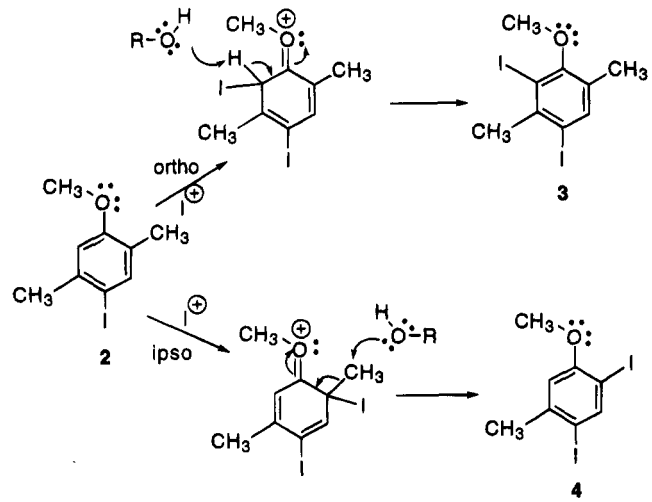
Scheme 2. Possible Mechanism for the Iododeformylation of 15[a]



[a] A referee has suggested an alternate deformylation via the hydrate:



Scheme 3. Classical Electrophilic Aromatic Substitution Mechanisms for Iodination and Iododemethylation



iodination of **11** is inferred since all products (except **16**) have a meta iodine. After monoiodination, three pathways may be taken (although each substrate shows products from only two): a *second iodination* at another unsubstituted position, an *iododemethylation*, or the *oxidation* of a methyl group to a formyl group. Compound **22** appears to result from iododemethylation of one methyl of **17**, along with oxidation of the other. (Compounds **22** and **16** are the only products which apparently did not undergo simple iodination.) Compound **23** could result from oxidation of **20**, iododemethylation of **21**, or iodination of **22**.

The unusual iododemethylation reactions can be rationalized by an ipso attack of I^+ occurring in competition with the classical electrophilic aromatic substitution process. As shown for substrate **2**, attack at the open ortho position gives the standard di-iodinated product **3**, while attack ipso to the ortho methyl leads to the demethylated product **4** (Scheme 3). Both pathways utilize a stabilized σ complex, which will result from electrophilic attack ortho or para to the methoxy group. Indeed, we observed iododemethylation of only methyl groups ortho (2 out of 5) or para (1 out of 1) to the methoxy, and never meta (0 out of 2).

An alternative iododemethylation mechanism to that shown in Scheme 3 involves aldehydes such as **15** as intermediates between aromatic methyls and iodides. Even though the partial conversion of **15** to **14** mentioned above (see Scheme 2) indicates that iodine attack ipso to formyl groups is possible, it is not clear that this is a major demethylation pathway.

The oxidation of aromatic methyls to formyl groups by a mixture containing periodic acid is the most extraordinary part of our results. Periodic acid is well-known for the conversion of glycols to aldehydes, polycyclic aromatics to quinones,[9] hydrazines to azo compounds,[10] and acetophenone or benzil to benzoic acid.[11] However, we could find no report of a periodic acid oxidation of an aryl methyl to a benzaldehyde.

A possible mechanism for the oxidation, similar to one proposed for the bromine oxidation of a hindered cresol,[12] is shown in Scheme 4 for the conversion of **12** to **15**. Electrophilic ipso attack makes an oxonium ion intermediate; elimination of HI gives an exocyclic alkene, **28**, which undergoes addition from water or acetic acid (ROH) to make an oxybenzylic species, **29**. A repeat of these three steps gives an acetal (or geminal diol), **30**, which will easily hydrolyze to the observed aldehyde, **15**, upon workup.

An alternative mechanism for production of these proposed exocyclic alkene intermediates involves single electron transfers (SET) from the aromatic π system to the iodine electrophile (which may be conveniently thought of as I^+, iodonium ion, although its actual identity is likely to be more complex). As shown for **12**, SET to iodonium gives a radical cation, **31**, and an iodine atom (Scheme 5). Deprotonation of **31** followed by SET to iodonium affords **28**. Such a sequence has been proposed, for example, for the oxidation of methylanthracenes.[13] Conjugate addition of either water or acetic acid (ROH) gives the oxybenzylic species, **29**. A repeat of these four steps gives the acetal (or geminal diol) **30**, which will hydrolyze to aldehyde product **15** upon workup.

Since, except for the conversion of **11** to **16**, oxidations were not observed on uniodinated products, we investigated the possibility that classical electrophilic monoiodination of the anisoles would produce monoiodo intermediates with lower oxidation potentials, thus making them susceptible to SET processes and subsequent oxidation. We performed PM3 semiempirical molecular orbital calculations on the five anisole substrates and their monoiodination products and compared the calculated HOMO energy levels. As shown in Table 1, four of the monoiodoanisoles had the four highest HOMO energies and should therefore be easiest to oxidize; however, two of these (**2** and **7**) did not yield isolable aldehydes and the fifth monoiodoanisole (**18**) had a low HOMO energy that did not fit the trend. The range of HOMO energies for all substrates was only 0.27 eV, suggesting that they are all potential candidates for SET reaction modes.

Indeed, the question arises whether SET processes might dominate the entire mechanistic scheme; SET

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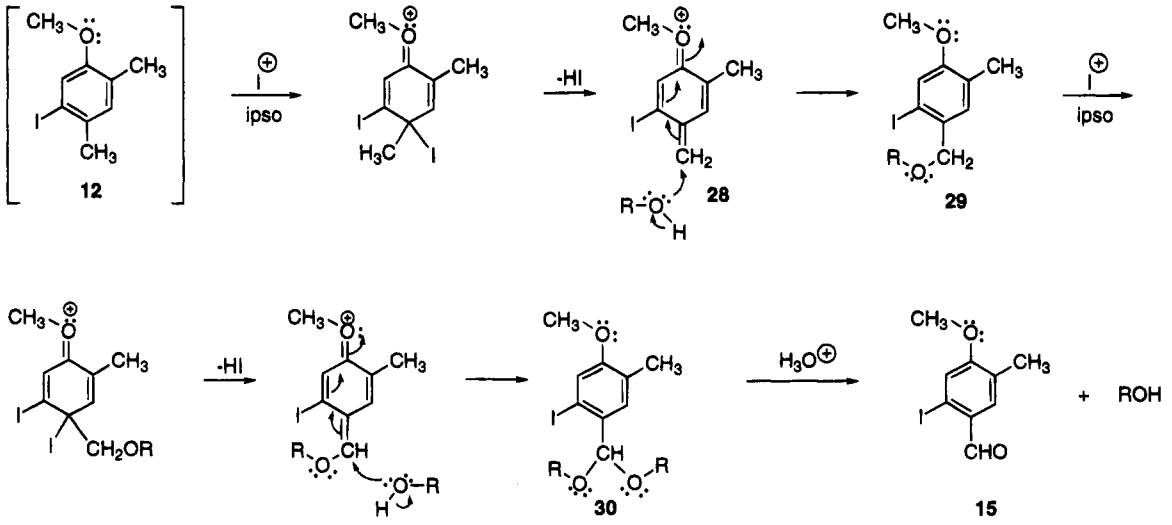
(11) Mattern, D. L. *J. Org. Chem.* **1984**, *49*, 3051.
(12) Coppinger, G. M.; Campbell, T. W. *J. Am. Chem. Soc.* **1953**, *75*, 734.
(13) Tolbert, L. M.; Khanna, R. K.; Popp, A. E.; Gelbaum, L.; Bottomley, L. A. *J. Am. Chem. Soc.* **1990**, *112*, 2373.

Scheme 4. Possible Mechanism for Methyl Oxidation via an Electrophilic Ipso Attack by Iodonium Ion



Scheme 5. Plausible Single-Electron-Transfer Mechanisms for Iododemethylation and Methyl Oxidation of 12

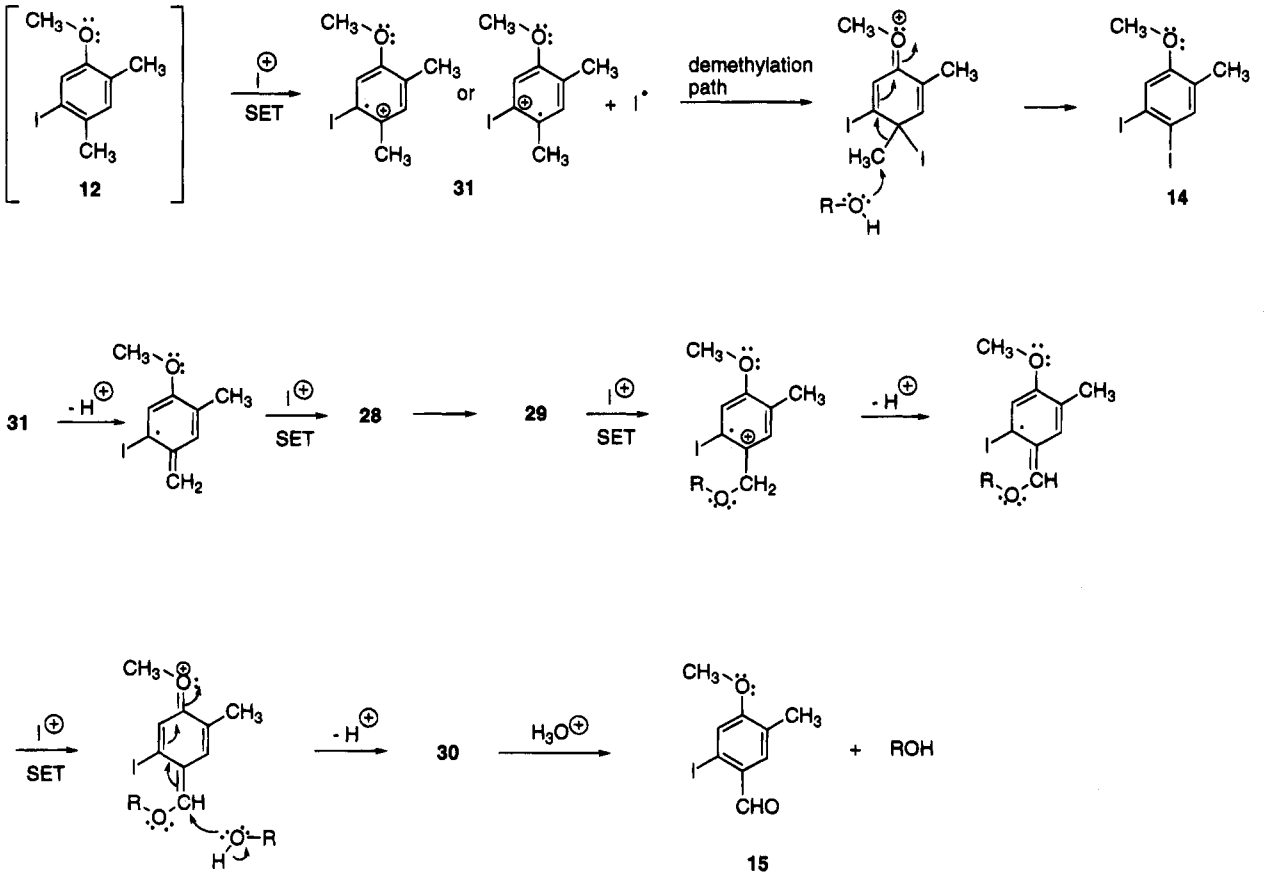


Table 1. HOMO Energy Levels of Several Anisoles

anisole	HOMO (eV)	monoiodinated anisole	HOMO (eV)
1	−8.857	2	−8.706
6	−8.944	7	−8.714
11	−8.798	12	−8.772
17	−8.894	18	−8.940
24	−8.980	25	−8.752

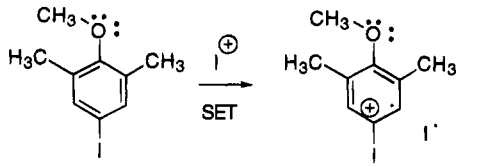
mechanisms have been proposed for aromatic substitutions involving strong electrophiles (such as nitronium) and activated arenes (such as toluene).[14,15] Scheme 6 shows how **18** could undergo apparent classical substitution via an SET step and a radical cation intermediate on the way to the σ complex. Further, the σ complex for iododemethylation is equally accessible from an SET process, as shown in Scheme 5 for the conversion of **12** to **14**.

Galli has argued that iodinations of mesitylene and durene are electrophilic, whereas SET processes lead to side-chain oxidation.[16] However, Hubig and co-workers[17]

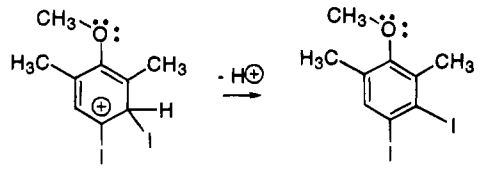
(14) Pederson, E. B.; Petersen, T. E.; Torsell, K.; Lawesson, S. *Tetrahedron* **1973**, *29*, 579.

(15) Perrin, C. L. *J. Am. Chem. Soc.* **1977**, *99*, 5516.
(16) Galli, C. *J. Org. Chem.* **1991**, *56*, 3238.
(17) Hubig, S. M.; Jung, W.; Kochi, J. K. *J. Org. Chem.* **1994**, *59*, 6233.
(18) Cohen, R. L.; Sisti, A. J. *Can. J. Chem.* **1964**, *42*, 1389.

Scheme 6. Possible Single-Electron-Transfer Mechanism for Aromatic Iodination



18



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have shown that radical cations of some anisoles and dimethoxybenzenes can be halogenation intermediates. Using iodine monochloride in CH_2Cl_2, they observed consistent para iodinations to methoxy groups, similar to our results. However, they observed no iododemethylations or methyl oxidations of their substrates (all of which were different from ours). This discrepancy is not surprising: their system avoids an excess of ICl in order to favor monohalogenated products, whereas in our system the deiodinations and oxidations follow initial iodination; further, they create Cl^- in a reactive triad with the radical cation and I·, thus providing ring chlorination as a major alternate path.

Finally, we used PM3 calculations to see if the unusual orientations and selectivities of some of the reactions could be explained by SET processes. We looked at the unpaired electron spin density of the radical cations of the anisoles and monoiodinated anisoles, as reflected by the squared coefficients of their singly occupied HOMOs. An iodine atom would be expected to preferentially react at unsubstituted or methylated ring positions where the spin density was highest. (Reaction at methoxy- or iodo-substituted positions would not lead to favorable products even if spin density was high.)

For the uniodinated anisoles, the para position always had the highest spin density of the unsubstituted positions, consistent with the para regioselectivity of iodinations of **1**, **6**, **17**, and **24**. For **11**, with the para position blocked, a meta position was attacked, rather than an ortho position with less spin density. This regioselectivity is consistent with a radical cation intermediate, but is counter to the expectation for electrophilic aromatic subsitution.

In the radical cations of **1**, **6**, **11** and **24**, methylated ring carbons had comparable or higher spin density than the open positions, suggesting that a radical process fostering iododemethylation might be competitive. However, such iododemethylations were not observed as the *initial* reaction of these substrates. It is conceivable that steric hindrance makes ipso attack leading to these iododemethylations noncompetetive, regardless of whether radical or ionic mechanisms control the initial iodinations.

Spin density analysis of the monoiodinated radical cations is complicated by the presence of 30 to 39% of the spin density on the iodine, as well as large amounts on the iodo- and methoxy-bearing carbons, leaving only small amounts in the other ring positions. Nonetheless, the calculated spin densities can rationalize some results. For example: compound **7**'s radical cation shows more spin density at the ortho position that is demethylated than at the unreactive *m*-methyl position; compound **18**'s radical cation shows spin density at its open meta positions comparable to that at its methyl-bearing ortho carbons, which may explain why this system prefers unusual meta iodination to ortho demethylation; compound **12**'s radical cation has its highest spin density at the para position, where iododemethylation and oxidation occur, whereas the ortho methyl's ring carbon has less density, explaining why it survives even though ortho methyls in the four other iodoanisoles—all with higher spin densities on their ring carbons—react; and compound **25**'s radical cation has comparable small densities at the three sites which react, including an unusual meta iodination.

In contrast, the calculated spin densities seem at odds with other findings. For example, the ring carbons for the ortho and meta methyls of **2** show similar large spin densities, but only the ortho position iododemethylates; further, there is only small density at the open ortho position of **2**, where simple iodination occurs. In compound **7**, the ortho and meta positions for simple iodination show comparable spin densities, but reaction occurs only at the ortho position. And finally, the question of how each reactive methyl determines whether to be demethylated (**2**, **7**), oxidized (**18**, **25**), or both (**12**) remains unclarified by the calculations.

Conclusion. We have shown that mono- and diiodinations of methylated anisoles with an iodine/periodic acid mixture are accompanied by intriguing iododemethylations, methyl oxidations to formyl groups, and unusual orientations of substitution. We have considered several mechanistic rationales, and it may well be that a mixture of ionic and radical mechanisms is in play.

Experimental Section

Melting points were run on a Thomas-Hoover apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Series 1600 FTIR and the NMR spectra on a Bruker AC300 instrument except for those of the mixture of **14**, **20**, and **25**, which were recorded on a Bruker DRX 500. TLC analyses were done on Analtech Silica Gel HLF plates, and elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, and Atlantic Microlab, Inc., Norcross, GA.

General Procedure for the Iodination of Methylated Anisoles. A mixture of 18 mmol of the methylated anisole, 2.35 g (9 mmol) of iodine, 2.5 g (11 mmol) of periodic acid, 24 mL of aqueous acetic acid (7:3 HOAc:H_2O), and 1.0 mL of concd H_2SO_4 was stirred and heated to 80–85 °C in an oil bath (stirred at 20–25 °C for product **2**) for 12 h. The iodine color was lost during the period. After cooling, the reaction mixture was partitioned between water and EtOAc. The residue from the organic layer was then fractionated by column (E. Merck Silica Gel 60, 9389) or preparative thin-layer chromatography (E. Merck Silica Gel 60 PF 254, 7749) using hexane, hexane–EtOAc (9:1), or hexane–benzene (9:1) as the eluting solvent. Melting/boiling points of the products are found in Table 2, yields are in Scheme 1, and spectral data and elemental analyses are given below.

4-Iodo-2,5-dimethylanisole (2): When the reaction mixture of **1** was stirred at rt for 12 h, **2** was isolated in 92% yield: IR (KBr) 2950, 2907, 1484, 1457, 1352, 1241, 1146, 1041, 941, 851, 572 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.50 (1H, s), 6.69 (1H,

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(20) Barnes, R. A.; Gerber, N. N. *J. Org. Chem.* **1961**, *26*, 4540.
(21) Butler, A. R.; Sanderson, A. P. *J. Chem. Soc., Perkin Trans. 2* **1974**, 1784.
(22) Bielig, H.-J.; Luetzel, G. *Justus Liebigs Ann. Chem.* **1957**, *608*, 140.

Table 2. Names and Melting Points of Anisole Products Prepared in This Work

no.	name	mp (°C)	crystallization solvent
2	4-iodo-2,5-dimethylanisole	49–50[a,b]	EtOAc
3	2,4-diiodo-3,6-dimethylanisole	49–51	hexane
4	2,4-diiodo-5-methylanisole	99–101[a]	hexane
7	4-iodo-2,3-dimethylanisole	28–30[c]	EtOAc–hexane
8	4,6-diiodo-2,3-dimethylanisole	68–69	EtOAc–hexane
9	2,4-diiodo-3-methylanisole	45–46	EtOAc–hexane
14	4,5-diiodo-2-methylanisole	73–74	hexane
15	2-iodo-4-methoxy-5-methylbenzaldehyde	99–100	hexane
16	4-methoxy-3-methylbenzaldehyde	233–234[d]	EtOAc
18	4-iodo-2,6-dimethylanisole	bp 53–56/0.08 Torr[e,f]	
19	3,4-diiodo-2,6-dimethylanisole	oil	
20	2,4-diiodo-6-methylanisole	mixture A	
21	5-iodo-2-methoxy-3-methylbenzaldehyde		
22	3-iodo-2-methoxybenzaldehyde	mixture B	
23	3,5-diiodo-2-methoxybenzaldehyde	mixture B	
25	4-iodo-2-methylanisole	mixture A	
27	5-iodo-2-methoxybenzaldehyde	140–141	$CHCl_3$-hexane

[a] Lit.[1]mp 102–103 °C. [b] Lit.[18] mp 47–49 °C. [c] Lit.[19] mp 32–33 °C. [d] 2,4-Dinitrophenylhydrazone, lit.[20] mp 235–237 °C. [e] Lit.[21] bp 74–76 °C/0.40 Torr. [f] Lit.[22] bp 87 °C/1.0 Torr.

s), 3.77 (3H, s), 2.37 (3H, s), 2.12 (3H, s); ^{13}C NMR ($CDCl_3$) δ 157.95, 139.96, 139.47, 126.35, 111.77, 89.14, 55.34, 28.10, 15.40.

2,4-Diiodo-3,6-dimethylanisole (3): IR (KBr) 2933, 1449, 1346, 1269, 1141, 1037, 980, 931, 863, 730, 630, 592, 504 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57 (1H, s), 3.67 (3H, s), 2.67 (3H, s), 2.20 (3H, s); ^{13}C NMR ($CDCl_3$) δ 158.50, 142.16, 141.16, 130.79, 98.86, 93.29, 59.98, 35.12, 16.35. Anal. Calcd for $C_9H_{10}I_2O$: C, 27.84; H, 2.58; I, 65.46. Found: C, 27.86; H, 2.62; I, 65.51.

2,4-Diiodo-5-methylanisole (4): IR (KBr) 2928, 1457, 1434, 1352, 1243, 1171, 1042, 879, 841, 714, 628 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10 (1H,s), 6.71 (1H, s), 3.85 (3H, s), 2.40 (3H, s); ^{13}C NMR ($CDCl_3$) δ 158.37, 147.28, 142.82, 112.36, 90.32, 83.13, 56.38, 28.20.

4-Iodo-2,3-dimethylanisole (7): IR (KBr) 2937, 2834, 1560, 1465, 1284, 1257, 1104, 1014, 809, 797, 691, 572 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.62 (1H, d), 6.46 (1H, d), 3.77 (3H, s), 2.42 (3H, s), 2.22 (3H, s); ^{13}C NMR ($CDCl_3$) δ 157.67, 140.03, 136.29, 126.49, 110.04, 91.40, 55.66.

4,6-Diiodo-2,3-dimethylanisole (8): IR (KBr) 2917, 1550, 1448, 1424, 1276, 1073, 1021, 797, 619 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.10 (1H, s), 3.72 (3H, s), 2.38 (3H, s), 2.34 (3H, s); ^{13}C NMR ($CDCl_3$) δ 158.09, 144.95, 141.67, 131.90, 96.96, 89.26, 60.56, 25.52, 15.24. Anal. Calcd for $C_9H_{10}I_2O$: C, 27.84; H, 2.58; I, 65.46. Found: C, 28.00; H, 2.66; I, 65.02.

2,4-Diiodo-3-methylanisole (9): IR (KBr) 2999, 2917, 1445, 1407, 1373, 1235, 1153, 1076, 989, 891, 861, 840, 743, 635, 558, 487 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.73 (1H, d), 6.37 (1H, d), 3.85 (3H, s), 2.79 (3H, s); ^{13}C NMR ($CDCl_3$) δ 158.54, 144.37, 139.17, 110.06, 92.71, 88.54, 56.71, 35.33. Anal. Calcd for $C_8H_8I_2O$: C, 25.74; H, 2.14; I, 68.10. Found: C, 25.84; H, 2.34; I, 68.19.

4,5-Diiodo-2-methylanisole (14):[23] IR (KBr) 3005, 2924, 2820, 1628, 1516, 1472, 1430, 1330, 1235, 1172, 1030, 862, 846 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.53 (1H, bs, J = <1.0 Hz), 7.23 (1H, bs, J = <1.0 Hz), 3.77 (3H, s), 2.10 (3H, s); ^{13}C NMR ($CDCl_3$) δ 157.97, 140.09, 129.14, 121.00, 103.86, 96.10, 55.63, 16.00. Anal. Calcd for $C_8H_8I_2O$: C, 25.68; H, 2.14; I, 67.90. Found: C, 25.95; H, 2.18; I, 67.63.

2-Iodo-4-methoxy-5-methylbenzaldehyde (15):[23] IR (KBr) 2960, 2860, 2770, 1682, 1663, 1590, 1483, 1238, 1145, 1019, 966, 893, 833, 780, 634 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.89 (1H, s), 7.68 (1H, s), 7.28 (1H, s), 3.91 (3H, s), 2.19 (3H, s); ^{13}C NMR ($CDCl_3$) δ 194.93, 162.79, 131.62, 128.06, 127.97, 121.18, 99.76, 55.96, 15.98. Anal. Calcd for $C_9H_9IO_2$: C, 39.14; H, 3.26; I, 45.99. Found: C, 39.12; H, 3.25; I, 46.08.

4-Methoxy-3-methylbenzaldehyde (16):[24] IR ($CHCl_3$) 3018, 2974, 2841, 1682, 1602, 1504, 1260, 1218, 1127, 1030, 928, 735, 669 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.86 (1H, s), 7.71 (1H, dd), 7.69 (1H, bs), 6.95 (1H, d), 3.92 (3H, s), 2.26 (3H, s); ^{13}C NMR ($CDCl_3$) δ 191.20, 162.87, 131.42, 130.69, 129.39, 127.58, 109.60, 55.63, 16.19.

(23) These products were purified by Mr. Dezhi Sha.
(24) This product was isolated and purified by Mr. Dezhi Sha.

4-Iodo-2,6-dimethylanisole (18): ^1H NMR ($CDCl_3$) δ 7.34 (2H, s), 3.69 (3H, s), 2.23 (6H, s); ^{13}C NMR ($CDCl_3$) δ 156.95, 137.47, 133.50, 87.61, 59.72, 15.72.

3,4-Diiodo-2,6-dimethylanisole (19): IR (oily film) 2935, 2855, 1456, 1398, 1206, 1150, 1007, 862, 836, 750, 701 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (1H, s), 3.66 (3H, s), 2.55 (3H, s), 2.18 (3H, s); ^{13}C NMR ($CDCl_3$) δ 155.84, 138.88, 137.78, 133.05, 111.90, 103.33, 60.12, 25.58, 15.75. Anal. Calcd for $C_9H_{10}I_2O$: C, 27.84; H, 2.58. Found: C, 28.00; H, 2.65.

2,4-Diiodo-6-methylanisole (20): This was obtained as a mixture with **14** and **25**: ^1H NMR ($CDCl_3$) δ 7.90 (1H, d, J = 2.14 Hz), 7.45 (1H, d, J = 2.14 Hz), 3.74 (3H, s), 2.28 (3H, s); ^{13}C NMR ($CDCl_3$) δ 158.14, 144.46, 140.21, 134.46, 93.24, 88.59, 60.28, 17.60.

5-Iodo-2-methoxy-3-methylbenzaldehyde (21): IR (KBr) 3447, 2860, 1680, 1465, 1233, 1213, 996, 875 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.26 (1H, s), 7.98 (1H, d), 7.76 (1H, d), 3.87 (3H, s), 2.31 (3H, s); ^{13}C NMR ($CDCl_3$) δ 188.75, 161.53, 145.77, 135.21, 135.06, 130.71, 88.21, 63.25, 15.26.

3-Iodo-2-methoxybenzaldehyde (22): A mixture of this and **23** was isolated, but the components were never separated: ^1H NMR ($CDCl_3$) δ 9.83 (1H, s), 8.31 (1H, d), 7.86 (1H, dd), 6.93 (1H, d), 3.98 (3H, s).

3,5-Diiodo-2-methoxybenzaldehyde (23): This was obtained as a mixture with **22**: ^1H NMR ($CDCl_3$) δ 10.32 (1H, s), 8.38 (1H, d), 7.37 (1H, d), 4.09 (3H, s).

4-Iodo-2-methylanisole (25): This product was obtained as a mixture with **14** and **20**: ^1H NMR ($CDCl_3$) δ 7.41 (2H, m), 6.60 (1H, d, J = 7–10 Hz), 3.78 (3H, s), 2.16 (3H, s).

5-Iodo-2-methoxybenzaldehyde (27): IR (KBr) 2865, 2825, 2755, 1671, 1472, 1453, 1267, 1244, 1171, 1010, 876, 812, 639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 10.35 (1H, s), 8.09 (1H, d), 7.81 (1H, dd), 6.79 (1H, d), 3.92 (3H, s); ^{13}C NMR ($CDCl_3$) δ 188.29, 161.41, 144.12, 137.07, 126.48, 114.12, 82.96, 55.84. Anal. Calcd for $C_8H_7IO_2$: C, 36.64; H, 2.67. Found: C, 36.92; H, 2.65.

Semiempirical molecular orbital calculations were performed using the HyperChem version of the PM3 program. The restricted Hartree–Fock method was used for geometry optimization of both neutral and radical cation molecules. The spin density on individual atoms was estimated as the square of their HOMO p_z coefficients.

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