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Surface-Mediated Reactions. 7. Unsupported Reagents[1]

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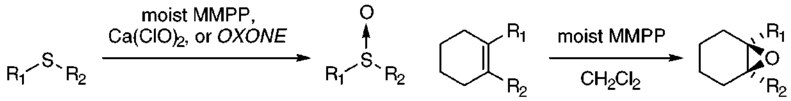
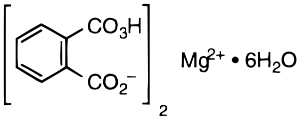
ABSTRACT

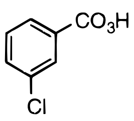


Some solid reagents traditionally supported on silica gel or alumina are also effective as heterogeneous reactants in the absence of a support. Moist magnesium monoperoxyphthalate (MMPP), either suspended in CH_2Cl_2 or solventless, is a convenient alternative to peroxycarboxylic acids for oxidation of sulfides and epoxidation of alkenes. The latter reaction exhibits an unusual order of reactivity: trisubstituted > disubstituted > tetrasubstituted. Unsupported moist $Ca(OCl)_2$ and OXONE are also effective oxidants.

The magnesium salt of monoperoxyphthalic acid (MMPP) is a commercially available alternative to the oxidant *m*-chloroperoxybenzoic acid (MCPBA) that is safer to handle (e.g., can be shipped by air) and, unlike MCPBA, does not require assaying for stoichiometric use.[2,3] It has received relatively little use, however, because it is only soluble in very polar solvents, thus usually necessitating the use of aqueous conditions.

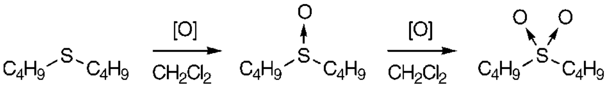


MMPP



MCPBA

Recently it was reported that adsorption of MMPP onto moist silica gel allows oxidation of sulfides to sulfoxides to be performed heterogeneously in CH_2Cl_2.[4] We have observed similar behavior with MMPP supported on moist alumina. Thus stirring a solution of sulfide **1** in CH_2Cl_2 with MMPP supported on moistened alumina readily afforded sulfoxide **2** in excellent yield with no observable over-oxidation to sulfone **3** (Table 1).[5]



1 **2** **3**

As with silica gel, a small amount of water is required. However, *the silica gel or alumina support is not needed*: a stirred suspension of solid MMPP, moistened with water, in CH_2Cl_2 readily afforded sulfoxide **2** (Table 1).[6] Similar results were obtained with moist MMPP under solvent-free conditions with the aid of microwave heating. Thus neither an adsorbent nor a solvent is needed!

Moist MMPP is a convenient alternative to MCPBA. In addition to the greater safety in handling and ease of use of MMPP, the product can be isolated by simple filtration through Celite and removal of the solvent, avoiding the

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[1] (1) Part 6: Kropp, P. J.; Breton, G. W.; Craig, S. L.; Crawford, S. D.; Durland, W. F., Jr.; Jones, J. E., III; Raleigh, J. S. *J. Org. Chem.* **1995**, *60*, 4146−4152.

[2] (2) (a) Brougham, P.; Cooper, M. S.; Cummerson, D. A.; Heaney, H.; Thompson, N. *Synthesis* **1987**, 1015−1016. (b) Heaney, H. *Aldrichimica Acta* **1993**, *26*, 35−45, and references therein.

[3] (3) MMPP is supplied in 80% pure form, while MCPBA is available only in several purity ranges, including 50−55%, 57−86%, and 70−75%.

[4] (4) Ali, M. H.; Stevens, W. C. *Synthesis* **1997**, 764−768.

[5] (5) To provide qualitative rate data, oxidations were terminated prior to total conversion. For preparative purposes, complete oxidation can be effected by using longer reaction times or employing a small excess of oxidant.

[6] (6) The concentration of water is critical. The amounts shown in Table 1 have been qualitatively optimized.

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Table 1. Oxidation of Sulfide **1**[a]

oxidant	adsorbent	water, μL	time, h	yield, %[b] **1**	**2**	**3**
MMPP	Al_2O_3		12	98		
MMPP	Al_2O_3	500	2	7	91	
MMPP			12	97		
MMPP		50	2	9	88	3
MMPP		50	c	2	95	2
$Ca(OCl)_2$		50	3	12	80	7
OXONE		17	4	16	81	3
$NaIO_4$[d]		25	2	100		

[a] Conducted at 25 °C by treating a solution of 1.0 mmol of sulfide **1** in 5 mL of CH_2Cl_2 with 2.5 g of Fisher A540 alumina (pH 9, 210 m^2/g), if used, and 0.5 mmol of oxidant that had been moistened with the indicated amount of water. [b] Determined by ^1H NMR analysis relative to diphenylmethane as an internal standard. [c] Conducted solvent-free by microwave heating for 40 s at 50% power of 0.5 mmol of MMPP moistened with 50 μL of water and to which 1.0 mmol of sulfide **1** had been adsorbed. [d] 1.7 mmol.

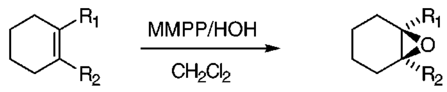
tedious extraction with aqueous base required to separate the carboxylic acid byproducts in oxidations involving peroxy acids.

Table 2. Epoxidation of Cyclohexenes **4** with Moist MMPP[a]

alkene	MMPP, mmol	time, h	yield, %[b] **4**	**5**
4a	1.0	7	5	93
4b	0.5	5	2	98
4c	1.0	24	49	41

[a] Conducted at 25 °C by treating a solution of 1.0 mmol of alkene **4** in 5 mL of CH_2Cl_2 with the indicated amount of MMPP that had been moistened with 100 μL of water/mmol. [b] Determined by ^1H NMR analysis relative to diphenylmethane as an internal standard.

Oxidation by moist MMPP is not limited to sulfides. Treatment of the cyclohexenes **4** afforded the epoxides **5** (Table 2). As expected, the trisubstituted analogue **4b** underwent epoxidation more rapidly than the less highly substituted cyclohexene (**4a**), but the rate *decreased* on going to the tetrasubstituted analogue **4c**, which underwent only slow oxidation. By contrast, in aqueous ethanolic solution the relative rates of oxidation followed the expected order: **4c** > **4b** > **4a** (Table 3). Thus for tetrasubstituted alkenes under heterogeneous conditions, steric hindrance apparently outweighs the favorable electronic effect of the substituents.



4 **5**

a, $R_1 = R_2 = H$; **b**, $R_1 = CH_3$, $R_2 = H$; **c**, $R_1 = R_2 = CH_3$

Table 3. Epoxidation of Cyclohexenes **4** with MMPP in Solution[a]

alkene	time, h	yield, %[b] **4**	**5**
4a	7	8	91
4b	4	2	90
4c	3	5	88

[a] Conducted with 1 mmol of alkene **4** and 0.5 mmol of MMPP in 95% ethanol according to the procedure of Gillard, J. R.; Newlands, M. J.; Bridson, J. N.; Burnell, D. J. *Can. J. Chem.* **1991**, *69*, 1337−1343. [b] Determined by ^1H NMR analysis relative to diphenylmethane as an internal standard.

Moist $Ca(OCl)_2$ and OXONE,[7] both of which also effect oxidation of sulfides as supported reagents,[8] displayed behavior analogous to MMPP as unsupported reagents (Table 1). However, not all solid reagents have the requisite physical properties to serve as unsupported heterogeneous reactants. Moist $NaIO_4$, another oxidant of sulfides when supported on silica gel or alumina,[9] afforded no oxidation of sulfide **1** as an unsupported reagent.

Solid reagents supported on silica gel and alumina have found wide use in numerous synthetic applications.[10] The present results indicate that in some, but not all, of these cases the adsorbent can be eliminated. This both simplifies the experimental procedure and indicates that the adsorbent may not be involved mechanistically. The role of water, which must be present in specific amounts that vary for each reagent, is apparently to both facilitate diffusion and impart requisite physical properties, especially dispersibility, to the solid reagent.[11] In addition to affording a convenient experimental procedure, unsupported heterogeneous reagents can retain the selectivities, including stereoselectivities, exhibited by supported reagents that complement those from traditional solution-phase methods. Our studies in the fascinating realm of surface-mediated reactivity continue.

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[7] OXONE is a product of the Du Pont Company consisting of a 2:1:1 mixture of the active ingredient $KOSO_2OOH$, along with $KHSO_4$ and K_2SO_4, respectively.

[8] $Ca(COCl)_2$: Hirano, M.; Yakabe, S.; Itoh, S.; Clark, J. H.; Morimotoa, T. *Synthesis* **1997**, 1161−1164. OXONE: Kropp, P. J.; Breton, G. W.; Fields, J. D.; Tung, J. C.; Loomis, B. R. Submitted.

[9] (a) Liu, K.-T.; Tong, Y.-C. *J. Org. Chem.* **1978**, *43*, 2717−2718. (b) Gupta, D. N.; Hodge, P.; Davies, J. E. *J. Chem. Soc., Perkins Trans. 1* **1981**, 2970−2973. (c) Varma, R. S.; Saini, R. K.; Meshram, H. M. *Tetrahedron Lett*. **1997**, *38*, 6525−6528.

[10] For reviews, see: (a) *Preparative Chemistry Using Supported Reagents*; Laszlo, P., Ed.; Academic: San Diego, 1987. (b) *Solid Supports and Catalysts in Organic Synthesis*; Smith, K., Ed.; Ellis Horwood: New York, 1992. (c) Clark, J. H. *Catalysis of Organic Reactions by Supported Inorganic Reagents*; VCH: New York, 1994.

[11] Reactions of solid-supported reagents are usually described as requiring moist silica gel or alumina. The present results suggest that the emphasis should be on the reagent as being moist.