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OXIDATION OF ENONES TO α'-ACETOXYENONES USING MANGANESE TRIACETATE[1]

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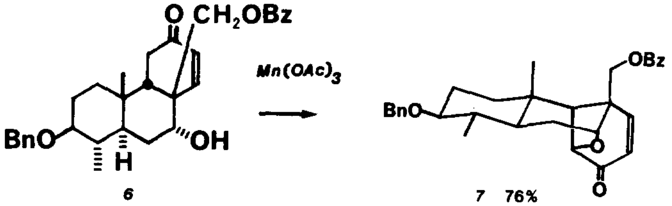
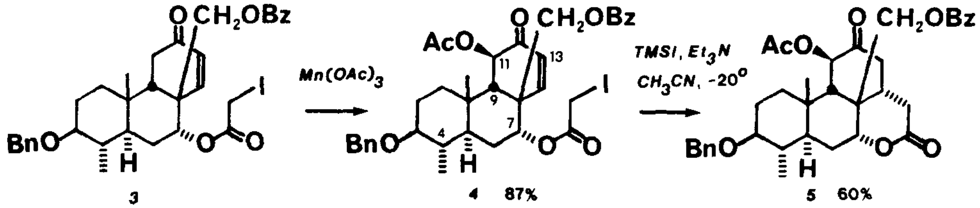
Abstract. The oxidation of α,β-unsaturated ketones with manganese (III) triacetate in benzene furnishes α'-acetoxyenones in good yields.

The regioselective α'-oxidation of enones 1 to α'-acetoxyenones 2 constitutes a valuable procedure for manipulating a common functional group. Previous efforts along these lines involve direct oxidations with lead tetraacetate,[2] mercuric acetate,[3] and manganese triacetate.[4] The modest yields reported[5] for many of these oxidations has undoubtedly detracted from the application of these materials in synthesis. In connection with synthetic work in the quassinoid area, we required a reliable procedure for the C-11 oxidation of a tricyclic intermediate[6] 3, and we found that manganese triacetate provided an efficient, general solution to this problem.

1 2

As shown in Table I, the addition of dried[7] manganese triacetate in portions to a benzene solution of various enones 1 furnishes the desired α'-acetoxyenones 2 in good yield. The process accommodates those enones possessing an α'-methylene site and zero, one, or two γ-hydrogens, but the yields are generally lower for those enones possessing an α'-methyl group (e.g., 1j) or more than two γ-hydrogens (e.g., 1a). As expected, the oxidation of enones bearing additional chiral centers produces a mixture of diastereomeric α'-acetoxyenones, and the oxidation of enones bearing proximal hydroxyl groups capable of intercepting the intermediate radical center[8] produces cyclic products such as 7. Of particular interest to us was the selective oxidation of the tricyclic enone 3 in the presence of the α-iodoester and benzyl ether functionality as well as the cyclization of the α'-acetoxyenone 4 using iodotrimethylsilane[6] (TMSI (2eq), Et$_3$N (1 eq), CH$_3$CN, -20°) to secure the tetracyclic quassinoid intermediate 5.

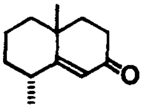
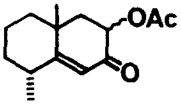
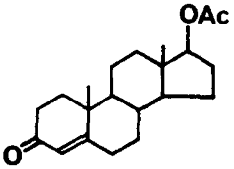
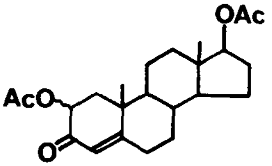
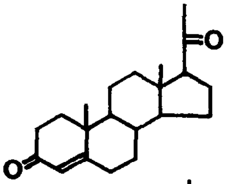
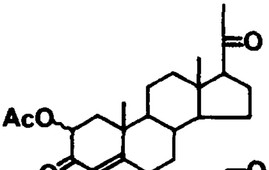
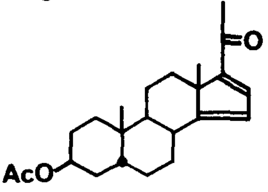
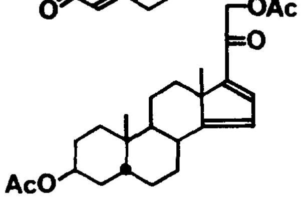




The following is a typical experimental procedure.[10] To 50 mg (0.08 mmol) of enone 3 in 1.4 mL of anhydrous benzene was added 67 mg of dried manganese acetate.[10] The brown suspension was refluxed for 1 h. An additional 47 mg of dried manganese acetate was added, and the mixture was refluxed for an additional 1.5 h. (Since manganese triacetate is a hydrate of unspecified composition, we arbitrarily use 1.5 g of $Mn(OAc)_3$ per mmol of substrate 1.) The product was cooled to room temperature, diluted with ethyl acetate, and decanted into a separatory funnel. The product was washed successively with 1 M hydrochloric acid, aqueous saturated sodium bicarbonate solution and brine, and dried over anhydrous magnesium sulfate. The product was chromatographed on one 20 cm x 20 cm preparative layer Macherey-Nagel silica gel F254 plate in 1:20 ethyl acetate-dichloromethane to afford 47 mg (87%) of 4: mp 147-148.5°C; IR (KBr) 1730, 1648 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (d, J = 5.9 Hz, 3, C-4α CH_3), 1.22 (s, 3, C-10β CH_3), 2.09 (s, 3, C-11 acetoxy CH_3), 2.59 (d, J = 5.1 Hz, 1, C-9β H), 3.69 (AB q, 2, CH_2I), 4.36-4.70 (m, 4, two overlapping AB q for CH_2Ph, CH_2OBz), 5.51 (m, 1, C-7β H), 5.59 (d, J = 5.1 Hz, 1, C-11α H), 6.34 (d, J = 10.3 Hz, 2, C-13 vinylic H), 7.06 (d, J = 11.0 Hz, 2, C-14 vinylic H), 7.2-8.0 (m, 10, aromatic H); mass spectrum (70 eV), m/e (relative intensity) 623(3), 497(9), 407(3), 127(9), 105(100).

Anal. Calcd. for $C_{35}H_{39}O_8I$: C, 58.83; H, 5.50. Found: C, 58.66; H, 5.56.

Table I. Manganese Triacetate Oxidation of Enones **1** to α'-Acetoxyenones[9] **2**.

Example	Substrate	Conditions[a]	Product (isolated yield, %)	
1a	3-methylcyclohexenone	19 h, 80°	6-acetoxy-3-methylcyclohexenone	51%
1b	4,4-dimethylcyclohexenone	19.5 h, 80°	6-acetoxy-4,4-dimethylcyclohexenone	81%
1c	5,5-dimethylcyclohexenone	24.5 h, 80°	6-acetoxy-5,5-dimethylcyclohexenone	70%
1d	4-methyl-4-n-propylcyclohexenone	27 h, 80°	6-acetoxy-4-methyl-4-n-propylcyclohexenone	71%
1e	4-methyl-4-phenylcyclohexenone	26.5 h, 80°	6-acetoxy-4-methyl-4-phenylcyclohexenone	83%
1f	spiro[5.5]undec-1-en-3-one	27 h, 80°	4-acetoxyspiro[5.5]undec-1-en-3-one	87%
1g[b]		21 h, 80°		84%
1h		25 h, 80°		83%
1i		19.5 h, 80°		48%
1j		23 h, 80°		25%

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a, oxidations were conducted in 0.1 M (initial concentration) of **1** in anhydrous benzene using 1.5 g of dried Mn(OAc)$_3$/mmole of enone **1** b, M. Voyle, K. S. Kyler, S. Arseniyadis, N. K. Dunlap, and D. S. Watt, *J. Org. Chem.*, 48, 470 (1983).

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References

1. This paper is the third in a series dealing with the synthesis of quassinoids. The second paper is reference 6 cited below.

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4. G. J. Williams and N. R. Hunter, *Can. J. Chem.*, 54, 3830 (1976).

5. The typical yields reported in the literature range from 3-42% for $Pb(OAc)_4$, 23-25% for $Hg(OAc)_2$, and 23-25% for $Mn(OAc)_3$ when recovered starting material is not taken into account. Ellis has, however, reported a considerably improved yield (78%) for isophorone using $Pb(OAc)_4$ in benzene (ref 2g).

6. M. Voyle, N. K. Dunlap, D. S. Watt, and O. P. Anderson, *J. Org. Chem.*, 48, 3242 (1983).

7. Manganese triacetate prepared according to the procedure in reference 4 was considerably less active than material dried *in vacuo* or dried over P_2O_5.

8. For mechanistic discussions involving Mn(III) oxidations, see (a) E. I. Heiba and R. M. Dessau, *J. Am. Chem. Soc.*, 93, 524 (1971); (b) E. I. Heiba and R. M. Dessau, *J. Org. Chem.*, 39, 3456 (1974); (c) G. I. Nikishin, M. G. Vinogradov, and T. M. Fedorova, *J. Chem. Soc., Chem. Commun.*, 693 (1973).

9. All products in this study had NMR and mass spectral data (high and low resolution) as well as C,H combustion analysis data in accord with assigned structures.

10. Oxidations conducted on a larger scale than this experiment were conducted in a 0.1 M benzene solution (initial concentration of **1**).

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