Microwave-Assisted Oxidation of Side Chain Arenes by Magtrieve™

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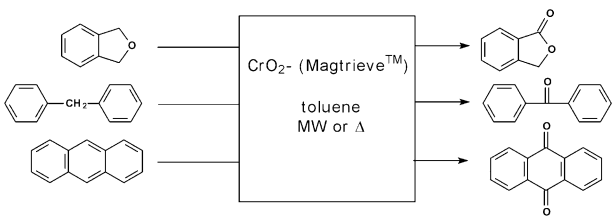
Abstract: A commercial tetravalent chromium dioxide (Magtrieve™) as a magnetically retrievable oxidant is shown to be a very useful compound for microwave-assisted and conventional transformation of aromatic and alkyl aromatic molecules into the corresponding aryl ketones, quinones or lactones.

Keywords: arenes; biphasic reactions; chromium dioxide; heterogeneous oxidation; microwave

The oxidation reactions of aromatic compounds are very useful transformations in organic synthesis as well as biochemistry and dyes synthesis.[1] For many years, the oxidation processes have been carried out in the presence of different oxidizing agents; for example, metal oxides, acids, and peracids.[2] Such methods very often have suffered from stoichiometric quantity of wastes, toxicity of oxidants, or tedious work-up procedures.

Magtrieve™ is DuPont's trademark for its magnetically retrievable oxidant based on tetravalent chromium dioxide (CrO_2).[3] The reagent has already been used in such chemical transformations as: oxidation of thiols,[4] generation of diphenyldiazomethane,[5] deprotection of acetals,[6] and aromatization of dihydropyridines.[7] These research results shows that Magtrieve™ should be considered as a readily available oxidant that is insoluble in most common organic solvents. Moreover, it can be easily separated by employing its magnetic properties, then recycled, and, in turn, reused for further processes.[8] In the oxidation of alcohols to aldehydes and ketones, Magtrieve™ can also serve as a very useful oxidant. Thus, using Magtrieve™ and employing microwave irradiation, we have recently shown[9] that oxidation of alcohols could be greatly improved. Strong interaction of Magtrieve™ with microwaves benefits in an efficient conversion of electromagnetic energy into heat according to the dielectric heating mechanism.[10] We now report that under microwave conditions Magtrieve™ can be used in the oxidation of anthracene and side chain arenes containing activated methylene groups (Scheme 1).



Scheme 1. Oxidations of arenas using Magtrieve™.

Microwave experiments confirmed that Magtrieve™ can be characterized by the strong interaction with microwaves which causes the rapid increase in temperature. For example, the irradiation of pure oxidant (2 g) by microwaves (with the power of 200 W) in an open

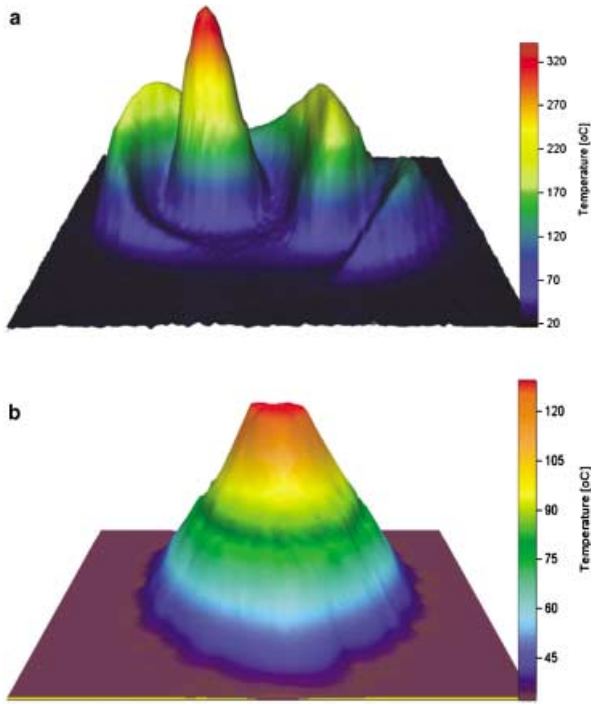


Figure 1. Temperature profiles after 2 min of the microwave irradiation of Magtrieve™ (**a**) and its suspension in toluene (**b**). Experiments conducted in a multimode microwave reactor (Plazmatronika, Poland)

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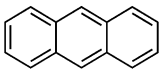
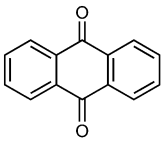
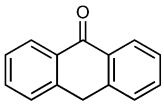
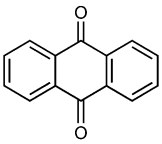
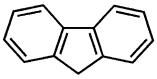
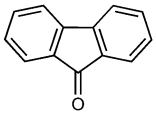
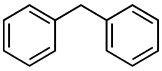
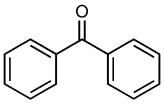
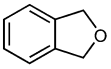
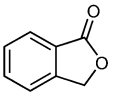
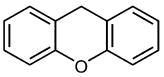
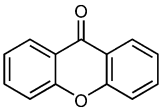
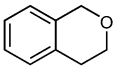
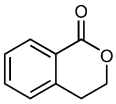
Table 1. Magtrieve™ oxidation of aromatic compounds.

Starting compound	Product	Microwave		Conventional		mp/lit mp[c]
		Time [min]	Yield[a, b] [%]	Time [min]	Yield[a, b] [%]	
		60	88	60	62	284 – 286/ 283 – 287
				150	83	
		45	97	45	81	
				120	97	
		60	57	60	29	79 – 82/ 80 – 83
				180	48	
		90	25	90	19	46 – 48/ 47 – 49
				180	25	
		70	65	70	48	69 – 72/ 71 – 74
				150	67	
		90	67	90	41	170 – 173/ 172 – 174
				200	58	
		90	80	90	52	34 – 35/ 35 – 37
				180	69	

[a] Isolated yield.
[b] All products were identified by standard spectroscopic analysis with comparison to authentic samples.
[c] R. Lide; CRC Handbook of Chemistry and Physics, CRC Press, **1997**

vessel (5 cm diameter) results in a very quick heating of the material up to 350 °C during 2 min of the experiment. The temperature profile recorded by means of the thermovision camera shows that the highest temperature is in the center of the reaction vessel but two other macro "hot spots" with temperatures of about 240 °C can be seen in the sample (Fig. 1a).

These results led us to the conclusion that strong interaction of microwaves with Magtrieve™ was the main reason of the heterogeneity of the heating making it difficult to control. Therefore, in order to maintain a more uniform temperature of reaction mixture, we decided to use as a solvent toluene, which is a very poor microwave absorber. In the Fig. 1b, in which temperature was recorded by a thermovision camera as well, it can be seen that the temperature of Magtrieve™ surface may be higher than the boiling point of toluene but boiling was not observed at all. This means that in heterogeneous systems (e.g., solid chromium oxide/ toluene) the temperature of the solid may be higher than the bulk temperature of reaction mixture, and, therefore, pyrometers as well as fiber-optics thermometers are not able to give correct information about the temperature. Moreover, a temperature gradient of the solid support can be observed with the highest temperature at the center of the samples so it is hard to say what the bulk temperature of reaction mixture is. Finally, the higher temperature of the solid could be responsible for the higher reaction rates and yields of products, which have been reported for a number of reactions.

All the reactions were carried out under heterogeneous conditions using Magtrieve™ as an oxidant and toluene as a medium, which was not oxidized under such conditions. The microwave and conventional reactions were conducted as described for the oxidation of 9*H*-fluorene which was representative for the general procedure of arene oxidations. The applied excess of the oxidant (5:1 weight ratio) is required since only its surface is reduced. The reactions were carried out during the time listed in Table 1. Additional experiments were run in solvent-free systems, but irradiation of Magtrieve™ and substrate mixtures results in poor yields (*ca.* 30% estimated by GC/MS) of the desired compound due to sublimation of the starting material at the very high temperature or ignition of the organic materials.

In the experiments employing toluene as a solvent the carbonyl compounds were obtained with satisfactory yields. Additionally, microwave experiments were carried out in a shorter time and with higher or comparable yields. Results of the experiments are listed in Table 1. In the conventional experiments, we did not observe such high yields as in the microwave system even though the reaction time was three times longer (as in the case of 9*H*-fluorene). In addition, the longer reaction times in the conventional experiments favor the creation of the side-products containing hydroxy groups in the aromatic ring (*ca.* 5% determined by GC/MS), which were not observed under microwave conditions.

In conclusion, we have discovered a very efficient method for the oxidation of side-chain aromatics to the corresponding carbonyl compounds using the solid and magnetically retrievable oxidant, chromium dioxide (Magtrieve™). The advantages of described methodology focus in a simple reaction set-up and application of commercially available reagents.

Finally, as shown in the experiments with the thermovision camera, high product yields and short reaction times can be attributed to the higher temperature of the solid support (i.e., Magtrieve™) during microwave experiments in comparison with conventional processes, which, in turn, can be the explanation of the higher reaction rates in a number of reactions reported for microwave protocols.

Experimental Section

All the chemicals were purchased from Aldrich and used as received. The reactions were carried out in a multimode microwave reactor with a continuous power regulation (Plazmatronika, Poland), which is equipped with a magnetic stirrer and two inlets on the top and one side of the reactor. The inlets allowed applying an upright condenser and introducing a fiber-optic sensor (ReFlex, Nortech) which was used to control the temperature during microwave experiments. IR spectra were recorded on FT-IR BIORAD FTS-165 spectrophotometer as liquids on NaCl disks. ^{1}H NMR spectra were collected on a Tesla 487C (80 MHz) spectrometer using TMS as an internal standard. GC/MS spectra were determined on GC/MS 5890 Series II Hewlett-Packard gas chromatograph equipped with Ultra 2 (25 m × 0.25 mm × 0.25 μm) column with a Hewlett-Packard 5971 Series Mass Selective Detector.

General Method for the Oxidation

All the reactions were carried out according to the oxidation procedure given for 9*H*-fluorene, which was representative of the general procedure employed for microwave and conventional conditions.

a) Microwave process: 9*H*-Fluorene (6 mmol, 1.07 g) was dissolved in toluene (30 mL), which was placed in a 100-mL round-bottom reaction flask. Then Magtrieve™ (5.34 g) was added to the solution. Next the magnetically stirred suspension was irradiated (450 W of microwave power) in an open vessel at reflux using the multimode microwave reactor (Plazmatronika, Poland) during 60 min. After completion of the process Magtrieve™ was isolated by a magnet, and the final solution was evaporated under vacuum. The crude product was purified by crystallization to afford 9-fluorenone; yield: 0.67 g (57%).

b) Conventional process: 9*H*-Fluorene (6 mmol, 1.07 g) was dissolved in toluene (30 mL), which was placed in a 100-mL round-bottom reaction flask. Then Magtrieve™ (5.34 g) was added to the solution. Next the magnetically stirred suspension was heated in a thermostatted bath in the vessel equipped with a reflux condenser during 180 min. After completion of the process Magtrieve™ was isolated by a magnet and the product were isolated and purified as described for microwave experiments to afford 9-fluorenone; yield: 0.56 g (48%).

9,10-Anthraquinodione: MS: $m/z = 209$ ($M^+ + 1$, 15%), 208 (M^+, 100%), 207 (13%), 180 (79%), 152 (48%), 151 (22%), 90 (6%), 76 (29%), 75 (9%), 63 (6%), 50 (8%); IR (KBr): $\nu = 3437$ (w), 3426 (w), 3074 (w), 1680 (s), 1624 (m), 1592 (m), 1474 (m), 1454 (m), 1333 (s), 1323 (m), 1286 (s), 1163 (w), 1094 (m), 912 (m), 810 (m), 696 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 8.56$ (m, 4H, 1,4,5,8-Ar), 7.59 (m, 4H, 2,3,6,7-Ar).

9-Fluorenone: MS: $m/z = 183$ ($M^+ + 1$, 15%), 180 (M^+, 100%), 152 (28%), 151 (13%), 126 (5%), 76 (13%), 75 (5%), 39 (1%); IR (KBr): $\nu = 3061$ (w), 3041 (w), 3013 (w), 1715 (s), 1666 (w), 1612 (s), 1600 (m), 1471 (w), 1451 (m), 1194 (m), 920 (m), 736 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.6$ (m, 2H, 1,8-Ar), 7.45 – 7.5 (m, 4H, 3,4,5,6-Ar), 7.26 (m, 2H, 2,7-Ar).

Benzophenone: MS: $m/z = 183$ ($M^+ + 1$, 7%), 182 (M^+, 50%), 181 (5%), 105 (100%), 77 (47%), 51 (14%), 50 (4%); IR (KBr): $\nu = 3291$ (w), 3088 (w), 3067 (m), 1666 (s), 1595 (m), 1449 (m), 1323 (m), 1281 (s), 1076 (w), 945 (m), 930 (m), 766 (m), 705 (s), 639 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$): $\delta = 7.83$ (m, 4H, *o*-Ar), 7.57 – 7.46 (m, 6H, *m, p*-Ar).

1-Isobenzofuranone (phthalide): MS: $m/z = 135$ ($M^+ + 1$, 3%), 134 (32%), 133 (11%), 105 (100%), 77 (41%), 76 (9%), 51(11%), 50(9%); IR (KBr): $\nu = 3491$ (m), 2945 (w), 1767 (s), 1468 (m), 1440 (m), 1341 (m), 1219 (m), 1111 (m), 1062 (s), 1002 (m), 743 (s) cm^{-1}; ^{1}H NMR ($CDCl_3$): $\delta = 7.5 – 7.9$ (m, 4H, Ar), 5.33 (s, 2H, CH_2).

9-Xanthenone: MS: $m/z = 198$ ($M^+ + 2$, 1%), 197 ($M^+ + 1$, 14%), 196 (M^+, 100%), 139 (27%), 84 (7%), 70 (4%), 63 (6%), 50 (4%); IR (KBr): $\nu = 3082$ (w), 1660 (s), 1618 (s), 1608 (s), 1481 (s), 1451 (s), 1347 (s), 1333 (m), 1218 (w), 1209 (w), 936 (m), 809

(w), 759 (s), 928 (m) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 8.31$ (m, 2H, 1,8-Ar), 7.35 – 7.67 (m, 6H, 2,3,4,5,6,7-Ar).

3,4,4a,8a-Tetrahydroisochroman-1-one: MS: $m/z = 149$ ($M^+ + 1$, 9%), 148 (M^+, 89%), 120 (100%), 92 (50%), 64 (13%), 63 (11%), 39 (4%); IR (KBr): $\nu = 2986$ (w), 2880 (m), 1697 (s), 1689 (s), 1604 (s), 1678 (m), 1479 (s), 1467 (m), 1460 (s), 1328 (s), 1300 (s), 1256 (m), 1216 (s), 1191 (m), 1039 (m), 926 (m), 817 (m), 766 (s), 672 (m), 558 (m) cm^{-1}; ^1H NMR ($CDCl_3$): $\delta = 7.86$ (m, 1H, Ar), 7.53 (m, 1H, Ar), 7.24 (m, 3H, Ar), 5.22 (m, 4H, aliphatic).

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