quinolines were separable by column chromatography on silica gel eluted with 2-butanol–14 M formic acid[8,9] or by fractional recrystallization from ethanol, ethanol–ether, or 2-propanol. The tetrahydroisoquinoline products **2–5** were identified by comparison with authentic samples synthesized by known methods or by the procedures described below. All tetrahydroisoquinolines except **4b** and **5d** were previously known (see references in Table I).

Authentic tetrahydroisoquinolines 2 and 4 which were difficult to obtain by literature procedures were synthesized by Pictet–Spengler reactions under strongly acidic conditions as follows: A formaldehyde solution (8.5 mmol, 120 mol %) was added to a solution of the phenethylamine 1 (7.0 mmol) dissolved in water (2–5 mL) at pH 0.5. When the reaction was essentially complete according to chromatography (5–20 days at 20 °C), 1 M $NaHCO_3$ was added to pH 2, the water was evaporated in vacuo, and the residue was sequentially triturated with 95% then 100% ethanol to afford crude product (80–100% yield). Recrystallization from ethanol, ethanol–ether, or 2-propanol afforded the pure product as the hydrochloride salt.

1,2,3,4-Tetrahydro-1,2-dimethyl-6-isoquinolinol hydrochloride (4b): mp 207–209 °C; ^{1}H NMR (D_2O) δ 1.70 (3 H, d), 3.00 (3 H, s), 3.12 (2 H, t), 3.60 (2 H, t), 4.60 (1 H, q), 6.8–7.2 (3 H, m); MS, *m/e* (relative intensity) 177.1159 (2, M^+, calcd 177.1154), 163 (19), 162 (100), 44 (33).

Authentic tetrahydroisoquinolines 3 and 5 which were difficult to obtain by literature procedures were synthesized by catalytic hydrogenolysis of the known 4-hydroxytetrahydroisoquinolines (see Table I) under the conditions described for synthesis of **1a**.

1,2,3,4-Tetrahydro-1,2-dimethyl-7,8-isoquinolinediol hydrochloride (5d): mp 157–160 °C; ^{1}H NMR (D_2O) δ 1.58 (3 H, d), 2.88 (3 H, s), 3.0 (2 H, m), 3.4 (2 H, m), 4.36 (1 H, q), 6.65 (2 H, s); ^{13}C NMR (D_2O, pH 5) δ 16.73, 22.86, 40.50, 45.32, 56.59, 116.75, 121.38, 121.94, 122.29, 141.97, 143.60; MS, *m/e* (relative intensity) 193.1106 (2, M^+, calcd 193.1103), 192 (4), 179 (18), 178 (100).

Acknowledgment. This investigation was supported in part by the U.S. Public Health Service, Grant AA05472, and Biomedical Research Support Grant 5 SO7 RR07067.

Registry No. **1a**·HCl, 3458-98-8; **1b**·HCl, 33543-61-2; **1c**, 51-61-6; **1d**·Br, 18191-22-5; **1e**, 536-21-0; **1f**, 532-38-7; **1g**, 586-17-4; **1h**, 6912-68-1; **2a**, 14446-24-3; **2b**, 14097-39-3; **2c**, 34827-33-3; **2d**, 37491-98-8; **2e**, 93202-93-8; **2f**, 23824-24-0; **2g**, 50988-14-2; **2h**, 82563-75-5; **3a**, 32999-37-4; **3b**, 14788-32-0; **3c**, 102830-09-1; **3d**, 102830-10-4; **3e**, 102830-11-5; **3f**, 23824-25-1; **3g**, 102830-12-6; **3h**, 82334-24-5; **4a**, 61562-93-4; **4b**, 102830-13-7; **4c**, 525-72-4; **4d**, 102830-14-8; **4e**, 102830-15-9; **4f**, 102830-16-0; **4g**, 33698-46-3; **4h**, 35589-37-8; **5a**, 102830-17-1; **5b**, 32999-47-6; **5c**, 102917-28-2; **5d**, 102830-18-2; **5e**, 102830-19-3; **5f**, 102830-20-6; **5g**, 102830-21-7; **5h**, 102830-22-8; CH_2O, 50-00-0; MeCHO, 75-07-0.

A Mild and Highly Selective Method for the Regeneration of Carbonyl Compounds from Oximes and (2,4-Dinitrophenyl)hydrazones

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Regeneration of carbonyl compounds from its derivatives under mild conditions is an important process in synthetic organic chemistry. Readily prepared and highly stable ketoximes are particularly useful both as protective groups and selective activating groups. Several oxidative methods are available for deoximation.[1] In the case of 2,4-DNP derivatives apart from exchange reactions with pyruvic acid[2] or levulinic acid,[3] ozonolysis at low temperature[4] and treatment with titanous ion[5] are the commonly employed methods of deprotection. Although these methods are generally useful they have limited applicability when extended to complex molecules having multifunctional groups which are prone to oxidation under the reaction conditions. Thus a need exists for the development of an oxidizing agent which is mild and selective and is capable of effecting the oxidative cleavage of the carbon–nitrogen double bond in the presence of other functional groups.

Recently, we reported on the usefulness in organic synthesis of an oxidizing agent—cetyltrimethylammonium permanganate (CTAP) for cis-hydroxylation of olefins[6] and for selective oxidation of benzylic alcohols.[7] In the course of our studies to explore the usefulness of this reagent in

Table I. Oxidative Cleavage of Oximes with CTAP

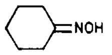
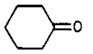
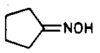
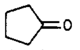
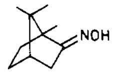
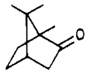
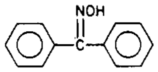
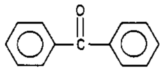
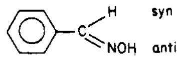
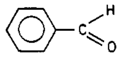
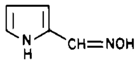
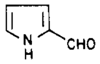
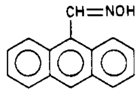
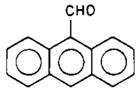
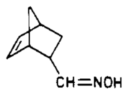
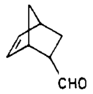
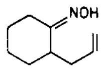
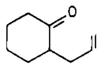
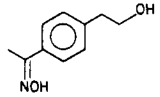
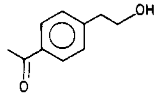
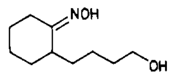
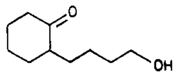
entry	oxime	condtn: time, min	carbonyl comp[a]	% yield[b]
1		15		98
2		60		94
3		20		89
4		40		95
5		20 35		90
6		15		88
7		15		96
8		15		92
9		20		90
10		30		86
11		30		88

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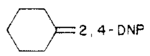
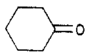
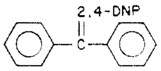
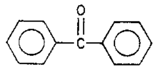
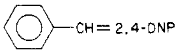
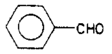
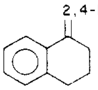
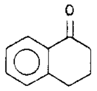
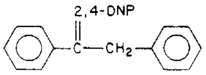
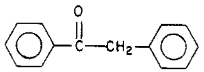
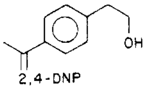
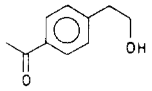
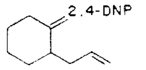
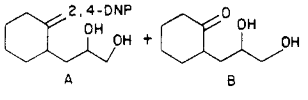
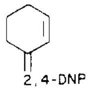
Table II. Oxidative Cleavage of 2,4-DNP with CTAP

entry	2,4-DNP deriv	condtns: time, h	carbonyl comp[a]	% yield[b]
1		4		80
2		7		79
3		4		72
4		4		76
5		4.5		78
6		8		70
7		5		(A) 30 (B) 32
8		6	no reaction	

[a] The carbonyl compounds were compared with authentic samples (mp, IR, NMR). [b] Yield refers to pure isolated products.

other organic transformations, we find that cetyltrimethylammonium permanganate (CTAP) is indeed a mild and selective reagent for the oxidative cleavage of carbon–nitrogen double bonds. Herein, we report our results on the regeneration of carbonyl compounds from oximes (Table I) and (2,4-dinitrophenyl)hydrazones (Table II) using CTAP.

In a typical reaction the derivative of the carbonyl compound (1 equiv) is stirred with 1.5 equiv of CTAP in dichloromethane or chloroform at room temperature (25 °C) for 0.1 to 6 h. At the end of the reaction, the reaction mixture is diluted with ether and filtered through a pad of Celite and silica gel. The filtrate is evaporated and purified by recrystallization, vacuum distillation, or chromatography. The deoximation with CTAP (Table I) is very fast at room temperature (<1 h) and the yield of the carbonyl compounds is high. The mildness of this methodology and selectivity of this reagent is exemplified by entries 5–11 in Table I. Reaction of aldoximes (entries 5–7) yields the aldehydes in good yield without overoxidation to carboxylic acids. The syn oximes react marginally faster than the anti oximes but there is no difference in the yield of the carbonyl compound formed. Entries 8 and 9 illustrate the selective cleavage of the carbon–nitrogen double bond of the aldoxime and ketoxime, respectively, in the presence of carbon–carbon double bond. Particularly noteworthy are the entries 10 and 11 containing readily oxidizable hydroxyl groups present in the molecule elsewhere. Under the conditions of oxidative cleavage with CTAP the carbonyl group is regenerated with the primary hydroxyl group intact.

Oxidative cleavage of (2,4-dinitrophenyl)hydrazones with CTAP (Table II) is equally effective although this reaction is much slower (1.5 to 6 h) compared to the deoximation reaction. Although the deprotection of 2,4-DNP under these conditions can be performed without difficulty when hydroxyl group is present in the molecule (entry 6), the regeneration of 2,4-DNP from compounds containing carbon–carbon double bonds is not selective (entry 7). 2,4-DNP derivatives of α,β-unsaturated carbonyl compounds (entry 8) are unaffected under the conditions of oxidation with CTAP.

In summary, the present methodology of regeneration of carbonyl compounds from their derivatives with CTAP is mild, highly selective, and proceeds in high yield.[8] The reagent itself is easily prepared[6] and can be handled with ease unlike some of the other quaternary ammonium permanganates.[9]

Experimental Section

General Procedure for the Regeneration of Carbonyl Compounds from Oximes and (2,4-Dinitrophenyl)hydrazones. To a stirred solution of cetyltrimethylammonium permanganate (CTAP) (3.0 mmol) in dichloromethane (8 mL) was added a solution of the oxime or 2,4-DNP (2 mmol) in dichloromethane (4 mL) at 25 °C. The reaction mixture was stirred (0.1–6 h) and then was diluted with ether (40 mL) and filtered through a pad of Celite and silica gel and the filtrate was concentrated on the rotary evaporator. The product was purified by chromatography on silica gel or recrystallization and was identified by melting point and by comparison of its infrared and NMR spectra with those of an authentic sample.

Registry No. CTAP, 73257-07-5; cyclohexanone, 108-94-1; cyclopentanone, 120-92-3; 1,7,7-trimethylbicyclo[2.2.1]heptan-2-one, 76-22-2; diphenylmethanone, 119-61-9; benzaldehyde, 100-52-7; 2-formylpyrrole, 1003-29-8; 9-formylanthracene, 642-31-9; 2-formyl-5-bicyclo[2.2.1]heptene, 5453-80-5; 2-(2-propenyl)cyclohexanone, 94-66-6; 1-[4-(1-hydroxyethyl)phenyl]ethanone, 15519-23-0; 2-(4-hydroxybutyl)cyclohexanone, 57548-42-2; 1,2,3,4-tetrahydronaphthalen-1-one, 529-34-0; 1,2-diphenylethanone, 451-40-1; 1-[4-(2-hydroxyethyl)phenyl]ethanone, 102494-25-7; 2-(2,3-dihydropropyl)cyclohexanone, 102494-27-9; cyclohexanone oxime, 100-64-1; cyclopentanone oxime, 1192-28-5; 1,7,7-trimethylbicyclo[2.2.1]heptan-2-one oxime, 13559-66-5; diphenylmethanone oxime, 574-66-3; *syn*-benzaldehye oxime, 622-31-1; *anti*-benzaldehyde oxime, 622-32-2; 2-formylpyrrole oxime, 32597-34-5; 9-formylanthracene oxime, 18004-57-4; 2-formyl-5-bicyclo[2.2.1]heptene oxime, 90086-80-9; 2-(3-

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(8) This oxidative cleavage is not selective if the reactions are performed with CTAP generated in situ under normal phase-transfer conditions.

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propenyl)cyclohexanone oxime, 59239-07-5; 4-(2-hydroxyethyl)benzaldehyde oxime, 102494-22-4; 2-(4-hydroxybutyl)cyclohexanone oxime, 102494-23-5; cyclohexanone (2,4-dinitrophenyl)hydrazone, 1589-62-4; diphenylmethanone (2,4-dinitrophenyl)hydrazone, 1733-62-6; benzaldehyde (2,4-dinitrophenyl)hydrazone, 1157-84-2; 1,2,3,4-tetrahydronaphthalen-1-one (2,4-dinitrophenyl)hydrazone, 853-95-2; 1,2-diphenylethanone (2,4-dinitrophenyl)hydrazone, 5637-51-4; 1-[4-(2-hydroxyethyl)phenyl]ethanone (2,4-dinitrophenyl)hydrazone, 102494-24-6; 2-(3-propenyl)cyclohexanone (2,4-dinitrophenyl)hydrazone, 1044-31-1; 2-cyclohexenone (1,2-dinitrophenyl)hydrazone, 1459-31-0; 2-(2,3-dihydroxypropyl)cyclohexanone (2,4-dinitrophenyl)hydrazone, 102494-26-8.

Communications

A General, Regiospecific Synthesis of Highly Substituted Quinones

Summary: A general route to a wide variety of substituted quinones (furyl, indolo, pyrrolo, quinolino, naphtho, and anthra) has been developed via the thermolysis (160 °C, xylene) and subsequent oxidation (air or Ce^{4+}) of 4-hydroxy-4-substituted-cyclobutenones (eq 1) and 2-hydroxy-2-substituted-benzocyclobutenones which were formed by the regioselective addition of an appropriate aryl or heteroaryl (etc.) lithium reagent to the corresponding cyclobutenedione.

Scheme I

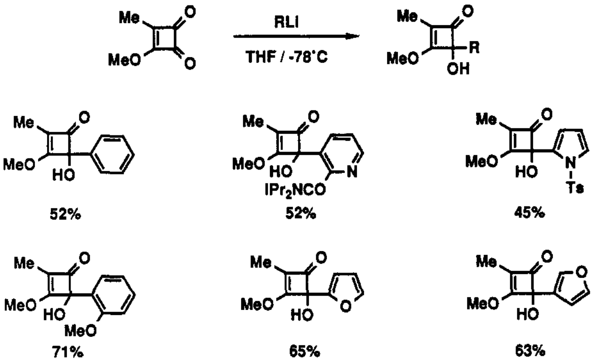
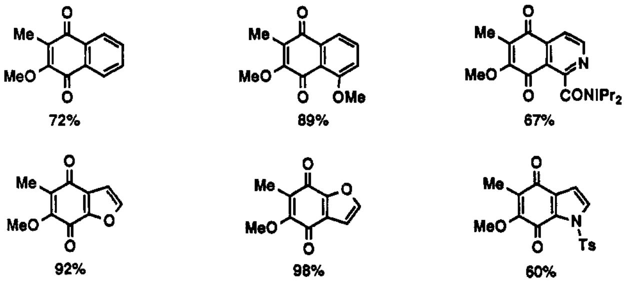
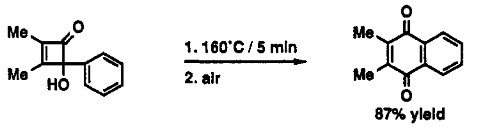


Table I. Quinones by Thermolysis of 4-Aryl(or hetero)-4-hydroxycyclobutenones



Sir: As a result of our long-standing interest in transition-metal complexes of cyclobutenediones and benzocyclobutenediones,[2] we began probing the reaction of derivatives of these very interesting organic molecules with low-valent metal species. In an attempt to prepare a new metallacycle, 4-hydroxy-4-phenyl-2,3-dimethylcyclobutenone (prepared by addition of PhLi to 3,4-dimethylcyclobutenedione in 44% yield) was heated with η^5-$CpCo(CO)_2$ at 160 °C in xylene for 5 min, when an exceptionally clean thermal transformation of the organic substrate occurred to give 2,3-dimethylnaphthohydroquinone. After exposure to air, 2,3-dimethylnaphthoquinone was isolated in 87% yield. A control reaction in the absence of η^5-$CpCo(CO)_2$ gave the same results. This unexpected reaction was particularily intriguing because thermal rearrangements of 4-vinylcyclobutenones have provided a significant synthetic route to highly substituted phenols,[3] but cyclobutenediones and benzocyclobutenediones (which can be readily prepared from simple starting materials[4]) have not been investigated in any detail as starting materials for a similar synthesis of highly functionalized quinones by thermal rearrangement of 4-hydroxy-4-vinyl(or aryl or hetero)cyclobutenones.[5]



(eq. 1)

A further investigation of the thermal reaction of 4-(aryl or heteroaryl)-4-hydroxy-2,3-disubstituted-cyclobutenones

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[1] Fellow of the Alfred P. Sloan Foundation, 1983–1987; Camille and Henry Dreyfus Teacher Scholar, 1986–1991.

[2] Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Blount, J. F. *J. Organomet. Chem.* **1980**, *202*, C73. Liebeskind, L. S.; Baysdon, S. L.; South, M. S. *J. Am. Chem. Soc.* **1980**, *102*, 7397. Baysdon, S. L.; Liebeskind, L. S. *Organometallics* **1982**, *1*, 771. South, M. S.; Liebeskind, L. S. *J. Am. Chem. Soc.* **1984**, *106*, 4181. Liebeskind, L. S.; Baysdon, S. L.; Chidambaram, R.; Goedken, V. L. *Organometallics*, in press. Liebeskind, L. S.; Leeds, J. P.; Baysdon, S. L.; Iyer, S. I. *J. Am. Chem. Soc.* **1984**, *106*, 6451. Liebeskind, L. S.; Baysdon, S. L.; South, M. S.; Iyer, S. I.; Leeds, J. P. *Tetrahedron, Symp.* **1985**, *41*, 5839. Liebeskind, L. S.; Jewell, C. F., Jr. *J. Organomet. Chem.* **1985**, *285*, 305. Jewell, C. F., Jr.; Liebeskind, L. S.; Williamson, M. *J. Am. Chem. Soc.* **1985**, *107*, 6715.

[3] Danheiser, R. L.; Gee, S. K. *J. Org. Chem.* **1984**, *49*, 1674. For earlier work on thermal rearrangements of cyclobutenones, see footnote 8 in this reference.

[4] Benzocyclobutenediones: South, M. S.; Liebeskind, L. S. *J. Org. Chem.* **1982**, *47*, 3815 and references therein. Cyclobutenediones: Liebeskind, L. S., Baysdon, S. L. *Tetrahedron Lett.* **1984**, *25*, 1747 and references therein.

[5] A novel variant of this chemistry using 4-alkynyl-2,3-dimethoxy-4-(trimethylsiloxy)cyclobutenones has been described recently by Moore: Karlsson, J. O.; Nguyen, N. V.; Foland, L. D.; Moore, H. W. *J. Am. Chem. Soc.* **1985**, *107*, 3392.

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