

Manganese-mediated Stereoselective and Chemoselective *trans*-Dichlorination of Alkenes with Tetradecyltrimethylammonium Permanganate–Trimethylchlorosilane

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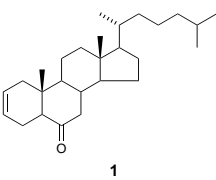
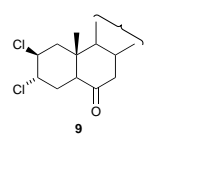
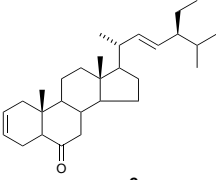
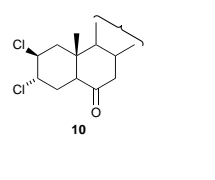
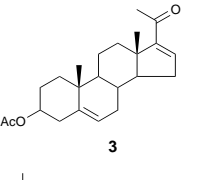
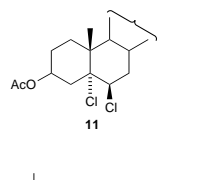
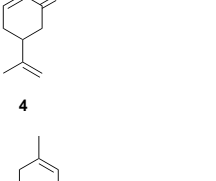
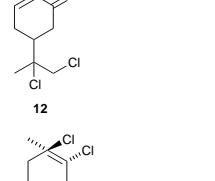
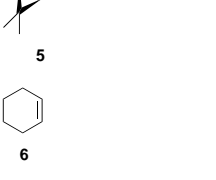
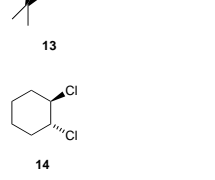
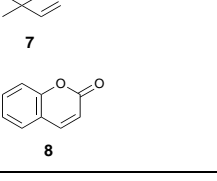
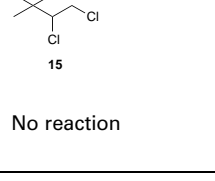
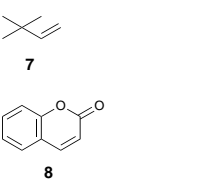
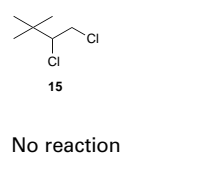
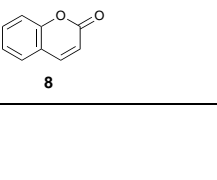
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An excellent reagent for the chemo- and stereo-selective *trans*-dichlorination of alkenes in high yield has been formulated by mixing tetradecyltrimethylammonium permanganate, a relatively stable crystalline solid, with trimethylchlorosilane in methylene dichloride.

Although not widely recognised, it is well established¹ that the formation of *vic*-dichlorides from addition of molecular chlorine to olefins has limited synthetic utility owing to the occurrence of side reactions. Moreover, reaction of gaseous chlorine with alkenes presents a potential environmental hazard and quantitative utilization of chlorine in this reaction is often hard to work out. Several other reagents add chlorine to double bonds. Sulfuryl chloride² reacts readily with most ethylenic compounds to yield saturated dichloro derivatives with evolution of sulfur dioxide. Reaction of trichloroamine³ with olefins provides a simple means for the preparation of *vic*-dichlorides. Phosphorus pentachloride,⁴ antimony pentachloride,⁵ iodobenzene dichloride,⁶ tetrabutylammonium iodotetrachloride⁷ and copper(II) chloride⁸ have been examined as chlorinating agents with good results in certain cases. *cis*-Vicinal dichlorinations of olefins by molybdenum(VI)-acetyl chloride⁹ and manganese(III) acetate–calcium chloride¹⁰ have been reported. *trans*-Vicinal dichlorinations of olefins with manganese dioxide–trimethylchlorosilane¹¹ and MnO₂–MnCl₂–acetyl chloride¹² and acetal chlorination with MnO₂–trimethylchlorosilane¹³ have been more recently documented. However non-homogeneity of these inorganic based reagents in commonly used organic solvents limits their wider synthetic applications. In order to overcome this difficulty Marko and Richardson have used^{14,15} benzyltriethylammonium permanganate and oxalyl chloride in methylene dichloride, a widely used organic solvent for the *trans*-dichlorination of alkenes. This reagent system is unstable above –35 °C. Moreover, use of benzyltriethylammonium permanganate has severe drawbacks in terms of safety due to its decomposition^{16–18} with explosive violence above 80–90 °C. This instability arises because the easily formed benzyl radical initiates a chain reaction, during drying or when the reagent is handled neat. In view of these factors it was expected that replacement of the aromatic functionality of the quaternary ammonium salt by a long-chain hydrocarbon moiety, *e.g.* tetradecyl, would give rise to a much safer quaternary permanganate salt of increased stability. We have recently prepared tetradecyltrimethylammonium permanganate (TDTAP) and demonstrated^{19a} its use as an excellent new reagent for the chemo- and stereo-selective *trans*-dibromination of alkenes. Differential thermal analysis of TDTAP has shown its decomposition to be a stepwise exothermic process which starts at 102.3 °C, with the thermogram reaching a maximum at 119.5 °C. This clearly indicates that TDTAP decomposes passively at a relatively higher temperature compared with earlier reported²⁰ quaternary permanganate salts. In fact, violet crystals of TDTAP are stable at room temperature for a few days and can be stored in a brown bottle at 0 °C for months which permits its ready access whenever required. In continuation of our earlier work towards

exploring the use of TDTAP as a reagent for important synthetic transformations,¹⁹ we report herein a highly stereo- and chemo-selective *trans*-dichlorination of alkenes with tetradecyltrimethylammonium permanganate (TDTAP) and trimethylchlorosilane (TMCS). Use of the non-hazardous

Table 1 *trans*-Dichlorination of alkenes with TDTAP–TMCS

Starting compound	Product	Yield (%)
		96
		88
		87
		62
		84
		92
		90
	No reaction	—

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and relatively stable TDTAP in combination with TMCS for *trans*-dichlorination of alkenes has not been reported earlier in the literature.

A violet-coloured solution of TDTAP in methylene dichloride at 0–3 °C changed immediately to brown on treatment with TMCS. A solution of the olefin in methylene dichloride was added to this mixture which was then stirred at 0–3 °C for 1.5 h. During this period the reaction mixture turned green. Along with the *trans*-dichlorinated products, we isolated hexamethyldisiloxane (Me₃Si–O–SiMe₃) as one of the end products in this reaction. The results are summarized in Table 1.

Our TDTAP–TMCS reagent displays high chemoselectivity as evidenced by a lack of reaction of the α,β -unsaturated double bond at C-16 of pregnenolone acetate **3**, the electron-deficient double bond of carvone **4** or with the benzylic as well as the electron-deficient double bond of coumarin **8**. In the stigmasterole derivative **2** the (22*E*)-double bond is sterically crowded by the (24*S*)-ethyl group and D-ring of the steroid, thus hindering the approach of the chlorinating species. The only product isolated in this case is the 2,3-diaxial dichloride **10** (88%).

The reaction of 16-dehydropregnenolone acetate **3** and carvone **4** in methylene dichloride with excess of chlorine gas at 0 to 3 °C for 1.5 h furnished a complex mixture of polychlorinated products. Allylic chlorination and chlorination α to the ketone along with addition of chlorine to the double bond took place in both cases. Column chromatographic purification of the polychlorinated products on silica gel using ethyl acetate–hexane (2:98) as an eluent afforded 3 β -acetoxy-5,6,16,17-tetrachloro-5 α -pregnan-20-one (0.127 g) and 3 β -acetoxy-5,6,16,17,21-pentachloro-5 α -pregnan-20-one (0.202 g) from 0.712 g of compound **3**. Both these compounds were obtained as foamy masses, which could not be crystallised. The structures of these two products were assigned from ¹H and ¹³C NMR and from elemental analysis. Further elution with the same solvent system furnished two more compounds (0.066 g and 0.096 g) which were not characterised. We failed to isolate any 5,6-dichlorinated product **11** from this reaction. In the case of carvone **4**, a mixture of polychlorinated compounds of identical polarity (41%) was isolated. IR, ¹H NMR and mass spectroscopic data suggested to be a mixture of 2,3,4,4,6,8,8,9,10-nonachloro- and 2,3,4,6,8,9,10-heptachloro-carvone. No trace of the 9,10-dichlorocarvone **12** was found in this chlorination reaction. Treatment of compounds **3** and **4** with excess of TDTAP–TMCS in methylene dichloride under identical conditions afforded the dichlorides **11** and **12**, respectively, as the only products in yields (78 and 53%) comparable with those obtained when a single equivalent of TDTAP had been employed. This excellent chemoselectivity, even with an excess of the reagent, clearly ruled out the possibility that molecular chlorine is generated in the reaction mixture and strongly suggests²¹ the formation of an oxochloro manganese intermediate as a chlorinating species in this *trans*-dichlorination reaction.

trans-Dichlorination of Alkenes: a Typical Procedure.—To a magnetically stirred violet solution of TDTAP (376 mg, 1 mmol) in methylene dichloride (10 cm³) was added trimethylchlorosilane (458 mg, 4.2 mmol) in methylene dichloride (2 cm³) at 0 °C. A brown solution resulted immediately. To this cholest-2-en-6-one²² **1** (384 mg, 1 mmol) in methylene dichloride (5 cm³) was added dropwise over 5 min and the reaction mixture was stirred at 0–3 °C for 1.5 h. During this period the brown colour of the reaction mixture changed to dark green. The mixture was then stirred with a 10% solution of sodium bisulfite (10 cm³) and was brought to room temp. and changed to colourless. From this mixture methylene

dichloride was removed under reduced pressure and the mixture was extracted with ethyl acetate (3 × 50 cm³). The ethyl acetate extracts were combined and washed with water (2 × 30 cm³), saturated brine (2 × 30 cm³) and dried over anhydrous Na₂SO₄. The solvent was evaporated under reduced pressure to afford a solid product (2*S*,3*S*)-2,3-dichlorocholestan-6-one **9** (437 mg, 96%); mp 134 °C (hexane–diethyl ether) (lit.,²³ 131 °C); [α]_D²⁸ = +34.9 (c 1.7, CHCl₃); ν_{\max} (nujol)/cm⁻¹ 1712 (C=O), 650; δ_{H} (200 MHz; CDCl₃) 0.75 (s, 3 H, 18-H₃), 0.94 (d, 6 H, *J* 7.0 Hz, 26-H₃, 27 H₃), 1.0 (d, 3 H, *J* = 7 Hz, 21-H₃), 1.12 (s, 3 H, 19-H₃), 2.9 (dd, 1 H, *J* 2.0, 12 Hz, 5-H), 4.43–4.65 (m, 2 H, 2,3-H); *m/z* 454 and 456 (M⁺), 439, 418, 403, 384, 367, 341, 247, 191, 107, 93 (100%). Compounds **10**–**15** were prepared using this general procedure.

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Techniques used: IR, ¹H NMR, MS, polarimetry, DTA

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- A manuscript consisting of EPR, UV–visible and other spectroscopic evidence for the reactants, chlorinating species and the end product is currently under preparation.