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# Baeyer−Villiger Oxidation with Potassium Peroxomonosulfate Supported on Acidic Silica Gel

María E. González-Núñez, Rossella Mello,
Andrea Olmos, and Gregorio Asensio*

*Departamento de Química Orgánica, Universidad de
Valencia, Avda. V. Andrés Estellés s/n,
46100 Burjassot, Valencia, Spain*

*gregorio.asensio@uv.es*

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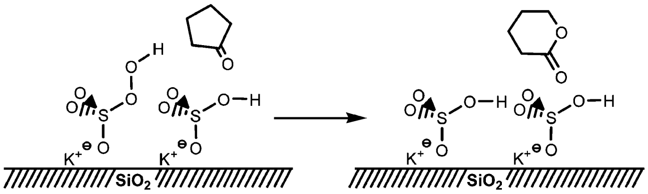
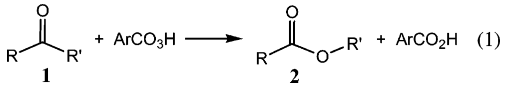


Potassium peroxomonosulfate deposited onto silica $SiO_2 \cdot KHSO_5$ efficiently reacts with ketones in dichloromethane at room temperature to give the corresponding esters or lactones in quantitative yields. This method avoids hydrolysis of the reaction products. The Baeyer−Villiger reaction is catalyzed by potassium hydrogensulfate present in the supported reagent.

The Baeyer−Villiger oxidation of ketones **1** into esters and lactones **2** is an important transformation in organic synthesis,[1] particularly for ring-expansion in the synthesis of natural products and the preparation of monomers for polymerization. The most common reagents for performing these transformations are organic peracids[1] such as *m*-chloroperbenzoic acid or trifluoroperacetic acid (eq 1). However, the hazards associated with these reagents have prompted the search for alternative approaches, such as the use of catalysts that activate hydrogen peroxide or dioxygen,[2] which circumvent both the environmental and safety issues associated with the classical Baeyer−Villiger oxidation.



(1)

Potassium peroxomonosulfate triple salt[3] ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) (Oxone, caroate) is a good alternative to organic peracids in the Baeyer−Villiger reaction since it is inexpensive and safe. In fact, Baeyer and Villiger used[4] persulfuric acid (Caro's acid) in their pioneering work on the oxidation of ketones to esters. Oxone is very efficient in the Baeyer−Villiger oxidation,[5] but it requires an aqueous reaction medium that leads to extensive hydrolysis of the reaction products. This side process can be minimized, but not completely avoided, by using biphasic conditions in the presence of a phase-transfer catalyst[6] or by using the sylilated derivative of peroxomonosulfuric acid.[7]

In this context, the use of Oxone supported on a solid inorganic matrix under anhydrous conditions could avoid undesired hydrolysis of the esters formed in the Baeyer−Villiger reaction, provided that the supported peracid remains reactive. Caro's acid supported on silica has been prepared[8] by treating silica with a mixture of potassium persulfate and concentrated sulfuric acid, but no details were provided concerning the nature of the supported active species. It has been reported that this reagent can be used in a variety of transformations such as the oxidation of thiols to disulfides[8h] and of sulfides to sulfoxides,[8e] aromatization of 1,4-dihydropyridines,[8c] and the conversion of oximes,[8f] hydrazones, and semicarbazones[8b] to carbonyl compounds, although other reactions, such as the deacetalization of carbonyl compounds[8a] or deprotection of silyl ethers,[8d] could be attributed to the strongly acidic character of the reagent rather than to its oxidizing capability. Recently, it has been reported that the surface of wet alumina[9a] or silica[9b,c] can activate Oxone for oxygen-transfer reactions to ketones,[9a] sulfides,[9b] and amines.[9c] However, the approach described in these reports[9] does not actually involve supported Oxone, but rather the existence in the medium of a heterogeneous mixture of wet silica or alumina, the inorganic triple salt ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) and the substrates.

We report here that anhydrous potassium peroxomonosulfate supported on silica ($SiO_2 \cdot KHSO_5$) efficiently oxidizes a variety of ketones **1** to the corresponding esters or lactones **2** in quantitative yields at room temperature. The Baeyer−Villiger reaction is catalyzed by potassium hydrogensulfate present in the supported reagent. This method also avoids hydrolysis of the reaction products.

Potassium peroxomonosulfate supported on silica was obtained by mixing a ca. 2 M aqueous solution of the

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[1] Krow, G. R. *Org. React.* **1993**, *43*, 251. (b) Renz, M.; Meunier, B. *Eur. J. Org. Chem.* **1999**, 737.

[2] (a) tenBrink, G.-J.; Arends, I. W. C. E.; Sheldon, R. A. *Chem. Rev.* **2004**, *104*, 4150. (b) Strukul, G. *Angew. Chem., Int. Ed.* **1998**, *37*, 1198−1209. Bolm, C. In *Advances in Catalytic Processes*; Doyle, M. P., Ed.; JAI Press: Greenwich, 1997; Vol. 2, p 43.

[3] Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 952.

[4] Baeyer, A.; Villiger, V. *Ber. Dtsch. Chem. Ges.* **1899**, *32*, 3265.

[5] Kennedy, R. J.; Stock, A. M. *J. Org. Chem.* **1960**, *25*, 1901.

[6] Camporeale, M.; Fiorentino, M.; Mello, R.; Curci, R. *XVII National Meeting of Organic Chemistry*; Italian Chemical Society: Fiuggi,Italy, 1987.

[7] Adam, W.; Rodríguez, A. *J. Org. Chem.* **1979**, *44*, 4969−4970.

[8] (a) Lakouraj, M. M.; Tajbakhsh, M.; Khojasteh, V.; Gholami, M. H. *Phosphorous, Sulfur Silicon Relat. Elem.* **2004**, *179*, 2645. (b) Tajbakhsh, M.; Lakouraj, M. M.; Gholami, M. H.; Ramzanian-Lehmali, F. *Phosphorous, Sulfur Silicon Relat. Elem.* **2004**, *179*, 1731. (c) Tajbakhsh, M.; Lakouraj, M. M.; Khojasteh, V. *Phosphorous, Sulfur Silicon Relat. Elem.* **2004**, *179*, 463. (d) Lakouraj, M. M.; Tajbakhsh, M.; Khojasteh, V. *Phosphorous, Sulfur Silicon Relat. Elem.* **2003**, *178*, 1865. (e) Lakouraj, M. M.; Movassagh, B.; Ghodrati, K. *Synth. Commun.* **2002**, *32*, 847. (f) Movassagh, B.; Lakouraj, M. M.; Ghodrati, K. *Synth. Commun.* **2000**, *30*, 4501. (g) f) Movassagh, B.; Lakouraj, M. M.; Ghodrati, K. *Synth. Commun.* **2000**, *30*, 2353. (h) Movassagh, B.; Lakouraj, M. M.; Ghodrati, K. *Synth. Commun.* **1999**, *29*, 3597.

[9] (a) Hirano, M.; Oose, M.; Morimoto, T. *Chem. Lett.* **1991**, 331−332. (b) Kropp, P. J.; Breton, G. W.; Fields, J. D.; Tung, J. C.; Loornis, B. R. *J. Am. Chem. Soc.* **2000**, *122*, 4280−4285. (c) Fields, J. D.; Kropp, P. J. *J. Org. Chem.* **2000**, *65*, 5937.

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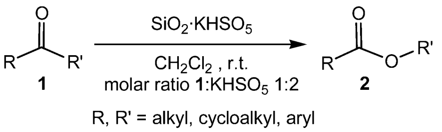
peroxide with chromatographic-grade silica gel (particle size 0.040−0.063 mm). The solvent was evaporated at room temperature under vacuum and the resulting free-flowing solid was dried under vacuum until it achieved a constant weight. The aqueous solution of potassium peroxomonosulfate was prepared by dissolving Oxone (potassium peroxomonosulfate triple salt: $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) in bidistilled water, cooling the mixture at 2 °C for several hours, and filtering the precipitated solids ($K_2SO_4$ and $KHSO_4$). This process was repeated with additional portions of Oxone until the iodometric titration of the solution indicated the desired peroxide concentration. The peroxidic content of the supported reagent was determined by iodometric titration, which revealed $SiO_2 \cdot KHSO_5$ values of 1.0−2.2 mmol of peracid/g.

The metallic traces present in the silica gel did not promote any significant decomposition of the peroxide along its deposition process, which was quantitative in all the essays. Acid−base titration of the reagent showed a total acid content of 1.6−3.0 mmol/g, indicating a potassium hydrogen sulfate content of 0.6−0.8 mmol/g. The reagent can be stored at 2 °C in a desiccator for several days without a noticeable loss of peroxidic content, but the peracid decomposes slowly at room temperature.

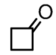
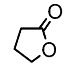
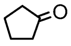
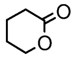
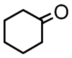
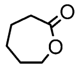
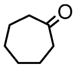
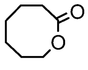
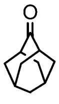
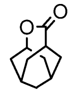
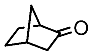
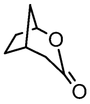
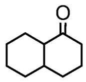
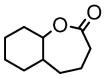
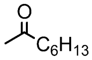
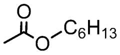
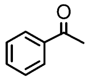
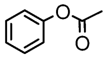
The oxidation of a series of ketones **1** (Table 1) was carried out by mixing potassium peroxomonosulfate supported on silica $SiO_2 \cdot KHSO_5$ with a solution of the substrate in dichloromethane at room temperature. The initial molar ratio of peracid:substrate was 2:1. The reaction was monitored by GC. The reaction mixtures were filtered and the solid was washed with dichloromethane. The solvent was removed under vacuum to give the corresponding esters or lactones **1** (Table 1).



(2)

The results show that cyclic ketones **1a**−**g** react with $SiO_2 \cdot KHSO_5$ to give exclusively the corresponding lactones **2a**−**g** (yield > 98% in all the cases) without significant hydrolysis of the reaction products. The reaction times show the relative reactivities of the different ketones, which depend on the ring size and the migratory ability of the substituents, but the reaction can be driven to completion by increasing the initial molar ratio peroxide:substrate. Thus, the less reactive cycloheptanone (**1d**) required 5 equiv of $SiO_2 \cdot KHSO_5$ 1.0 mmol of peracid/g and 8 h for its quantitative conversion into 2-oxocanone (**2d**) (run 6, Table 1). *trans*-Decalone (**1g**), 2-octanone (**1h**), and acetophenone (**1i**) also required an excess of peracid to achieve a quantitative conversion (runs 10−13, Table 1). Heating of the reaction mixture at 40 °C did not improve the results but enhanced the decomposition of the peracid and acid-catalyzed aldol condensation of the ketone. A higher loading of peracid on the silica led to faster reactions. Thus, the conversion of cyclobutanone (**1a**) took 8 h with $SiO_2 \cdot KHSO_5$ 1.0 mmol of peracid/g, but only 1 h with $SiO_2 \cdot KHSO_5$ 2.2 mmol of peracid/g (runs 1 and 2, Table 1). On the other hand, the reaction of cyclopentanone (**1b**) with nonsupported Oxone ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$) in dichloromethane at room temperature for 24 h gave only a 10% conversion of the substrate.

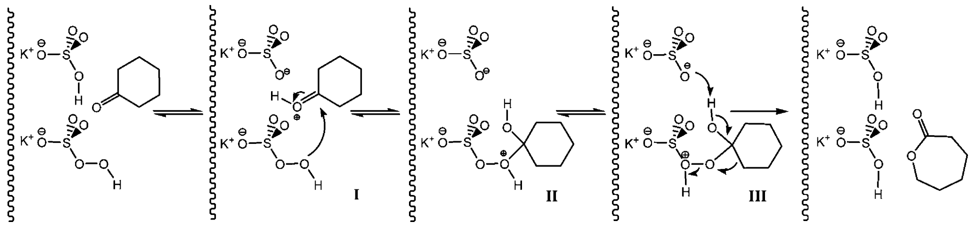
**TABLE 1. Oxidation of Ketones 1 with $SiO_2 \cdot KHSO_5$** [a]

| Run | Substrate | $SiO_2 \cdot KHSO_5$ ($KHSO_5$:**1**) t(h) | Product[b] | Conv.[c] (%) |
|---|---|---|---|---|
| 1 |  **1a** | A (2:1) 8 |  **2a** | >99 |
| 2 | | B (2:1) 1 | | >99 |
| 3 |  **1b** | B (2:1) 2 |  **2b** | 96 |
| 4 |  **1c** | B (2:1) 3 |  **2c** | 95 |
| 5 | | C (2:1) 48 | | 70 |
| 6 |  **1d** | A (5:1) 8 |  **2d** | 93 |
| 7 | | B (2:1) 48 | | 13 |
| 8 |  **1e** | A (2:1) 1 |  **2e** | 99 |
| 9 |  **1f** | A (2:1) 8 |  **2f** | 95 |
| 10 |  **1g** | A (3:1) 2 |  **2g** | 98 |
| 11 |  **1h** | A (3:1) 1.5 |  **2h** | 87 |
| 12 |  **1i** | A (3:1) 16 |  **2i** | 86 |
| 13 | | A (4:1) 16 | | >99 |

[a] Reactions in dichloromethane at room temperature with $SiO_2 \cdot KHSO_5$: (A) 1.0 mmol of peracid/g; (B) 2.2 mmol of peracid/g; (C) 2.0 mmol of peracid/g previously neutralized with *n*-butylamine. [b] Yield >98% in all the cases. [c] Determined by GC analysis of the reaction mixtures.

The structure of the supported reagent deserves further study. Our results suggest that the peroxomonosulfate species are oriented in part on the solid support with the hydroperoxide groups pointing outward from the surface; otherwise, the nucleophilic attack on the carbonyl group of the substrate would not be feasible. In fact, iodometric titration of the supported reagent recovered after reacting with a 6-fold excess of cyclopentanone (**1b**) for 3 h evidenced ca. 50% of unreacted peroxide on the silica matrix, indicating that only a half of the peracid is available for the oxygen transfer reaction. These results can be attributed either to a partial adsorption of the peracid on the silica through the reactive hydroperoxide group, which would then not be exposed to the ketone substrate in solution, or to adsorption of the peracid within the inner pores of the solid support, which is inaccessible to the substrate. We also cannot exclude the possibility that some of the additional potassium salts present in Oxone ($KHSO_4$ and $K_2SO_4$) could be deposited to cover the peroxide in the supported reagent.

**SCHEME 1. Proposed Reaction Pathway for the Oxidation of Ketones 1 with Silica-Supported Oxone**[a]



[a] The wavy line represents the silica surface.

To determine the role of surface-adsorbed potassium hydrogen sulfate in the Baeyer−Villiger reaction, we neutralized a sample of the supported reagent containing $SiO_2·KHSO_5$ 2.2 mmol of peracid/g and potassium hydrogen sulfate 0.8 mmol of acid/g by treatment with the stoichiometric amount of *n*-butylamine with respect to potassium hydrogen sulfate in dichloromethane solution, at 0 °C, followed by filtration, washing of the solid with dichloromethane, and drying under vacuum. The amount of base adsorbed onto the supported reagent was monitored by disappearance of the amine from the organic solution. The reagent maintained the peroxidic titer, indicating that protonation of the amine with adsorbed potassium hydrogen sulfate occurs faster than oxidation under these conditions. The reaction of this neutral supported reagent with cyclohexanone under the usual conditions (initial molar ratio peracid:ketone 2:1, dichloromethane, room temperature) was significantly slower, and required 2 days to achieve a 70% conversion of the substrate. An analysis of the residue from the dichloromethane solution showed no evidence of detachment of the ammonium salt from the solid reagent under these conditions. This result indicates that adsorbed potassium hydrogen sulfate helps to catalyze the Baeyer−Villiger reaction with ketones.

The reaction pathway can be depicted in terms of the initial equilibrium between the ketone adsorbed on the acidic surface of the reagent and the ketone in solution. This initial acid−base process provides an activated carbonyl that then reacts with a proximate hydroperoxide group. The leaving-group ability is also favored by interaction of the peroxidic intermediate with the adjacent acidic hydrogen atoms (Scheme 1).

The change of the solvent has dramatic effects on the course of the reaction. Thus, highly polar protic solvents such as methanol partially detached the reactive species from the solid support, leading to strongly acidic solution with high peroxidic content. On the other hand, in apolar solvents such as hexane, the aldol condensation of the ketones becomes the preferred reaction pathway. The poor solvating ability of hexane strongly favors the adsorption of the substrate onto the acidic centers of the active surface and reduces the concentration of the protonated ketone available at the proximity of the supported hydroperoxide. Thus, the reaction of cyclohexanone (**1c**) with $SiO_2·KHSO_5$ 2.2 mmol of peracid/g in hexane at room temperature and with an initial molar ratio of peracid:ketone 2:1 led to low substrate conversion and 2-cyclohexylidene cyclohexanone as the main reaction product, with only minor amounts of the corresponding $\epsilon$-caprolactone (**2c**). Also, under these conditions recovery of the reaction products required a thorough washing of the solid with dichloromethane to detach the organic material that was strongly adsorbed on the surface of the reagent.

In summary, anhydrous potassium peroxomonosulfate supported on silica $SiO_2·KHSO_5$ efficiently converts ketones **1** into esters **2** at room temperature and avoids the hydrolysis of the reaction products. The reaction is acid-catalyzed by potassium hydrogen sulfate present at the reactive surface of the reagent.

## Experimental Section

**General Procedures.** Water was distilled twice from potassium permanganate. Dichloromethane was purified following described procedures. The glass containers for the aqueous solutions of caroate were carefully cleaned and washed with a solution of EDTA in bidistilled water (0.25 g $L^{-1}$) before use to remove traces of metals.

Aqueous solutions of potassium peroxomonosulfate were prepared by mixing 800 g of Oxone in 1.5 L of a solution of EDTA in bidistilled water (0.25 g $L^{-1}$) at rt under stirring. The mixture was allowed to stand overnight at 2 °C. The solids were filtered off, and the solution was treated with an additional 400 g of Oxone at rt under stirring. The procedure was repeated with successive 200 g portions of Oxone until the solution reached the desired peroxidic titer. The solution was stored at 2 °C and titered[10] before use. The aqueous solutions of Oxone are strongly corrosive and should be handled with care. Metallic traces can initiate the decomposition of the peroxide.

**Preparation of $SiO_2·KHSO_5$.** A 100-mL round-bottomed flask charged with 10 g of silica gel (Merck, 0.040−0.063 mm) and a magnetic stirrer was placed in an ice−water bath. Twenty-five milliliters of a 1.8 M aqueous solution of potassium peroxomonosulfate (45 mmol) was then added portionwise under stirring, and the mixture was maintained at 0 °C for 15 min. The reaction mixture was dried under vacuum ($10^{-3}$ mbar) at rt until it reached a constant weight to obtain 17 g of $SiO_2·KHSO_5$. Iodometric titration of the solid indicated 2.0 mmol of peracid/g (76% of the initial peracid). The supported reagent was stored at 2−3 °C in a desiccator. After 1 month, iodometric titration indicated 38% decomposition of the peroxidic reagent. The reagent is corrosive, and exposure to its dust should be minimized. Thermal and mechanical shocks should be avoided.

**Oxidation of Ketones to Esters with $SiO_2·KHSO_5$. General Procedure.** To a stirred mixture of 0.64 g of $SiO_2·KHSO_5$ (2.2 mmol of peracid/g) in 7 mL of dichloromethane at rt was added 52.2 $\mu$L (0.7 mmol) of cyclobutanone (**1b**). The reaction was monitored by GC analysis. After 2 h, the conversion of the substrate was complete. The mixture was filtered, and the solid was washed twice with dichloromethane. The solvent was removed under vacuum to give 0.06 g of pure $\gamma$-butyrolactone (>99% yield) as a colorless oil. The reaction product was characterized by GC−MS and $^1H$ and $^{13}C$ NMR.

**2-Oxocanone (2d).** $^1H$ NMR ($CDCl_3$, 300 MHz): 1.5 (m, 4H), 1.7 (m, 4H), 2.4 (tr, 2H), 4.3 (tr, 3H). $^{13}C$ NMR ($CDCl_3$, 75

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[10] Mendham, J.; Denney, R. C.; Barnes, J. D., Thomas, M. J. K. *Vogel's Textbook of Quantitative Chemical Analysis*, 6th ed.; Prentice Hall: Upper Saddle River, NJ, 2000.

MHz): 24.9, 26.1, 29.0, 31.6, 32.6, 68.4, 177.4. GC−MS (EI+, 70 eV): *m/z* 128 ($M^{\bullet+}$, 2), 110 (10), 100 (30), 98 (35), 83 (14), 82 (16), 80 (20), 69 (55), 55 (100), 42 (60).

**4-Oxatricyclo[4.3.1.1$^{3,8}$]undecan-5-one (2e).** $^1$H NMR ($CDCl_3$, 300 MHz): 1.7−2.1 (m, 12H), 3 (bs, 1H), 4.4 (bs, 1H). $^{13}$C NMR ($CDCl_3$, 75 MHz): 26.4, 31.28, 34.1, 35.9, 41.6, 73.6, 179.0. GC−MS (EI+, 70 eV): *m/z* 166 ($M^{\bullet+}$, 5), 122 (15), 107 (7), 93 (17), 80 (100), 67 (13), 53 (8), 41 (16).

**2-Oxabicyclo[3.2.1]octan-3-one (2f).** $^1$H NMR ($CDCl_3$, 300 MHz): 1.5−2.2 (m, 7H), 2.4−2.7 (m, 2H), 4.8 (bs, 1H). $^{13}$C NMR ($CDCl_3$, 75 MHz): 29.8, 32.2, 32.8, 35.7, 41.1, 81.4, 171.2. GC−MS (EI+, 70 eV): *m/z* 126 ($M^{\bullet+}$, 15), 111 (1), 98 (19), 82 (85), 67 (100), 55 (50), 41 (55).

**2-Oxabicyclo[4.5.0]undecan-3-one (2g).** $^1$H NMR ($CDCl_3$, 300 MHz): 0.9−2.2 (m, 15 H), 2.4−2.7 (m, 2H), 3.9−4.1 (m, 1H). $^{13}$C NMR ($CDCl_3$, 75 MHz): 22.8, 24.8, 25.1, 33.3, 33.7, 35.5, 38.3, 42.3, 82.5, 176.2. GC−MS (EI+, 70 eV): *m/z* 168 ($M^{\bullet+}$, 10), 150 (8), 125 (13), 111 (9), 97 (20), 84 (100), 67 (27), 54 (17), 41 (19).

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**Supporting Information Available:** Gas chromatograms and NMR spectra of the reaction crudes. This material is available free of charge via the Internet at http://pubs.acs.org.

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