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High-Throughput Purification of Solution-Phase Periodinane Mediated Oxidation Reactions Utilizing a Novel Thiosulfate Resin

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Abstract: *A simple and efficient methodology for sequestering byproducts and excess starting reagent from the solution-phase Dess-Martin and Grieco-Dess-Martin periodinane mediated oxidation of primary or secondary alcohols to aldehydes or ketones is described. The periodinane oxidations are carried out under mild conditions followed by treatment with a novel thiosulfate resin which reduces any remaining I(V) and I(III) periodinane species to an I(I) species. Quantitative removal of the I(I) species from the solution is achieved by using a base functionalized resin followed by filtration and evaporation to afford highly pure aldehyde or ketone products. Utilization of this sequestration methodology for periodinane mediated oxidations allows for the high-throughput purification and work-up of parallel reaction chambers and is highly amenable to automation procedures.* © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Periodinane, Oxidation, Ketones, Aldehydes

INTRODUCTION

The use of combinatorial chemistry for the generation of small molecule libraries has become an area of intense research.[1] Many early disclosures focused on the use of solid-phase organic chemistry techniques for the synthesis of chemical libraries.[1] More recently, chemical library synthesis methodologies have been described that rely on performing reactions in the solution-phase.[2] We have recently reported a solution-phase chemical library synthesis/purification strategy based on the principles of functional group molecular recognition and chemoselective sequestration.[3] One aspect of this general strategy is the use of functionalized

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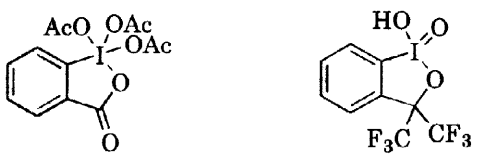
resins to chemoselectively sequester excess reagent and reagent byproducts from parallel, solution-phase reactions. The reagent and reagent byproduct contain a common functional group *tag* which enables them to be sequestered by a functionalized resin containing a molecular recognition element complementary to that of the *tag*. This allows the purified solution-phase products to be obtained by simple filtration away from the sequestered reagents and reagent byproducts. We report here a resin system that conveniently allows solution-phase periodinane mediated oxidation reactions to be performed in a parallel format.

Oxidation of alcohols to aldehydes or ketones is a very important reaction in organic chemistry and numerous methods utilizing a variety of reagents and conditions have been developed. Hypervalent iodine species have received particular attention for these oxidation reactions because of their chemoselectivity and the mild reaction conditions required. Examples of these hypervalent iodine oxidants include the Dess-Martin periodinane (DMP) **1** (1,1,1-triacetoxy-1,1-dihydro-1,2benziodoxol-3-(1H)-one) and the Grieco-Dess-Martin periodinane (GDMP) **2** (1-hydroxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole-1-oxide), figure 1.[4]

Figure 1



1 **2**

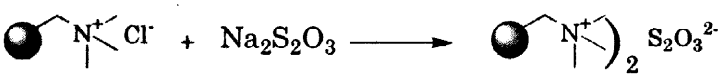
Polymer-bound reagents have an advantage of being easily removed from the solution-phase product by filtration. Several examples of polymer-bound oxidizing reagents have been published,[5] however none are as general and selective as the aforementioned periodinane reagents for the oxidation of alcohols.

Several disadvantages are associated with the utilization of periodinane reagents. These include the excess reagents required, the liquid-phase extraction protocols needed for reaction work-up, and the chromatographic separations necessary to obtain pure product. During the preparation of libraries of compounds in a parallel format, the need to pace all reaction wells through a liquid-phase extractive protocol and/or chromatographic separation can be a very time-consuming process. In an effort to eliminate these problems, we have developed a general, solution-phase synthesis/purification strategy for the periodinane oxidants.[6] After the oxidation of the alcohol to the aldehyde or ketone, a novel Amberlyst® A-26 thiosulfate resin is used to reduce the I(V) and I(III) periodinane species to the I(I) species. This is followed by treatment with a base-functionalized resin which quantitatively sequesters the I(I) species, leaving the pure aldehyde or ketone in solution. Utilization of this purification method allows for the high-throughput purification and work-up of parallel reaction chambers and is highly amenable to automation procedures.[7]

RESULTS AND DISCUSSION

A typical work-up for an oxidation reaction using the DMP reagent **1** involves a solution-phase extraction with aqueous sodium thiosulfate/sodium bicarbonate to reduce the periodinane reagent and concomitantly extract the 2-iodobenzoic acid. A typical purification for an oxidation reaction using the GDMP reagent **2** usually involves a time-consuming chromatographic separation. The DMP reagent **1** contains an inherent masked carboxylic acid group such that reduction of the I(V) species to the I(I) species unmasks the acid group, allowing for its sequestration. Similarly, the GDMP reagent **2** contains an inherent masked carbinol. Reduction of the I(V) species to the I(I) species unmasks the carbinol, and the resulting weakly acidic proton permits its sequestration with an appropriate base-functionalized resin.

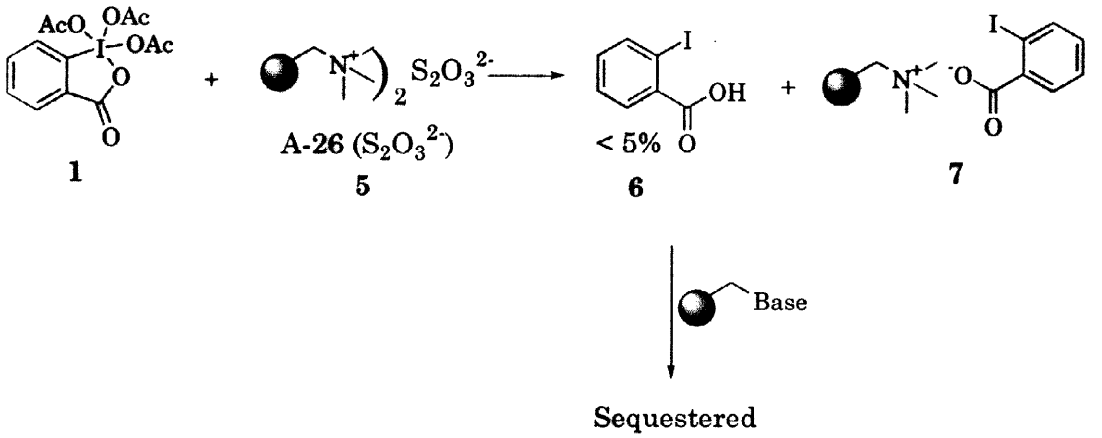
A reducing resin was desired that would quantitatively reduce the periodinane reagents to their corresponding sequesterable I(I) species. The polymer-bound thiosulfate resin **5** was prepared as shown in Scheme 1. Amberlyst® A-26 (chloride form) **3** was converted to the thiosulfate form **5** by treating with aqueous sodium thiosulfate. The exchange proceeded quantitatively as elemental analysis indicated a nitrogen to sulfur ratio of 1:1 with only trace amounts of chlorine or sodium. It was envisioned that the thiosulfate resin **5** would reduce the DMP reagent **1** to the 2-iodobenzoic acid, thereby unveiling the inherent masked carboxylic acid *tag*, allowing for its sequestration with a base-functionalized resin. Likewise, reaction of the thiosulfate resin **5** with the GDMP reagent **2** would afford the 2-iodocarbinol (unveiling the inherent masked carbinol *tag*) which could be sequestered through the acidic proton of the carbinol.



A-26 (Cl^-) **3** | **4** | A-26 ($S_2O_3^{2-}$) **5**

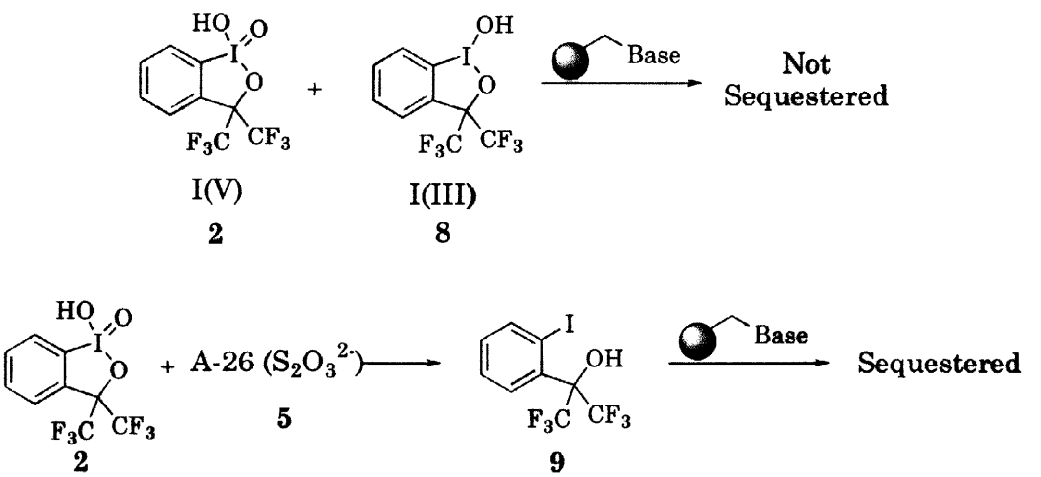
Scheme 1. Preparation of Amberlyst® A-26 thiosulfate resin.

Scheme 2 illustrates the reaction of the thiosulfate resin **5** with the DMP reagent **1** resulting in quantitative reduction of **1** to the I(I) species **6** after two hours of incubation, as indicated by LC/MS analysis and ^{1}H NMR. In addition, the thiosulfate resin **5** sequestered most of the resulting 2-iodobenzoic acid **6** (I(I) species), with typically less than 5% of the acid **6** remaining. Apparently, after reduction exchange of the thiosulfate ion occurs with 2-iodobenzoic acid **6** to afford the polymer-bound quaternary ammonium benzoate salt **7**. The remaining 2-iodobenzoic acid **6** is sequestered by addition of a base-functionalized resin (see Table 1) followed by filtration and evaporation to afford a residue-free vial.



Scheme 2. Reaction of Amberlyst® A-26 thiosulfate resin with DMP reagent **1**.

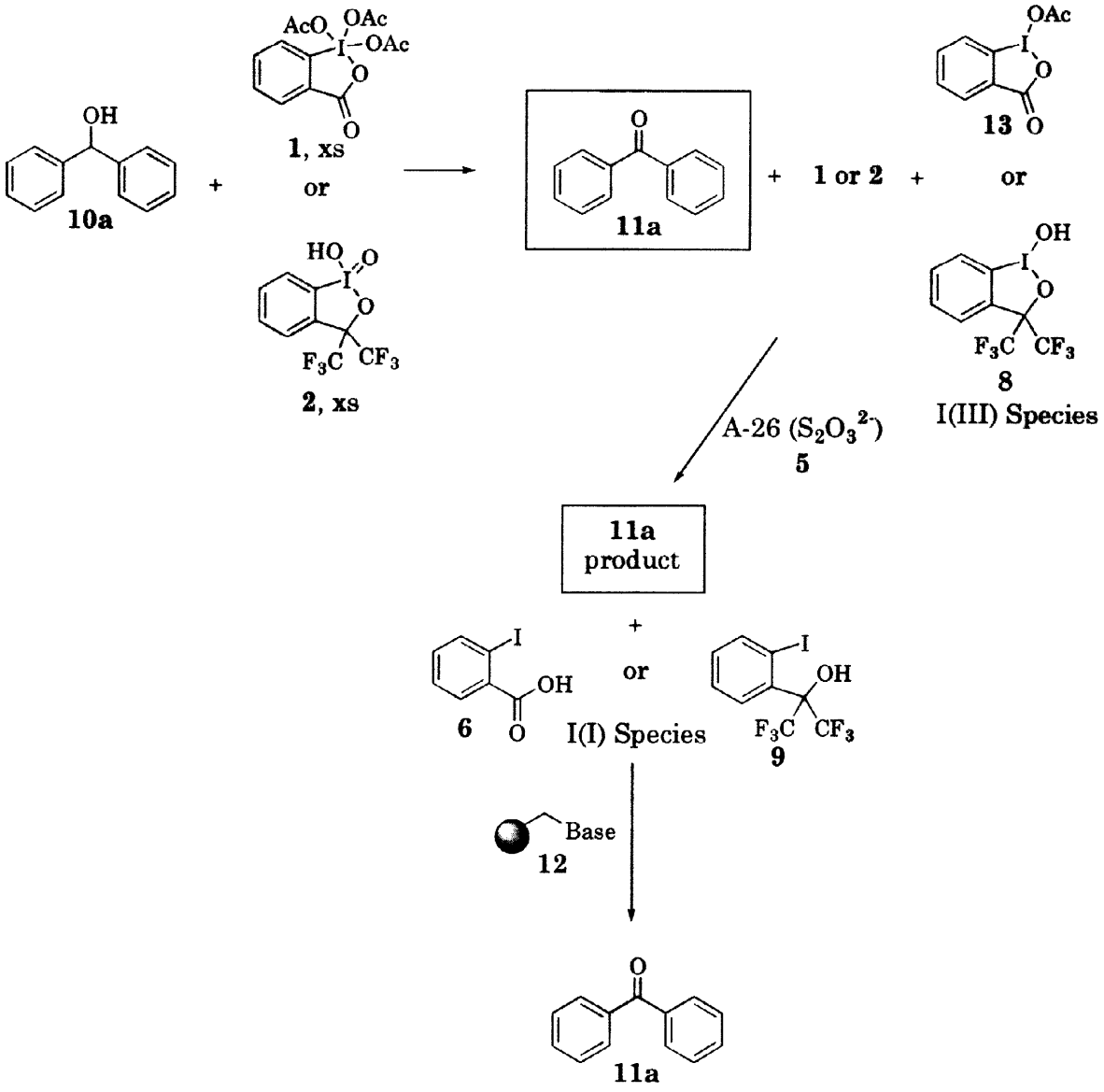
It was initially thought that the GDMP reagent **2** and its I(III) byproduct **8** could be directly sequestered at the end of a reaction *via* the acidic proton present on both. However, attempts to directly sequester **2** and **8** from a product mixture with base-functionalized resins did not afford quantitative sequestration (Scheme 3). Thus, use of the thiosulfate resin **5** was required as shown in Scheme 3. Reduction of the GDMP reagent **2** with the thiosulfate resin **5** afforded carbinol **9** quantitatively after two hours of incubation, as determined by ^{19}F NMR and LC/MS. Addition of a sufficiently basic functionalized resin (see Table 1) resulted in greater than 99% sequestration of the reduced GDMP species **9** as determined by LC/MS, ^{1}H and ^{19}F NMR.



Scheme 3. Reaction of Amberlyst® A-26 thiosulfate resin with GDMP reagent **2**.

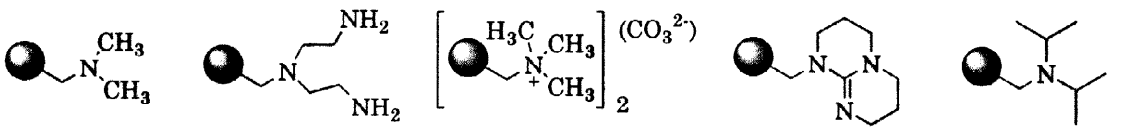
A study was conducted to determine which of the basic functionalized resins would be most suitable for the sequestration of each of the I(I) species **6** and **9**. The oxidation of benzhydrol **10a** to benzophenone **11a** was chosen as the model reaction (Scheme 4). A series of reactions using both periodinane reagents **1** and **2** to oxidize benzhydrol **10a** to benzophenone **11a** was investigated. The product mixtures were purified by a

sequential addition of two resins. The thiosulfate resin **5** was added to reduce the periodinanes to their sequesterable I(I) species **6** or **9** followed by addition and incubation with a basic resin **12** to sequester the reduced I(I) species (Scheme 4). The results are listed in Table 1. As indicated, all five resins were able to efficiently purify the product mixtures from the reactions using the DMP reagent **1**. In the reactions involving the GDMP **2**, only the carbonate resin **12c** and P-TBD resin **12d** were sufficiently basic enough to sequester the carbinol **9** to afford products with acceptable purities. Although LC/MS showed 0% of the carbinol **9** remaining after incubation with P-TBD **12d** (Table 1), ^{19}F NMR indicated a small amount of the carbinol **9** present.



Scheme 4. Model study using a variety of base-functionalized resins to sequester the I(I) species **6** and **9**.

A ^{19}F NMR study was undertaken to quantitatively determine the amount of carbinol **9** that was unsuccessfully sequestered after treatment with resin **12d**. GDMP **2** and a reference 4,4'-difluorobiphenyl were dissolved in CD_3CN. The solution was analyzed by ^{19}F NMR to determine the relative areas of the signals due to the two fluorinated species. The 3,4,5-trimethoxybenzyl alcohol **10g** was added to the solution. After complete oxidation of the alcohol **10g**, the product mixture was treated with the thiosulfate resin **5** and the reduced periodinane **9** sequestered with P-TBD resin **12d**. The area of the remaining GDMP species relative to the reference was determined from ^{19}F NMR analysis of the CD_3CN solution. The amount of GDMP species remaining was calculated to be less than $1.2x10^{-3}$ mmol, or less than 0.5%.



12a A-21 | **12b** Polyamine Resin | **12c** A-26(CO_3^{2-}) | **12d** P-TBD | **12e** PS-DIEA

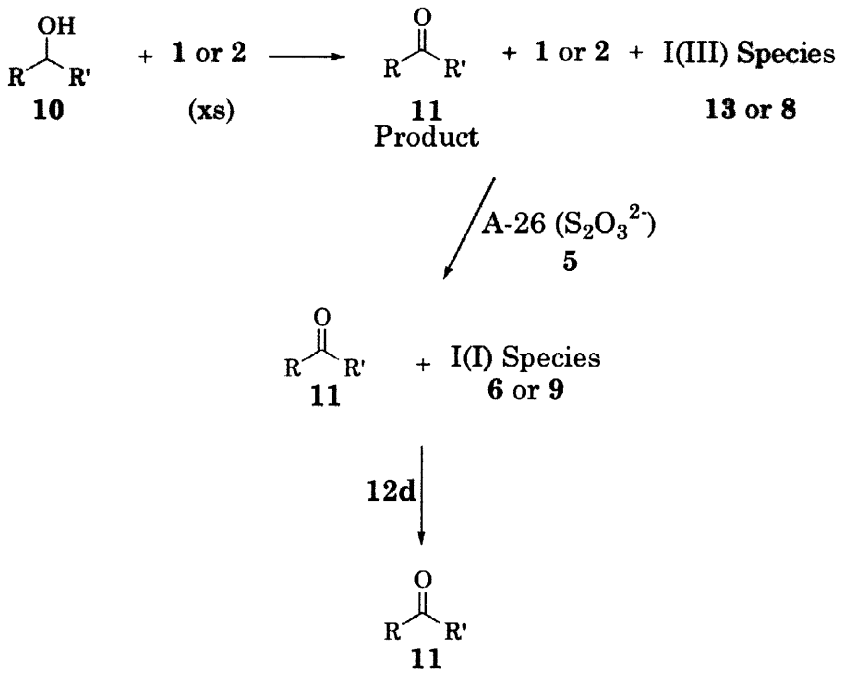
	DMP Reagent 1		GDMP Reagent 2	
Basic Resins **12a-e**	% Product[a] **11a**	% I(I) Species **6**	% Product **11a**	% I(I) Species **9**
12a	100	0	94.7	3.9
12b	100	0	92.9	5.2
12c	100	0	100	0
12d	100	0	100	0
12e	98.5	1.5	91.5	6.5

[a]Relative amounts of benzophenone product and I(I) species are based on LC/MS analysis.

Table 1. Sequestration of reduced DMP **1** and GDMP **2** species with base-functionalized resins.

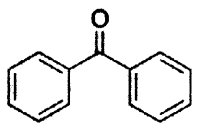
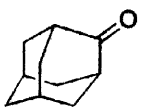
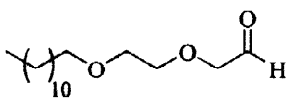
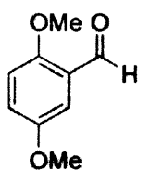
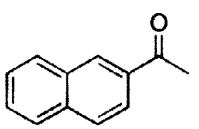
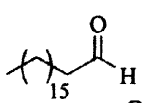
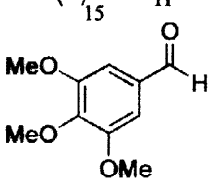
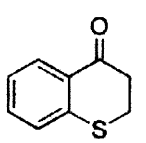
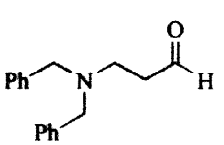
A series of primary and secondary alcohols **10** with various functionalities was oxidized using the periodinanes **1** and **2** to demonstrate this periodinane oxidation/purification strategy. The periodinane reagent (**1** or **2**) was used in excess and reacted with the alcohols **10** as shown in Scheme 5. The oxidations were monitored by TLC and GC/MS or LC/MS and were complete in less than ten minutes. Two work-up protocols were investigated. The first involved a sequential addition where the thiosulfate resin **5** was added directly to the product mixture to reduce the periodinanes to their sequesterable I(I) species. After the

reduction was complete, P-TBD resin **12d** was added to the product mixture to sequester the reduced I(I) species **6** or **9**. Filtration and evaporation afforded purified products **11** in excellent yields and purities, as shown in Table 2. The single exception was the oxidation of alcohol **11i** which resulted in a complex product mixture which was also observed in a previous report using a traditional workup procedure.[8] The second work-up protocol involved the simultaneous use (mixed-bed system)[2u] of the thiosulfate resin **5** and the P-TBD **12d** which worked equally well to afford purified products **11**. In both the sequential and mixed-bed methods, the small percentage (<1%) of remaining I(I) species **9**, from reactions using the GDMP reagent **2**, could be sequestered with a second P-TBD **12d** treatment. Alcohols **10d,g,h** were selected for comparison studies in which the resulting products were previously reported using a liquid-phase extraction purification.[4] Proton NMR and GC/MS indicated the use of the thiosulfate resin **5** and the P-TBD **12d** afforded products with acceptable purities to that of the corresponding products obtained by a traditional purification.



Scheme 5. Demonstration of procedure using a variety of primary and secondary alcohols.

In summary, we have demonstrated a simple and efficient method for sequestering byproducts and excess starting reagents from the periodinane mediated oxidation of alcohols to aldehydes and ketones. Treatment of the reaction solution with thiosulfate resin **5** followed by a basic resin results in essentially quantitative removal of the reduced periodinane species. This purification method allows for the high-throughput purification and work-up of parallel reaction chambers and is highly amenable to automation.[12] Utilization of this purification strategy in a multi-step synthesis involving oxidation of an alcohol with the DMP reagent **1** will be described in a future publication.

	Product 11	DMP (1) % Purity[b]	DMP (1) % Yield[c]	GDMP (2) % Purity[b]	GDMP (2) % Yield[c]
a[d]		>99	96	97	98
b[d]		>99	97	90	65
c[e]		>99	68	31	65
d[d]		>99	93	94	91
e[d]		>99	89	97	96
f[f]		83	72	>99	88
g[d]		>99	94	97	98
h[d]		>99	82	81	69
i[g]		--	--	--	--

[a] ^{1}H NMR spectra and MS data for all compounds prepared were identical to previously reported values (see experimental section). [b] Purity is reported from GC/MS analysis which is in agreement with ^{1}H NMR. [c] Yields are based on mass recovery. [d] See reference 9. [e] See reference 10. [f] See reference 11. [g] See reference 8.

Table 2. Oxidation of Alcohols with DMP 1 and GDMP 2.[a]

EXPERIMENTAL SECTION

General: ^{1}H NMR spectra were recorded using 300 MHz NMR spectrometer. HPLC purities were determined with a Hewlett Packard HP1100 equipped with a series 1100 MSD and an ODS Eclipse XDB-C18 3.5um 30 x 2.1 mm C18 column, eluting with a gradient system of 0/100 to 95/5 acetonitrile/H_2O with 0.1% TFA over 6 min at 1 mL/min, and detected by UV at 254 nm using a diode array detector. GC purities were determined with a Hewlett Packard HP 6890 equipped with an MSD utilizing a capillary column (0.25 mm i.d., 5 % phenyl methyl siloxane, 0.25 um film thickness, 30 m, temperature program from 100 to 300 °C at 20 °C per min). Reported yields are unoptimized with emphasis on purity of products rather than quantity. Amberlyst A-21 **12a** was purchased from Aldrich Chemical Co. and washed three times with dimethylformamide, three times with dichloromethane, three times with tetrahydrofuran, three times with diethyl ether, and dried *in vacuo*. *N,N*-(Diisopropyl)aminomethylpolystyrene resin **12e** (PS-DIEA) was purchased from Argonaut Technologies and used without purification. Dess-Martin periodinane (DMP) reagent **1** (1,1,1-triacetoxy-1,1-dihydro-1,2benziodoxol-3-(1H)-one) was purchased from Lancaster Synthesis Inc. and the Grieco-Dess-Martin periodinane (GDMP) reagent **2** (1-hydroxy-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole-1-oxide) was prepared as described in reference 4a.

Preparation of thiosulfate resin (5). Amberlyst A-26® (Cl^-) **3** (1.0 meq/mL) (~1100 mL, ~ 1.1 mol) purchased from Alfa Æsar was packed in a column and flushed with deionized water. Twelve liters of a 1 M solution of $Na_2S_2O_3{\cdot}5H_2O$ in deionized water was passed through the resin-packed column. The resin was rinsed with deionized water until the eluent was neutral. The resin was removed from the column and rinsed four times with tetrahydrofuran, three times with diethyl ether, and dried *in vacuo*. Anal. Obsd.: N, 4.81 %, 3.4 mmol/g; S, 11.18 %, 3.5 mmol/g; Cl, 0.15%; Na, 0.19%.

Washing of polymer-bound 1,5,7-triazabicyclo[4.4.0]dec-5-ene (P-TBD) resin (12d). Polymer-bound TBD resin **12d** was purchased from Fluka. The polymer was rinsed three times with dimethylformamide, three times with dichloromethane, soaked in dichloromethane for 1 hour, rinsed with dichloromethane two times, rinsed three times with tetrahydrofuran, three times with diethyl ether, three times with methanol, three times with ether, and dried *in vacuo*. Anal. Obsd.: N, 11.43 %, 2.7 mmol/g.

General Procedure A. Oxidation of alcohols using DMP 1. Benzhydrol **10a** (18 mg, 0.10 mmol) and DMP **1** (85 mg, 0.20 mmol) were dissolved in 2-3 mL of dichloromethane. The solution was stirred for 20 min, at which time TLC and LC/MS analyses indicated the oxidation was complete. The A-26 ($S_2O_3^{2-}$) resin **5** (~1.72 meq/g) (0.54 g, 0.93 mmol) was added and the mixture was agitated at room temperature on an orbital shaker for 16 hours. TLC and LC/MS analyses indicated complete reduction of the DMP species. The reduced DMP **6** was sequestered by adding P-TBD resin **12d** (~2.7 meq/g, 0.46 g, 1.2 mmol) and agitating the mixture on an orbital shaker for 8 hours. TLC and LC/MS analyses showed essentially complete sequestration (> 98.5% based on LC/MS). The solution was filtered and the polymer was rinsed with five 2 mL portions of dichloromethane. The combined filtrate and washings were evaporated to give 17.1 mg (96%) of **11a** as a white solid: ^{1}H NMR ($CDCl_3$) ppm 7.47-7.57 (m, 4H), 7.58-7.68 (m, 2H), 7.80-7.89 (m, 4H); HPLC 98.7 % (3.6 min); HPLC ES-MS 183 (M^++H); GC >99% (5.7 min).

Data for 11a: See above.

Data for 11b: General procedure A; 14.8 mg, 97 %. ^{1}H NMR ($CDCl_3$) ppm 1.87-2.21 (m, 12H), 2.57 (br s, 2H); HPLC >99% (2.7 min); HPLC ES-MS 151 (M^++H); GC >99 % (3.9 min).

Data for 11c: General procedure A; 18.9 mg, 68%. ^{1}H NMR ($CDCl_3$) ppm 0.9 (t, 3H), 1.2-1.4 (m, 18H), 1.55 (m, 2H), 3.35-3.70 (m, 6H), 4.2 (s, 2H), 9,6 (s, 1H); GC >99 % (7.2 min); GC EI-MS 113 (M^+ - $(CH_2)_4O(CH_2)_2)CH_2CHO$).

Data for 11d: General procedure A; 17.4 mg, 93%. ^{1}H NMR ($CDCl_3$) ppm 3.84 (s, 3H), 3.93 (s, 3H), 6.97 (d, J = 9.1 Hz, 1H), 7.17 (dd, J = 3.2, 9.1 Hz, 1H), 7.36 (d, J = 3.2 Hz, 1H), 10.47 (s, 1H); HPLC ES-MS 167 (M^++H); GC >99 % (4.6 min).

Data for 11e: General procedure A; 15.2 mg, 89%. ^{1}H NMR ($CDCl_3$) ppm 2.77 (s, 3H), 7.62 (m, 2H), 7.87-8.11 (m, 4H), 8.51 (s, 1H); HPLC 96.7 % (3.6 min); HPLC ES-MS 171 (M^++H); GC >99 % (5.6 min).

Data for 11f: General procedure A; 18.3 mg, 72%. ^{1}H NMR ($CDCl_3$) ppm 0.92 (t, J = 6.7 Hz, 3H), 1.18-1.44 (m, 28H), 1.66 (t, J = 7.3 Hz, 2H), 2.45 (dt, J = 1.8, 7.3 Hz, 2H), 9.80 (t, J = 1.8 Hz, 1H); GC-MS 250 (M^+ - H_2O); GC 83.3 % (7.6 min).

Data for 11g: General procedure A; 19.9 mg, 94%. ^{1}H NMR ($CDCl_3$) ppm 3.96 (s, 6H), 3.97 (s, 3H), 7.16 (s, 2H), 9.90 (s, 1H); HPLC ES-MS 197 (M^++H); GC >99% (5.4 min).

Data for 11h: General procedure A; 13.8 mg, 82%. ^{1}H NMR ($CDCl_3$) ppm 3.02 (m, 2H), 3.28 (m, 2H), 7.21 (m, 1H), 7.31 (m, 1H), 7.41 (m, 1H), 8.14 (dd, J = 1.4, 8.1 Hz, 1H); HPLC ES-MS 165 (M^++H); GC >99 % (5.2 min).

General Procedure B. Oxidation of alcohols using GDMP 2. Benzhydrol **10a** (18 mg, 0.10 mmol) and GDMP **2** (80 mg, 0.20 mmol) were dissolved in 2-3 mL of acetonitrile. The solution was stirred for 20 min, at which time TLC and LC/MS analyses indicated the oxidation was complete. The A-26($S_2O_3^{2-}$) resin **5** (~1.72 meq/g, 0.52 g, 0.89 mmol) was added and the mixture was agitated at room temperature on an orbital shaker for 16 hours. TLC and LC/MS analyses indicated complete reduction of the GDMP species. The reduced GDM **9** was sequestered by adding P-TBD resin **12d** (~2.7 meq/g, 0.45 g, 1.2 mmol) and agitating the mixture on an orbital shaker for 8 hours. TLC and LC/MS analyses showed essentially complete sequestration (> 98.5% based on LC/MS). The solution was filtered and the polymer was rinsed with five 1 mL portions of acetonitrile. The combined filtrate and washings were evaporated to give 17.6 mg (98%) of **11a** as a white solid: ^{1}H NMR ($CDCl_3$) ppm 7.46-7.58 (m, 4H), 7.58-7.68 (m, 2H), 7.80-7.89 (m, 4H); HPLC 98.6 % (3.6 min); HPLC ES-MS 183 (M^++H); GC 96.5 % (5.7 min). To obtain higher purities the solution can be treated a second time with P-TBD resin **12d**.

Data for 11a: See above.

Data for 11b: General procedure B; 9.6 mg, 65%. ^{1}H NMR ($CDCl_3$) ppm 1.87-2.21 (m, 12H), 2.60 (br s, 2H); HPLC >99 % (2.7 min); HPLC ES-MS 151 (M^++H); GC 90.2 % (3.9 min).

Data for 11c: General procedure B; 18.2 mg, 65%. GC EI-MS 272 (M^+); GC 30.5 % (7.2 min).

Data for 11d: General procedure B; 19.2 mg, 91%. ^{1}H NMR ($CDCl_3$) ppm 3.84 (s, 3H), 3.93 (s, 3H), 6.97 (d, J = 9.1 Hz, 1H), 7.18 (dd, J = 3.2, 9.1 Hz, 1H), 7.37 (d, J = 3.2 Hz, 1H), 10.46 (s, 1H); HPLC ES-MS 167 (M^++H); GC 94 % (4.6 min).

Data for 11e: General procedure B; 16.8 mg, 96%. ^{1}H NMR ($CDCl_3$) ppm 2.78 (s, 3H), 7.63 (m, 2H), 7.85-8.10 (m, 4H), 8.50 (s, 1H); HPLC 97.3 % (3.5 min); HPLC ES-MS 171 (M^++H); GC 97.1 % (5.6 min).

Data for 11f: General procedure B; 26.1 mg, 88%. ^{1}H NMR ($CDCl_3$) ppm 0.92 (t, J = 6.7 Hz, 3H), 1.15-1.44 (m, 28H), 1.66 (m, 2H), 2.45 (dt, J = 1.8, 7.4 Hz, 2H), 9.79 (t, 1.8 Hz, 1H) ; GC EI-MS 268 (M^+) GC >99 % (7.6 min).

Data for 11g: General procedure B; 21.1 mg, 98%. ^{1}H NMR ($CDCl_3$) ppm 3.96 (s, 6H), 3.97 (s, 3H), 7.16 (s, 2H), 9.90 (s, 1H); HPLC ES-MS 197 (M^++H); GC 97.0 % (5.5 min).

Data for 11h: General procedure B; 10.4 mg, 69%. ^{1}H NMR ($CDCl_3$) ppm 3.02 (t, J = 6.4 Hz, 2H), 3.28 (t, J = 6.4 Hz, 2H), 7.21-7.50 (m, 3H), 8.14 (d, J = 7.5 Hz, 1H); HPLC 96.6 % (3.1 min); HPLC ES-MS 165 (M^++H); GC 81.2 % (5.1 min).

Determination of amount of GDMP species (8 and 9) remaining after sequestration with P-TBD resin 12d. GDMP **2** (87 mg, 0.22 mmol) and the reference 4,4'-difluorobiphenyl (4 mg, 0.02 mmol) were dissolved in deuterated acetonitrile. The solution was analyzed by ^{19}F NMR and the relative areas of the peaks at -71 ppm (GDMP **3**) and -113 ppm (4,4'-difluorobiphenyl reference) were calculated to be 72.0 and 1.0, respectively. The 3,4,5-trimethoxybenzyl alcohol **10g** (19 mg, 0.10 mmol) was added and the solution was stirred at room temperature for 25 min TLC and LC/MS analyses showed the oxidation was complete. The GDMP **2** was reduced by adding A-26($S_2O_3^{2-}$) resin **5** (0.58 g, 1.0 mmol) to the solution and agitating the mixture overnight on an orbital shaker. The reduced GDMP species was sequestered by adding P-TBD resin **12d** (0.50 g, 1.1 mmol) to the mixture and agitating for 3.5 hours on an orbital shaker. The relative areas of the remaining GDMP species (0.41) and reference (1.0) were determined from ^{19}F NMR analyses of the deuterated acetonitrile solution. The amount of GDMP species remaining corresponds to less than 1.2×10^{-3} mmol, or less than 0.5%.

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6. Another periodinane reagent that is of late receiving more attention is 1-hydroxy-1,2-benziodoxol-3(1H)-one 1-oxide (IBX). IBX should behave similarly and would be purified using the same protocol.

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12. A limitation to this purification method is substrates that contain an acidic functionality are sequestered by the base-functionalized resin.

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