

Chemical Manganese Dioxide (CMD): Its Application to the Oxidative Iodination of Benzene, Halobenzenes and Some Deactivated Arenes[†]

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Abstract: After comparing our previous and newer results for numerous oxidative aromatic iodination experiments using *various brands* of active MnO₂ as the oxidants, we recommend the use of a Chemical Manganese Dioxide (Aldrich CMD; 90+% MnO₂) as the oxidant of choice, since it is satisfactorily pure and chemically active, and is *notably less costly* than other options.

Keywords: Iodinated arenes; arenes; oxidative aromatic iodination; chemical manganese dioxide as oxidant.

Introduction

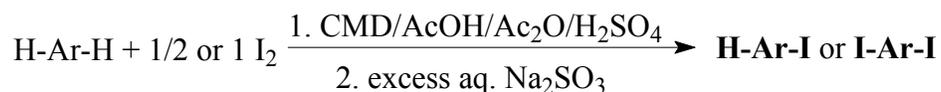
In a previous paper [1] we reported some easy laboratory methods for the mono- or diiodination of several activated and deactivated arenes, using either *freshly-prepared activated* MnO₂ [2] or commercial KMnO₄ (Aldrich, 99+%) [3] as suitable oxidants to obtain either 62-89% or 73-87%

yields, respectively, of the corresponding *purified* iodinated products. Starting our earlier iodination experiments with MnO₂, we had previously checked out *various brands* of this oxidant experimentally. An ordinary technical grade MnO₂ (Aldrich, 75% MnO₂) [3] was not usable. The best iodination yields (*vide supra*) were attained with *activated* MnO₂ freshly prepared by us prior to use [2]. An Activated Manganese Dioxide (Aldrich AMD, suitable for organic reactions, ca. 85% MnO₂) [3] gave *lower* iodination yields by ca. 5-10%. In this work, we have experimentally checked out *two brands* of the so-called **Chemical Manganese Dioxide** (CMD), viz. (1) Wako CMD, min. 75% MnO₂ and (2) Aldrich CMD, 90+% MnO₂ [3]. CMD has been produced industrially mainly as a component of dry batteries [4], and is now available as an inexpensive, stable laboratory reagent for the oxidation of a wide variety of organic compounds, although the price of the Wako product in Europe is however ca. 10-12 times higher than that of the Aldrich CMD [3,5].

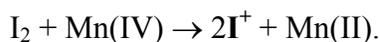
In 1998, four Japanese papers were published [6-9] in which selective oxidations of various classes of organic compounds were reported, using Wako CMD as the effective oxidant. These *heterogeneous* reactions, carried out in hexane, CH₂Cl₂ or acetone, often proceeded in nearly quantitative yields under relatively mild conditions. Usually, *a large excess* of CMD was required for smooth completion of the reactions. In some cases, Wako CMD proved to be much superior to the usual AMDs commercially available from the Aldrich, Fluka, Merck, Nakarei and Wako companies [6]. These papers prompted us to repeat our earlier iodination experiments [1], but using the said two CMD brands as the oxidants (see Experimental). In all our iodination experiments, however, both the CMD oxidants were always *dissolved fully* (or nearly so) in the anhydrous, strongly acidic reaction mixtures containing also diiodine and a chosen arene to be oxidatively iodinated. Hence, *all possible contaminants* present in the two CMDs used were transferred in full into the iodinating reaction mixtures, and they therefore contaminated, more or less, the crude iodinated products. Apparently, Wako CMD is less concentrated and more contaminated than Aldrich CMD, as has been shown in our subsequent aromatic iodination experiments (*vide infra*).

Results and Discussion

As previously described [1], our novel iodination experiments proceed as follows:



For the monoiodination of benzene and four halobenzenes, using either Wako CMD or Aldrich CMD as the oxidants, the following reaction stoichiometry was applied (**Procedure 1**):



Presumably, only transient *iodine(I)* species, briefly denoted as I⁺ [10], preponderantly act upon the reacted arenes to form the respective iodoarenes. After adding all the reactants, viz. Wako CMD (*used at first*), powdered diiodine, a chosen arene, and an appropriate amount of concd. H₂SO₄, to *anhydrous* AcOH/Ac₂O solvent mixtures cooled below 10°C, the resulting reaction mixtures were stirred for two

hours at 70°C, and they were then poured into stirred excess aqueous Na₂SO₃ solutions. After more laborious isolation (cf. [1]) and purification of the crude iodination products, the purified iodoarenes were obtained in only 40-56% yields. When we halved the amount of the benzene added to the reaction mixtures (with respect to that used for its monoiodination), the purified 1,4-diiodobenzene was obtained in only 41% yield (see Table).

Table. Iodinated pure products prepared.

Substrate Ar-H	Reaction conditions ^a	Product (Arabic denotation) Ar-I/ I-Ar-I	Yield (%)	Analysis/I% Calcd (Found)	Mp °C/solvent ^b (lit. mp) [11]
C ₆ H ₆	<i>I</i> ; <u>7.99</u> (150); 2	PhI (1)	56 [46]	62.23 (61.7)	bp. 80-82/27 (bp. 63- 64 /8; 188/760)
C ₆ H ₆	<i>I</i> ; <u>10.65</u> (200); 2	1,4-I ₂ C ₆ H ₄ (2)	41 [61]	76.95 (77.2)	131-133/E (129)
PhI	<i>I</i> ; <u>13.32</u> (250); 2	1,4-I ₂ C ₆ H ₄ (2)	42	76.95 (76.8)	131-133/E (129)
PhI	<i>2</i> ; <u>7.99</u> (150); 1	1,4-I ₂ C ₆ H ₄ (2)	57 [73]	76.95 (76.9)	131-133/E (129)
PhBr	<i>I</i> ; <u>13.32</u> (250); 2	4-BrC ₆ H ₄ I (3)	48 [64]	44.86 (44.8)	90-91/E (91-92)
PhBr	<i>2</i> ; <u>7.99</u> (150); 1	4-BrC ₆ H ₄ I (3)	53 [91]	44.86 (44.7)	90-91/E (91-92)
PhCl	<i>I</i> ; <u>7.99</u> (150); 2	4-ClC ₆ H ₄ I (4)	40 [48]	53.22 (53.0)	54-56/E (57)
PhCl	<i>2</i> ; <u>5.33</u> (100); 1	4-ClC ₆ H ₄ I (4)	41 [46]	53.22 (53.1)	54-56/E (57)
PhF	<i>I</i> ; <u>5.33</u> (100); 2	4-FC ₆ H ₄ I (5)	50 [60]	57.18 (57.2)	bp. 82-84/38 (bp. 182-184/760)
PhCOOH	<i>2</i> ; <u>10.65</u> (200); 2	3-IC ₆ H ₄ COOH (6)	84 [81]	51.17 (51.3)	189-191/C (187-188)
PhCOOEt	<i>2</i> ; <u>10.65</u> (200); 2	3-IC ₆ H ₄ COOEt (7)	64	45.97 (45.4)	bp. 158-164/26 (bp. 150.5/15)
4-MeC ₆ H ₄ COOH	<i>2</i> ; <u>10.65</u> (200); 2	3-I-4-MeC ₆ H ₃ COOH (8)	82 [85]	48.43 (48.0)	211-212/C (210-212)
PhCF ₃	<i>2</i> ; <u>18.64</u> (350); 3	3-IC ₆ H ₄ CF ₃ (9)	50 [37]	46.65 (46.1)	bp. 73-76/25 (bp. 182-183/760)
PhNO ₂	<i>2</i> ; <u>26.63</u> (500); 3	3-IC ₆ H ₄ NO ₂ (10)	52 [52]	50.96 (50.4)	bp. 161-164/24 (bp. 153/14; 38)

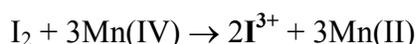
Table 1. Cont.

PhCONH ₂	2; <u>23.97</u> (450); 3	3-IC ₆ H ₄ CONH ₂ (11)	70 [77]	51.37 (51.9)	180-183/E (186.5)
PhCOPh	2; <u>7.99</u> (150); 2	3-IC ₆ H ₄ COC ₆ H ₄ I-3' (12)	59 [47]	58.48 (58.1)	147-149/A (152.5-153.5)

^a The following data are given: **Procedure** (either **1** or **2**); the amount [mL (mmol)] of concd. (98%) H₂SO₄ added dropwise to the reaction mixture below 10 °C; the reaction time (h) of the main iodination reaction at 70 °C.

^b Solvents used for recrystallization: **A**: Me₂CO; **C**: CCl₄; **E**: EtOH.

For the monoiodination of six deactivated arenes and also three halobenzenes (used here for comparison), using either Wako CMD or Aldrich CMD as the oxidants (in a threefold excess), the following reaction stoichiometry was applied (**Procedure 2**):



which strongly favors the formation of more electrophilic transient *iodine(III)* species, briefly denoted as **I³⁺** [10], which act upon the reacted arenes to form some organic iodine(III) intermediates ArISO₄ (*not isolated*) [10]. After adding all the reactants, viz. Wako CMD (*used at first*), powdered diiodine, a chosen arene, and an appropriate amount of concd. H₂SO₄, to anhydrous AcOH/Ac₂O solvent mixtures cooled below 10°C, the resulting reaction mixtures were stirred for 1-3 hours at 70°C. After pouring the cooled reaction mixtures into stirred excess aqueous Na₂SO₃ solutions, the said organic iodine(III) intermediates were readily *reduced* to the corresponding iodoarenes, ArI. After more laborious isolation (cf. [1]) and purifications of the crude iodination products, the purified monoiodinated arenes were obtained in 41-84% yields. We also oxidatively diiodinated benzophenone to obtain, after laborious isolation and purification, 3,3'-diiodobenzophenone in only 39% yield (see Table).

Lower yields obtained generally in this work when using Wako CMD as the oxidant (see Table and cf.[1]), are mainly due to the fact that Wako CMD is apparently *considerably contaminated*. This resulted in *greater losses* during the troublesome purification of the dark-colored crude iodinated products, evidently more impure than those obtained in our earlier work [1].

Finally, we also carried out a number of analogous aromatic iodination reactions, covering benzene, three halobenzenes and seven deactivated arenes, but using Aldrich CMD as the oxidant. The same **Procedures 1** and **2** described in Experimental were applied. The final yields attained for the purified mono- and diiodinated products (46-90%) are given in Table (*in square brackets*). These yields are usually higher than those obtained with Wako CMD, and are comparable (or sometimes even higher) than those previously reported by us in the earlier paper [1]. It is also noteworthy that the crude products isolated from the final reaction mixtures, when we used Aldrich CMD, were evidently less contaminated (only slightly colored), and were easier to purify.

Conclusions

Though the *self-prepared* AMD [2] is (mostly) somewhat more efficient in the oxidative aromatic iodination reactions than either the commercial Aldrich CMD or Wako CMD products [3,5], its tedious preparations are relatively expensive and time consuming. The more impure Wako CMD [5] gave dark-colored and heavily contaminated crude iodinated products, which resulted in *considerable losses* during their troublesome isolation and purification. Consequently, we would recommend the use of Aldrich CMD as the oxidant of choice in these oxidative aromatic iodination reactions, since it has quite satisfactory chemical reactivity and purity, and is *notably less costly* [3].

Experimental

General

Melting or boiling points given in the Table are uncorrected. The commercial reagents and solvents (Aldrich, Fluka) were used without purification. Both CMD brands (Wako, Aldrich) [3,5] were neither preheated nor otherwise pretreated prior to their use in the iodination reactions. Molecular iodine (diiodine) was *finely powdered* to facilitate its dissolution in the reaction mixtures. Elemental analyses were carried out at the Institute of Organic Chemistry, The Polish Academy of Sciences, Warsaw, Poland. After checking their purities and homogeneities by TLC, the structures of the purified iodinated products, all known in the literature, were checked by comparison of their melting points (or boiling points) with those reported in the literature (see Table), as well as by their mixed melting points with authentic specimens [1]. The structures were also corroborated by elemental microanalyses (see Table). As previously [1], all the yields reported in the Table represent potentially optimal values.

Procedure 1 for the iodination of benzene and halobenzenes using Wako CMD

Wako CMD (2.78 g; ca 24 mmol MnO₂; 20% excess) and powdered diiodine (5.08 g, 20 mmol; 0% excess) [for the diiodination of benzene: 5.59 g I₂, 22 mmol; 10% excess] were suspended in a stirred mixture of AcOH (40 mL) and Ac₂O (10 mL) cooled to 5-10°C. Next, *varied quantities* (see Table 1) of concd. (98%) H₂SO₄ were very slowly added dropwise with vigorous stirring while keeping the temperature at 5-10°C (*exothermic reactions*). An appropriate *arene* (44 mmol; 10% excess) [for the diiodination of benzene: 1.56 g benzene, 20 mmol, 0% excess] was added with stirring, then the stirring was continued for 2 h at 70°C. The anhydrous reaction mixtures were poured into ice-water (200 mL) containing previously dissolved Na₂SO₃ (1.0 g, 7.94 mmol) (*under a fume hood*). After ca. 30 min, the precipitated oily or semi-solid crude products **1-5** were extracted with CHCl₃, the collected extracts were dried (MgSO₄), filtered, and the solvent was distilled off, and the oily residues of compounds **1** and **5** were fractionated under vacuum (see Table). The solidified in part residues of compounds **2**, **3** and **4** were triturated with ethanol, the precipitated solids were collected by filtration, air-dried, and recrystallized from appropriate solvents (see Table).

Procedure 2 for the iodination of deactivated arenes and some halobenzenes using Wako CMD

Wako CMD (4.96 g; ca 43 mmol MnO₂; 43% excess) [for the monoiodination of halobenzenes, and for the diiodination of benzophenone: CMD (4.18 g; ca 36 mmol MnO₂; 20% excess)] and powdered diiodine (2.80 g, 11 mmol; 10% excess) were suspended in a stirred mixture of AcOH (40 mL) and Ac₂O (10 mL) cooled to 5-10°C. Next, *varied quantities* (see Table) of concd. (98%) H₂SO₄ were very slowly added dropwise with vigorous stirring while keeping the temperature at 5-10°C (*exothermic reactions*). An appropriate *arene* (20 mmol; 0% excess) [for the diiodination of benzophenone: 1.82 g benzophenone, 10 mmol; 0% excess] was added with stirring and this stirring was continued for 1-3 h (see Table) at 70°C. The anhydrous reaction mixtures were poured into ice-water (200 mL) containing previously dissolved Na₂SO₃ (5.0 g, 39.7 mmol) (*under a fume hood*). After ca 30 min, the precipitated oily crude products **7**, **9** and **10**, and the precipitated semi-solid crude products **2**, **3** and **4** were worked up as above in **Procedure 1**. The precipitated semi-solid crude product **12** was also extracted with CHCl₃, but after removal of the solvent, this was recrystallized from acetone. The precipitated solid crude products **6**, **8** and **11** were collected by filtration, washed with water, air-dried, extracted with boiling acetone in a Soxhlet apparatus, the solvent was distilled off, and the residues were recrystallized from the appropriate solvents (see Table).

All our iodination experiments using Aldrich CMD were similar to those described above. The crude iodinated products were however less contaminated, hence they were easier to purify. The final yields for the purified products are also given in the Table (in square brackets). The yields for the purified iodinated products given in the Table were calculated from the total amounts of those reagents (diiodine or arenes) which were used in the reactions in strictly stoichiometric quantities (0% excess).

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Sample Availability: Available from the authors.

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