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Reactions of η^2-(2-acylaryl-C,O)tetracarbonylmanganese(I) complexes with some vinyl sulfur compounds

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Abstract

The thermally promoted reactions of some phenyl and diterpenoid η^2-(2-acylaryl-C,O)tetracarbonylmanganese(I) complexes with phenyl vinyl sulfone, methyl vinyl sulfone, or phenyl vinyl sulfoxide, have been investigated. The major products from the diterpenoid complexes arise from insertion followed by reductive demetallation; cyclopenta-annulation, when it occurs, is a minor process. Liberation of the metal-free adducts from their Mn-containing precursors requires treatment with either acid or photolysis-oxidation.

Key words: Sulfur; Vinyl; Manganese; Carbonyl

1. Introduction

Previously we [1–3] and others [4–6] have shown that indane or indene derivatives can be made from η^2-(2-acylaryl-C,O)tetracarbonylmanganese(I) complexes by reaction with an alkene or alkyne. This one-pot cyclopenta-annulation results from initial insertion of the unsaturated reagent into the aryl–Mn bond to give an alkyl–Mn or vinyl–Mn intermediate, followed by addition across the ketone (or aldehyde) carbonyl group. Ethene and monosubstituted deactivated alkenes (*e.g.* methyl propenoate) react well, the desired annulated product usually being isolated in good yield without the need for any deliberate decomplexation step to effect liberation of the metal-free organic product. (The silica gel used in chromatographic purification apparently promotes protolytic cleavage of the O–Mn bond.) Application of this chemistry to some ring-C aromatic diterpenoid complexes [1–3] was directed at developing a simple and direct route to ring-C aromatic steroidal (18-nor-androstane) analogues [7]. However, the use of methyl propenoate, for example, while operationally straightforward, affords a 17-hydroxy-16-methoxycarbonyl tetracycle in which the 16-ester group is redundant. Demethoxycarbonylation of such a system was not expected to be a straightforward procedure, and so an alternative functionalized alkene was sought. Ideally, such an alkene would allow not only insertion in high yield but also facile removal of the functional group after cyclization. A suitable potential alternative to the use of gaseous ethene appeared to be phenyl vinyl sulfone (a solid at ambient temperature), since a variety of mild procedures are available to effect reductive desulfonylation of either alkyl phenyl sulfones [8,9] or vinyl phenyl sulfones [10]. Furthermore, the substituted sulfonyl moiety can provide a locus for subsequent reaction with Grignard reagents under catalysis by either $Ni(acac)_2$ or $Fe(acac)_3$ to give sulfur-free products of *ipso* substitution. Alternatively, the β-alkyl vinyl sulfone resulting from dehydration of the initial 1-indanol derivative could be deprotonated to give a stabilized anion. Reaction with an electrophile at either the α or γ (exocyclic) carbon atoms could then provide a route to specifically functionalized indane or indene derivatives. For any of these possibilities the phenylsulfonyl substituent in the initially used alkene is central to the success of the intended subsequent reactions. The availability of such diverse chemistry, leading poten-

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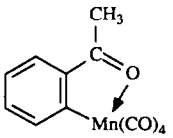
tially to a range of ring-C aromatic steroidal analogues carrying substituents at predictable sites in or on ring D, stimulated the investigations reported herein.

2. Results and discussion

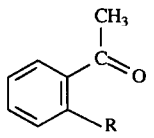
Initially η^2-(2-acetylphenyl-C,O)tetracarbonylmanganese(I) (**1**)



(**1**)

[11] was used as a model substrate. Thus, a solution of **1** and phenyl vinyl sulfone was heated to reflux in dried benzene with a slow stream of argon passing over the system. Removal of the solvent and chromatography (flash column, then PLC) of the crude material on silica gel [1] resulted in a very low recovery of product mixtures. On the premise that the poor mass balance was caused by the failure of silica gel to cleave C–Mn and/or O–Mn bonds in the organomanganese adducts, leading to an intractable polar mixture, alternative demetallation procedures were investigated. Irradiation of the crude material in acetonitrile at 350 nm, followed by exposure of the photolysate to air and addition of water [12,13] resulted in a mixture with significantly improved chromatographic behaviour. Multiple elution PLC was, however, still required to ensure good separation of the products.

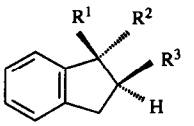
The least polar product recovered was a mixture (1:1) of *E* and *Z* 1-[2-[2-(phenylsulfonyl)ethenyl]-phenyl]ethanone (**2**)



(**2**: R = *E*/*Z* CH=CHSO$_2$Ph
3: R = CH$_2$CH$_2$SO$_2$Ph)

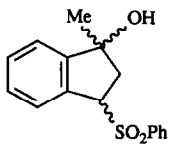
(2%) resulting from Heck-type insertion–elimination, and was followed by the saturated analogue **3** (7%).

The first of the two cyclopenta-annulated products to be eluted was assigned as the *trans* 1-indanol, (1*R**,2*S**)-2,3-dihydro-1-methyl-2-phenylsulfonyl-1*H*-inden-1-ol (**4**)



(**4**: R^1 = Me, R^2 = OH, R^3 = SO$_2$Ph
5: R^1 = OH, R^2 = Me, R^3 = SO$_2$Ph
6: R^1 = Me, R^2 = OH, R^3 = SOPh
7: R^1 = OH, R^2 = Me, R^3 = SOPh)

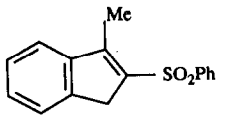
(12%), while the compound of lower R_f was assigned as the (1*S**,2*S**) diastereoisomer **5** (17%). Both **4** and **5** gave ions at $(M + NH_4)^+$ in their chemical ionization (NH_3) mass spectrum, as well as at *m/z* 288 ($M^{+\bullet}$) having the correct (accurate mass measurement) elemental composition for $C_{16}H_{16}O_3S$. Absorptions characteristic of hydroxy and sulfonyl groups were present in their IR spectra. The regiochemistry of these 1-indanols, with the bulky phenylsulfonyl substituent attached to C(2) rather than to C(3), was assigned by analogy with that of the 1-indenols isolated by Liebeskind *et al.* [4] from the reaction of **1** with some unsymmetrical alkynes. Moreover, this orientation of insertion of the unsymmetrical alkene moiety into the aryl–Mn bond is consistent with that shown unambiguously (single crystal X-ray analysis) to result from reaction of a diterpenoid η^2-(2-acetyl)Mn(CO)$_4$ complex with methyl propenoate [1]. Furthermore, the one-proton signal resulting from an alicyclic methine group in the ^{1}H NMR spectra (3.85; 3.94 ppm) would resonate further downfield in the spectrum of the regioisomer **8**,



(**8**)

in which such a methine proton is also benzylic. Therefore, the above signals were assigned to H(2) in **4** and **5** respectively. The relative stereochemistry of **4** and **5** was deduced from the expectation [1] that the ^{1}H NMR signal resulting from the 1-Me group would occur at higher field when this substituent is *vicinal* and *cis* to a pendant phenylsulfonyl group (**4**, 1.62; **5**, 1.86 ppm).

In an alternative demetallation procedure, electrophilic cleavage of C–Mn/O–Mn was promoted by treatment (without photolysis) of the crude reaction mixture with trifluoroacetic acid. This procedure yielded **3** (5%), and 3-methyl-2-(phenylsulfonyl)-1*H*-indene (**9**) (25%),

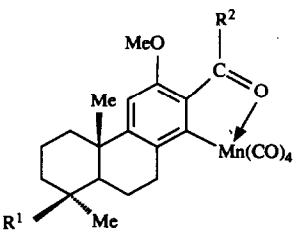


(9)

whose structure followed easily from its spectroscopic data, and which clearly arose from elimination of water from **4**/**5**.

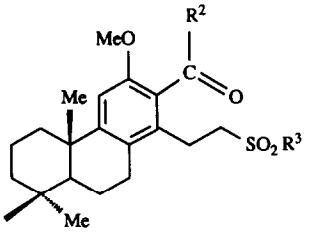
Although cyclopenta-annulation had occurred in the above reactions, the yields of the 1-indanol or 1*H*-indene derivatives were only moderate. In order to determine whether the use of a less electron-poor alkene would increase the yield from at least the initial insertion step, complex **1** was refluxed in benzene with phenyl vinyl sulfoxide. It was recognized that the use of the sulfoxide instead of the sulfone would result in the generation of a third stereogenic centre (at sulfur) in the desired cyclopenta-annulated products. However, this consequence was not considered to complicate the eventual overall aim since the phenylsulfinyl group was destined to be removed anyway. In the event, extensive chromatography of the crude mixture on silica gel afforded the phenylsulfinyl analogues **6** (7%) and **7** (12%) of **4** and **5** respectively. The NMR spectra confirmed that **6** and **7** were single compounds, but the relative configuration at sulfur is not known. Obviously, however, the isolated yields of the 1-indanols **6** and **7** derived from phenyl vinyl sulfoxide were lower than those of their analogues from phenyl vinyl sulfone. Moreover, the phenylsulfinyl group in **6** and **7** ($M^{+\bullet}$ 272 absent, EI spectrum) showed a marked tendency to oxidize to a phenylsulfonyl group ($M^{+\bullet}$-Me$^\bullet$, *m*/*z* 273) on exposure to air during multiple elution PLC. Therefore, subsequent reactions on diterpenoid complexes were carried out using a vinyl sulfone as the alkene.

Treatment of (13-acetyl-12,19-dimethoxypodocarpa-8,11,13-triene-C^{14},O^{13})tetracarbonylmanganese(I) (**10**) [14]



(**10**: R^1 = $MeOCH_2$, R^2 = Me
11: R^1 = MeO_2C, R^2 = Et)

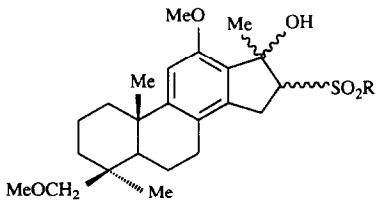
with phenyl vinyl sulfone (1.3 molar equivalent) in refluxing benzene followed directly by chromatography of the crude material on silica gel gave the insertion–protolytic cleavage product (**12**) (33%).



(**12**: R^1 = $MeOCH_2$, R^2 = Me, R^3 = Ph
13: R^1 = MeO_2C, R^2 = Et, R^3 = Ph
14: R^1 = $MeOCH_2$, R^2 = Me, R^3 = Me)

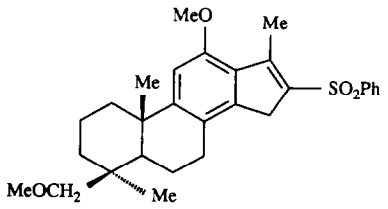
Accurate measurement of the molecular ion ($M^{+\bullet}$ 498) of **12** in the EI mass spectrum was consistent with the molecular formula $C_{29}H_{38}O_5S$. The mass spectrum also contained peaks at $M^{+\bullet}$-43 and at *m*/*z* 43; cyclopenta-annulation had not, therefore, occurred. The IR spectrum (ν_{max} 1306, 1151 cm^{-1}) confirmed the incorporation of the phenylsulfonyl group, while the NMR data was consistent with that expected for the non-cyclized C(14)-substituted adduct. Thus, the pairs of diastereotopic hydrogen atoms $CH_2CH_2SO_2Ph$ and $ArCH_2CH_2$ gave rise to two multiplets, the former centred at 3.3 ppm and partially obscured by the resonances because of $H(19)_2$ and to the 19-OMe group, and the latter centred at 2.7 ppm and hidden partially by the absorption caused by H(7eq). The ^{13}C NMR spectrum included peaks caused by these side-chain methylene carbons at 55.8 ppm and 27.2 ppm respectively. The NMR signals characteristic of the remaining diterpenoid aromatic methine group [C(11)] occurred at δ(H) 6.72 and δ(C) 106.5.

In order to increase the potential yield of **12**, and perhaps also to allow formation of the more desirable tetracyclic products, the above reaction conditions were modified by adding a solution of **10** in benzene dropwise to a solution of phenyl vinyl sulfone in refluxing benzene. This protocol was chosen in an attempt to minimize thermally promoted decomposition of **10** before it could react with the alkene. Trifluoroacetic acid was then added to the cooled crude solution in order to liberate metal-free products. The saturated non-cyclized adduct **12** was again isolated, and, gratifyingly, in higher yield (63%), but none of the desired tetracyclic products were formed. When the crude solution was subjected instead to demetallation by photolysis-oxidation, **12** was formed (23%), but now a mixture of the 17-hydroxy steroidal analogues **15**



(15: R = Ph
16: R = Me)

and the derived indene **17** was also isolated. This mixture was treated with *p*-toluenesulfonic acid in refluxing benzene to afford, after PLC, pure 12-methoxy-4β-methoxymethyl-4α,17-dimethyl-16-phenylsulfonyl-18-nor-5α-androsta-8,11,13,16-tetraene (**17**) (20%).



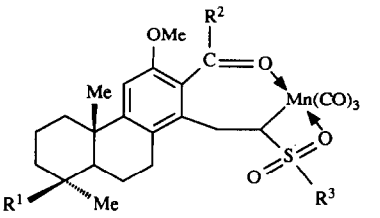
(17)

Accurate measurement of the molecular ion ($M^{+\bullet}$ 480, 23%) in the mass spectrum confirmed the molecular formula $C_{29}H_{36}O_4S$; no fragment ion corresponding to (m/z-H_2O) was detected. Signals from the vinyl carbons C(16) and C(17) were observed at 142.75 and 152.3 ppm respectively, in the ^{13}C NMR spectrum.

Reaction of phenyl vinyl sulfone in refluxing benzene with the related homologous 13-propanoyl complex **11** (synthesized in 98% yield using the standard [14] procedure), followed by PLC on silica gel, gave the non-cyclized congener **13** (25%).

In order to assess whether the phenyl substituent in the vinyl sulfone was sterically retarding the second insertion step (into the ketone carbonyl) necessary for cyclization, and thereby leading to low yields of the cyclopenta-annulated product, the 13-acetyl complex **10** was refluxed with methyl vinyl sulfone in benzene, followed by photolysis-oxidation. PLC then gave a mixture (1 : 1) of the 18-nor-androstan-17-ols **16** (11%) and the non-cyclized adduct **14** (26%). When trifluoroacetic acid was used instead of the photolytic work-up the isolated yield of **14** increased to 79%.

It is apparent, therefore, that reaction of the diterpenoid (13-acyl)tetracarbonylmanganese(I) complexes **10** and **11** with phenyl vinyl sulfone or methyl vinyl sulfone afforded mainly a saturated but non-cyclized adduct. Furthermore, these reactions were in general complicated practically by the tendency of the initial product(s) to bind manganese strongly, perhaps *via* a relatively stable *bis* η^2-$Mn(CO)_3$ intermediate such as **18**.



(18)

The cleanest, highest-yielding, and practically most straightforward work-up included the use of trifluoroacetic acid, but this procedure did not result in cyclopenta-annulation. Although use of the alternative photolysis-oxidation work-up did allow conversion of, for example, **18** into the ring-C aromatic 18-norandrostane analogues **15**, **16**, or **17** (presumably *via* dissociation of CO) these tetracycles were always accompanied by the non-cyclized saturated Heck-type adduct as the major product. Therefore, this approach to functionalized indane or indene derivatives offers no advantage over the use of ethene directly [1].

3. Experimental details

For general experimental details see Refs. 15 and 16. High field NMR spectra were measured on a Bruker AM400 instrument operating at 9.2 T. Multiplicities were determined from DEPT spectra.

3.1. Reaction of η^2-(2-acetylphenyl-C,O)tetracarbonylmanganese(I) (1) with phenyl vinyl sulfone

3.1.1. Photolytic-oxidative work-up

A solution of the yellow complex **1** (0.77 g, 2.71 mmol) in dried benzene (4 mL) was added during 30 min to a refluxing degassed solution of phenyl vinyl sulfone (0.59 g, 3.56 mmol) in benzene (16 mL). A slow sweep of argon was maintained *via* a bubbler. After refluxing for a further 3 h, TLC (hexanes : Et_2O, 4 : 1) indicated that all of **1** had been consumed. The benzene was evaporated from the deep red solution, and the brown-red oily-solid residue was dissolved in MeCN (200 mL). This deep orange solution was photolysed (Rayonet) at 350 nm while being flushed continuously with argon. After 6 h no IR carbonyl peaks resulting from Mn–C≡O could be detected. The milky brown solution (which contained a small amount of brown precipitate) was then opened to the air in laboratory light, water (4 mL) was added and stirring was continued for 1.5 h. Removal of the solvents gave a brown residue which was triturated with Et_2O and the result-

ing solution filtered through a plug of silica gel. Evaporation of the eluate gave a yellow oil (0.57 g) which was chromatographed on silica gel (Et_2O) to give a mixture containing **2**, **3**, **4** and **5**. PLC (benzene:Et_2O, 3:1) gave, in order of decreasing R_f:

(i) A mixture (1:1) of *E*- and *Z*-1-[2-[2-(phenylsulfonyl)ethenyl]phenyl]ethanone (**2**) (18 mg, 2%). ^1H NMR: 5.60 and 5.63 (two d, $J = 17.4$ Hz, *E*, H(2'), H(1')); 5.32 and 5.33 (two d, $J = 11$ Hz, *Z*, H(2'), H(1')) ppm. *m/z* 286 ($M^{+\bullet}$).

(ii) 1-[2-[2-(phenylsulfonyl)ethyl]phenyl]ethanone (**3**) (53 mg, 9%), m.p. 89–90°C. Anal. Found: [(M)$^+$, CI, NH_3] 289.0915. $C_{16}H_{17}O_3S$ calc.: M, 289.0898. IR: ν_{max} (KBr) 1677 (CO), 1295, 1159, and 1143 cm^{-1} (-SO_2-). ^1H NMR: 2.52 (COMe); 3.15–3.27 (m, 2, $ArCH_2$); 3.43–3.52 (m, 2, CH_2SO_2); 7.25–7.49 (m, ArH); 7.52–7.76 (m, 3, *meta* and *para* $PhSO_2$); 7.96 (dd, $J = 6.6$, 1.1 Hz, 2, *ortho* $PhSO_2$) ppm. ^{13}C NMR: 28.5 ($COCH_3$); 29.1 ($ArCH_2$); 57.0 (CH_2SO_2); 127.2, 130.2, 132.1, 132.4 (*C*H, Ar); 128.1 (two *C*H, *ortho* $PhSO_2$); 129.2 (two *C*H, *meta* $PhSO_2$); 133.6 (CH, *para* $PhSO_2$); 136.8, 138.3 (quaternary, Ar); 139.2 (quaternary, *ipso* $PhSO_2$) ppm.

(iii) A mixture (1.0:1.4) of the diastereoisomeric 1-indanols **4** and **5** (0.23 g, 30%). PlC (hexanes:Et_2O, 1:1, five elutions) of this mixture gave:

(a) (1*R**,2*S**)-2,3-dihydro-1-methyl-2-(phenylsulfonyl)-1*H*-inden-1-ol (**4**) (95 mg, 12%) as a clear oil. Anal. Found: $M^{+\bullet}$(CI, NH_3) 288.1066. $C_{16}H_{16}O_3S$ calc: M, 288.1058. IR: ν_{max} (film) 3489 (OH), and 1306, 1149 cm^{-1} (-SO_2-). ^1H NMR 1.62 (Me); 3.15 (dd, $J = 16.3$, 8.4 Hz, H(3) *cis* to SO_2Ph); 3.64 (dd, $J = 16.3$, 8.3 Hz, H(3) *trans* to SO_2Ph); 3.85 (t, $J = 8.4$ Hz, H(2)); 7.15–7.36 (m, 4, ArH); 7.52–7.72 (m, 3, *meta* and *para* $PhSO_2$); 8.01 (dd, $J = 7.4$, 0.9 Hz, 2, *ortho* $PhSO_2$) ppm. ^{13}C NMR: 27.7 (Me); 3.19 (C(3)); 71.3 (C(2)); 81.0 (C(1)); 122.8, 124.7, 127.9, 129.3 (*C*H, Ar); 128.8 (two *C*H, *ortho* $PhSO_2$); 129.1 (two *C*H, *meta* $PhSO_2$); 133.8 (*para* $PhSO_2$); 138.0, 139.6 (quaternary, Ar); 145.7 (*ipso* $PhSO_2$) ppm. *m/z* 288 (< 1%, M^+); 273 (100, M–Me); 146 (50, 273-$PhSO_2H$).

(b) (1*S*,2*S**)-2,3-dihydro-1-methyl-2-(phenyl-sulfonyl)-1*H*-inden-1-ol (**5**) (132 mg, 17%) as a clear oil. Anal. Found: $M^{+\bullet}$(CI, NH_3) 288.1058. $C_{16}H_{16}O_3S$ calc.: M, 288.1058. IR: ν_{max} (film) 3488 (OH), and 1310, 1147 cm^{-1} (-SO_2-). ^1H NMR: 1.86 (Me); 2.88 (dd, $J = 15.3$, 10.9 Hz, H(3) *cis* to -SO_2Ph); 3.20 (br OH); 3.34 (dd, $J = 15.3$, 10.9 Hz, H(3) *trans* to -SO_2Ph); 3.94 (dd, $J = 10.9$, 7.8 Hz, H(2)); 7.11–7.39 (m, 4, ArH); 7.53–7.72 (m, 3, *meta* and *para* $PhSO_2$); 7.98 (dd, $J = 6.6$, 1.7 Hz, 2, *ortho* $PhSO_2$) ppm. ^{13}C NMR: 26.4 (Me); 31.9 (C(3)); 74.7 (C(2)); 82.7 (C(1)); 122.4, 124.5, 127.95, 128.0 (*C*H, Ar); 128.0 (two *C*H, *ortho* $PhSO_2$); 129.4 (two *C*H, *meta* $PhSO_2$); 133.85 (*para* $PhSO_2$); 135.7; 140.0 (quaternary Ar); 146.5 (*ipso* $PhSO_2$) ppm. *m/z*(EI) 288 (< 1%, M^+); 273 (100, M–Me); 146 (50, 273-$PhSO_2H$).

3.1.2. Trifluoroacetic acid work-up

The reaction was carried out using complex **1** (0.56 mmol) and phenyl vinyl sulfone (0.56 mmol), refluxing for 3 h, then evaporating the benzene. The residue was dissolved in trifluoroacetic acid (5 mL) and the solution stirred at room temperature for 2.5 h. Chromatography afforded:

(i) 3-methyl-2-(phenylsulfonyl)-1*H*-indene (**9**) (37 mg, 25%), m.p. 148–149°C (hexanes/CH_2Cl_2). Anal. Found: C, 71.2; H, 5.5; $M^{+\bullet}$ 270.0711. $C_{16}H_{14}O_2S$ calc.: C, 71.1; H, 5.2%; M, 270.0715. IR: ν_{max} (KBr) 1304, 1152 cm^{-1} (-SO_2-). ^1H NMR: 2.60 (t, $J = 2.4$ Hz, Me); 3.67 (q, $J = 2.4$ Hz, $H(3)_2$); 7.33–7.40 (m, 2, H(5), H(6)); 7.43–7.60 (m, 5, H(4), H(7), *meta* and *para* $PhSO_2$); 7.97 (dd, $J = 6.1$ Hz, *ortho* $PhSO_2$) ppm. ^{13}C NMR: 11.5 (Me); 39.1 (C(3)); 121.6, 124.0, 127.1, 128.4 (*C*H, Ar); 127.1 (two *C*H, *ortho* $PhSO_2$); 129.2 (two *C*H, *meta* $PhSO_2$); 133.0 (*para* $PhSO_2$); 136.9 (*ipso* $PhSO_2$); 142.1, 143.6, 143.9 (C(3a)*, C(7a)*, C(2)*); 150.4 (C(1)) ppm. *m/z* 270 (10%, M^+); 129 (100, M–$PhSO_2$).

(ii) **3** (8 mg, 5%).

3.2. Reaction of η^2-(2-acetylphenyl-C,O)tetracarbonylmanganese(I) (1) with phenyl vinyl sulfoxide

A degassed solution of the complex **1** (0.45 g, 1.7 mmol) and phenyl vinyl sulfoxide (0.34 mL, 2.53 mmol) in benzene was refluxed for 2 h. Solvent removal and PLC (hexanes:EtOAc, 1:1) afforded:

(i) (1*R**,2*S**)-2,3-dihydro-1-methyl-2-(phenylsulfinyl)-1*H*-iden-1-ol (**6**) (32 mg, 7%) as an oil. ^1H NMR: 1.77 (Me); 2.59 (dd, $J = 16.8$, 8.8 Hz, H(3) *cis* to -SOPh); 3.3 (t, $J = 8.2$ Hz, H(2)); 3.3 (bs, OH); 3.70 (dd, $J = 16.8$, 7.7 Hz, H(3) *trans* to -SOPh); 7.18 (dd, $J = 5.0$, 3.5 Hz, H(7)); 7.24 (t, $J = 3.6$ Hz, H(6)*); 7.26 (t, $J = 3.6$ Hz, H(5)*); 7.36 (dd, $J = 5.2$, 3.5 Hz, H(4)); 7.45–7.60 (m, PhSO) ppm. ^{13}C NMR: 25.6 (C(3)); 27.5 (Me); 72.9 (C(2)); 81.2 (C(1)); 122.8, 125.0, 127.5, 129.0 (*C*H, Ar); 124.3, (*ortho* PhSO); 129.2 (*meta* PhSO); 130.7 (*para* PhSO); 139.7 (C(3a)); 146.1 (C(7a)); 142.6 (*ipso* PhSO) ppm. *m/z* 272 (< 1%, M^+); 147 (58, M–PhSO); 129 (100, 147–H_2O); 77 (29, Ph).

(ii) (1*S**,2*S**)-2,3-dihydro-1-methyl-2-(phenylsulfinyl)-1*H*-inden-1-ol (**7**) (56 mg, 12%) as a clear oil. Anal. Found: $M^{+\bullet}$-15, 257.0657. $C_{15}H_{13}O_2S$ calc.: M–Me, 257.0636. ^1H NMR: 1.88 (Me); 2.56 (dd, $J = 16.4$, 8.4 Hz, H(3) *cis* to -SOPh); 3.02 (dd, $J = 16.4$, 7.9 Hz, H(3) *trans* to -SOPh); 3.47 (t, $J = 8.2$ Hz, H(2)); 3.67 (bs, OH); 7.10 (d, $J = 7.0$ Hz, H(7)*); 7.24 (td, $J = 7.3$, 1.3 Hz, H(6)*); 7.28 (btd, $J = 7.1$ Hz, H(5)*); 7.40 (bd,

J = 6.8 Hz, H(4)*); 7.53–7.55 (m, *meta* and *para* PhSO); 7.80 (dd, J = 6.4, 2.8 Hz, *ortho* PhSO) ppm. ^{13}C NMR: 29.2 (Me); 31.4 (C(3)); 73.4 (C(2)); 82.2 (C(1)); 122.9, 124.6, 127.7, 129.0 (*C*H, Ar); 125.5 (*ortho* PhSO); 129.2 (*meta* PhSO); 131.6 (*para* PhSO); 139.0 (C(3a)); 143.1 (C(7a)); 146.4 (*ipso* PhSO) ppm. m/z 272 (< 1%, $M^{+\bullet}$); 257 (M–Me); 147 (100, M–PhSO); 129 (80, 147-H_2O); 77 (45).

3.3. Reaction of (13-acetyl-12,19-dimethoxypodocarpa-8,11,13-triene-C^{14},O^{13})tetracarbonylmanganese(I) (10) with phenyl vinyl sulfone

3.3.1. Silica gel work-up

A solution of the diterpenoid complex **10** (73 mg, 0.15 mmol) and phenyl vinyl sulfone (34 mg, 0.2 mmol) in dried benzene (10 mL) was refluxed for 1.5 h under a continuous flush of argon. Removal of the solvent gave an orange oil, PLC (hexanes:Et_2O, 2:1, three elutions) of which afforded 13-acetyl-12-methoxy-4β-methoxymethyl-4α-methyl-14-[2-(phenylsulfonyl)-ethyl]-podocarpa-8,11,13-triene (**12**) (24 mg, 33%) as a clear oil. Anal. Found: $M^{+\bullet}$ 498.2422. $C_{29}H_{38}O_5S$ calc.: M, 498.2440. IR: ν_{max} 1694 (CO), 1594, 1493, 1408, and 1306, 1151 cm^{-1} (-SO_2-). ^{1}H NMR: 0.95 (td, J = 13.3, 3.9 Hz, H(3ax)); 1.01 (s, H(18)$_3$); 1.15 (s, H(20)$_3$); 1.29 (bd, J = 11.5 Hz, H(5)); 1.34 (td, J = 13.0, 3.7 Hz, H(1ax)); 1.50–1.75 (m, H(2eq), H(2ax), H(6ax)); 1.83 (bd, J = 13.5 Hz, H(3eq)); 1.99 (dd, J = 13.4, 7.4 Hz, H(6eq)); 2.22 (bd, J = 12.6, H(1eq)); 2.32 (s, 13-COMe); 247 (ddd, J = 17.0, 11.4, 7.4 Hz, H(7ax)); 2.67 (dd, J = 15.9, 6.0 Hz, H(7eq)); 2.7 (m, Ar*C*H_2); 3.21 (d, J = 9.1 Hz, H(19)); 3.3 (m, CH_2SO_2); 3.30 (s, 19-OMe); 3.46 (d, J = 9.1 Hz, H(19)); 3.73 (s, 12-OMe); 6.72 (s, H(11)); 7.56 (t, J = 7.4 Hz, *meta* $PhSO_2$); 7.65 (t, J = 7.4 Hz, *para* $PhSO_2$); 7.93 (d, J = 7.4 Hz, *ortho* $PhSO_2$) ppm. ^{13}C NMR: 19.12 (C(2)); 19.16 (C(6)); 23.6 (C(7)); 25.5 (C(20)); 27.2 (Ar*C*H_2); 27.6 (C(18)); 32.1 13-COMe; 35.8 (C(3)); 38.0 (C(10)); 38.6 (C(4)); 39.4 (C(1)); 50.6 (C(5)); 55.5, 12-OMe; 55.8, *C*H_2SO_2; (59.4, 19-OMe); 75.9 (C(19)); 106.5 (C(11)); 126.0 (C(13)); 128.1 (*ortho* $PhSO_2$); 129.2 (*meta* $PhSO_2$); 129.8 (C(8)); 132.4 (C(14)); 133.6 (*para* $PhSO_2$); 139.0 (*ipso* $PhSO_2$); 153.2 (C(9)); 154.4 (C(12)); 205.6 (*C*OMe) ppm. m/z 498 (4%, M^+); 455 (3, M–MeCO); 423 (9, 455-MeOH); 357 (100, M–$PhSO_2$); 43 (31, $MeCO^+$).

3.3.2. Trifluoroacetic acid work-up

A solution of the complex **10** (80 mg, 0.16 mmol) in benzene (2 mL) was added over 30 min to a solution of phenyl vinyl sulfone (35 mg, 0.21 mmol) in refluxing benzene (8 mL). After 1.5 h trifluoroacetic acid (0.5 mL) was added to the cooled solution and refluxing was resumed for 15 min. Flash chromatography (silica gel) afforded the adduct **12** (50 mg, 63%).

3.3.3. Photolytic-oxidative work-up

A solution of the complex **10** (80 mg, 0.16 mmol) and phenyl vinyl sulfone (35 mg, 0.21 mmol) in benzene (10 mL) was refluxed over dried finely ground 4 Å molecular sieves (80 mg) for 1 h, with continuous stirring and flushing by argon. The sieves were filtered off, and the solvent removed from the filtrate. The residue was photolysed at 350 nm for 8 h in MeCN (150 mL). The solution was opened to the atmosphere in laboratory light, water (2.5 mL) was added and the mixture was stirred for 1.5 h. Removal of the solvents and PLC gave:

(i) The adduct **12** (18 mg, 23%);

(ii) A mixture of the 17-hydroxy-18-nor-androstatrienes **15** together with the derived alkene **17**. Treatment of this mixture (35 mg) with *p*-toluenesulfonic acid (3 mg) in refluxing benzene (10 mL) for 35 min gave 12-methoxy-4β-methoxymethyl-4α,17-dimethyl-16-phenylsulfonyl-18-nor-5α-androsta-8,11,13,16-tetraene (**17**) (16 mg, 20%) as an oil. Anal. Found: $M^{+\bullet}$ 480.2328. $C_{29}H_{36}O_4S$ calc.: 480.2334. IR: ν_{max} 1301, 1150 cm^{-1} (-SO_2-). ^{1}H NMR: 0.99 (td, J = 13.7, 4.1 Hz, H(3ax)); 1.04 (s, H(18)$_3$); 1.21 (s, H(20)$_3$); 1.39–1.45 (m, H(1ax), H(5)); 1.6–1.17 (m, H(2ax), H(2eq), H(6ax)); 1.87 (bd, J = 15.1 Hz, H(3eq)); 2.02–2.09 (m, H(6eq)); 2.29 (bd, J = 13.0 Hz, H(1eq)); 2.58 (ddd, J = 17.6, 11.4, 7.4, Hz, H(7ax)); 2.69–2.75 (m, H(7eq)); 2.72 (t, J = 2.5 Hz, 17-Me); 3.25 (d, J = 9.1 Hz, H(19)); 3.33 (s, 19-OMe); 3.44–3.50 (m, H(15)$_2$); 3.51 (d, J = 9.1 Hz, H(19)); 3.82 (s, 12-OMe); 6.75 (s, H(11)); 7.45–7.57 (m, *meta* and *para* $PhSO_2$); 7.91–7.96 (6 lines, J_o = 6.9 Hz, *ortho* $PhSO_2$) ppm. ^{13}C NMR: 14.8 (17-Me); 18.8 (C(2)*); 19.2 (C(6)*); 25.5 (C(20)); 27.2 (C(7)); 27.7 (C(18)); 35.9 (C(3)); 38.1 (C(10)); 38.4 (C(4)); 38.6 (C(15)); 39.3 (C(1)); 51.4 (C(5)); 55.3 (12-OMe); 59.4 (19-OMe); 75.9 (C(19)); 106.0 (C(11)); 123.2 (C(13)); 126.9 (*ortho* $PhSO_2$); 128.8 (C(8)); 129.1 (*meta* $PhSO_2$); 132.7 (*para* $PhSO_2$); 133.9 (C(14)); 142.75 C(16)); 143.6 (*ipso* $PhSO_2$); 152.3 (C(17)); 152.4 (C(9)); 155.1 (C(12)) ppm. m/z 480 (23%, M^+); 339 (100, M–$PhSO_2$).

3.4. Tetracarbonyl(methyl 12-methoxy-13-propanoyl-podocarpa-8,11,13-trien-19-oate-C^{14},O^{13})-manganese(I) (11)

Methyl 12-methoxy-13-propanoylpodocarpa-8,11,13-trien-19-oate (105 mg, 0.29 mmol) was refluxed in heptane (13 mL) for 5 min to effect dissolution and the solution was degassed by purging with argon. A solution of $PhCH_2Mn(CO)_5$ (0.14 g, 0.49 mmol, 1.7 molar equivalent, optimum) in heptane was added to the refluxing solution during 1.2 h. Work-up and flash

chromatography (silica gel, hexanes:Et_2O, 1:1) afforded tetracarbonyl(methyl 12-methoxy-13-propanoylpodocarp-8,11,13-trien-19-oate-C^{14},O^{13})manganese-(I) (**11**) (151 mg, 98%) as a yellow oil. Anal. Found: 524.1223. $C_{26}H_{29}MnO_8$ calc.: 524.1234. IR: ν_{max} 2073, 1970, 1925 (Mn–C≡O), 1580, 1548 cm^{-1} (COMe). ^1H NMR: 1.04–1.09 (m, H(3ax)); 1.12 (t, $J = 7$ Hz, CH_2CH_3); 1.14 (s, $H(20)_3$); 1.32 (s, $H(18)_3$); 1.44 (td, $J = 13.0$, 3.6 Hz, H(1ax)); 1.56 (bd, $J = 12.3$ Hz, H(5)); 1.67 (bd, $J = 13.7$ Hz, H(2eq)); 1.97 (qd, $J = 12.9$, 5.3 Hz, H(6ax)); 2.06 (qt, $J = 13.9$, 4.0 Hz, H(2ax)); 2.22 (bd, $J = 12.7$ Hz, H(1eq)); 2.30 (m, H(6eq)); 2.86 (ddd, $J = 16.4$, 12.5, 6.3 Hz, H(7ax)); 3.02 (bdd, H(7eq)); 3.05 (q, $J = 7$ Hz, CH_2CH_3); 3.68 (s, 19-OMe); 3.86 (s, 12-OMe); 6.57 (s, H(11)) ppm. ^{13}C NMR: 8.7 (CH_2CH_3); 20.1 (C(2)); 22.35 (C(6)); 22.41 (C(20)); 28.4 (C(18)); 36.8 (CH_2CH_3); 37.4 (C(3)); 38.8 (C(7)); 39.9 (C(1), C(10)); 44.0 (C(4)); 51.2 (19-OMe); 51.8 (C(5)); 54.7 (12-OMe); 104.9 (C(11)); 131.4 (C(13)); 138.8 (C(8)); 155.0 (C(9)); 160.3 (C(12)); 178.0 (C(19)); 197.5 (C(14)); 218.6 (13-COEt); 212.1, 212.4, 215.0, 221.4 ($Mn(CO)_4$) ppm. m/z 524 (3%, M^+); 412 (8, M-4CO); 358, 18, M–$Mn(CO)_4$ + H); 329 (100, 358-Et).

3.5. Methyl 12-methoxy-14-[2-(phenylsulfonyl)ethyl]-13-propanoylpodocarpa-8,11,13-trien-19-oate (13)

A solution of the complex **11** (75 mg, 0.14 mmol) and phenyl vinyl sulfone was refluxed for 4 h in benzene (10 mL) as above. Removal of the solvent and PLC (hexanes:Et_2O, 4:1) gave methyl 12-methoxy-14-[2-(phenylsulfonyl)ethyl]-13-propanoylpodocarpa-8,11,-13-trien-19-oate (**13**) (19 mg, 25%) as a clear oil. Anal. Found: $M^{+\bullet}$ 526.2388. $C_{30}H_{38}O_6S$ calc.: 526.2389. IR: ν_{max} 1690 (COMe), and 1310, 1148 cm^{-1} (-SO_2-). ^1H NMR: 0.96 (t, $J = 7.3$ Hz, CH_2CH_3); 1.02 (s, $H(20)_3$); 1.05 (td, $J = 13.5$, 4.2 Hz, H(3ax)); 1.27 (s, $H(18)_3$); 1.33 (td, $J = 12.9$, 4.1 Hz, H(1ax)); 1.44 (bd, $J = 11.6$ Hz, H(5)); 1.62 (bd, $J = 14.0$ Hz, H(2eq)); 1.88 (qt, $J = 13.0$, 5.1 Hz, H(6ax)); 1.99 (qt, $J = 14.0$, 4.0 Hz, H(2ax)); 2.16–2.30 (m, H(1eq), H(3eq), H(6eq)); 2.48 (ddd, $J = 16.6$, 12.9, 6.2 Hz, H(7ax)); 2.55–2.63 (m, CH_2CH_3); 2.60–2.70 (m, $CH_2CH_2SO_2Ph$); 2.75 (dd, $J = 16.5$, 4.3 Hz, H(7eq)); 3.25 (ddd, $J = 14.7$, 9.9, 6.2 Hz, 1, $CH_2CH_2SO_2Ph$); 3.37 (ddd, $J = 14.0$, 10.5, 6.7 Hz, 1, $CH_2CH_2SO_2Ph$); 3.66 (s, 4-CO_2Me); 3.72 (s, 12-OMe); 6.72 (s, H(11)); 7.58 (t, $J = 7.4$ Hz, *meta* $PhSO_2$); 7.66 (t, $J = 7.4$ Hz, *para* $PhSO_2$); 7.96 (d, $J = 7.4$ Hz, *ortho* $PhSO_2$) ppm. ^{13}C NMR: 7.7 (CH_2CH_3); 19.9 (C(2)); 20.7 (C(6)); 22.7 (C(20)); 23.8 (CH_2CH_3); 28.1 (C(7)); 28.4 (C(18)); 37.3 (C(3)*); 37.8* ($CH_2CH_2SO_2Ph$); 39.2 (C(10)); 39.8 (C(1)); 43.9 (C(4)); 51.3 (19-OMe); 55.8 ($CH_2CH_2SO_2Ph$); 107.3 (C(11)); 126.4 (C(13)); 128.1 (*ortho* $PhSO_2$); 129.2 (*meta* $PhSO_2$); 130.1 (C(8)); 132.3 (C(14)); 133.6 (*para* $PhSO_2$); 138.8 (*ipso* $PhSO_2$); 151.0 (C(9)); 154.1 (C(12)); 177.7 (C(19)); 208.8 (COEt) ppm. m/z 526 (6%, M^+); 497 (24, M–Et); 385 (100, M–$PhSO_2$); 57 (23, $^+$COEt).

3.6. Reaction of (13-acetyl-12,19-dimethoxypodocarpa-8,11,13-triene-C^{14},O^{13})tetracarbonylmanganese(I) (10) with methyl vinyl sulfone

3.6.1. Photolytic-oxidative work-up

The complex **10** (0.13 g, 0.26 mmol) was refluxed with methyl vinyl sulfone (73 mg, 0.69 mmol) in benzene (10 mL) for 45 min. Photolysis (5.5 h)-oxidation as before followed by flash chromatography (hexanes:Et_2O, 1:1) and then PLC (hexanes:Et_2O, two elutions) afforded:

(i) A mixture (13 mg, 11%) of the diastereoisomers of 12-methoxy-4β-methoxy-methyl-4α,17ζ-dimethyl-16ζ-methanesulfonyl-18-nor-5α-androsta-11,13,16-tetriene (**16**). Anal. Found: $M^{+\bullet}$ 436.2272. $C_{24}H_{36}O_5S$ calc.: 436.2283.

(ii) 13-acetyl-12-methoxy-4β-methoxymethyl-4α-methyl-14-[2-(methanesulfonyl)ethyl]podocarpa-8,11,13-triene (**14**) (32 mg, 26%) as a clear oil. Anal. Found: $M^{+\bullet}$ 436.2276. $C_{24}H_{36}O_5S$ calc.: M, 436.2283. IR: ν_{max} 1691 (COMe), 1593, 1567, and 1307, 1136 cm^{-1} (-SO_2-). ^1H NMR: 1.01 (m, H(3ax)); 1.05 (s, $H(18)_3$); 1.22 (s, $H(20)_3$); 1.39 (m, H(1ax), H(5)); 1.57–1.76 (m, H(2ax), H(2eq), H(6ax)); 1.88 (d, $J = 12.7$ Hz, H(3eq)); 2.09 (dd, $J = 12.7$ Hz, H(3eq)); 2.09 (dd, $J = 11.9$, 7 Hz, H(6eq)); 2.29 (d, $J = 13.3$ Hz, H(1eq)); 2.51 (s, COMe); 2.67 (m, H(7ax)); 2.86 (m, H(7eq), $CH_2CH_2SO_2$); 2.96 (s, SO_2Me); 3.21 (m, H(19), $CH_2CH_2SO_2$); 3.39 (s, 19-OMe); 3.51 (d, $J = 8.9$ Hz; H(19)); 3.82 (s, 12-OMe); 6.81 (s, H(11)) ppm. ^{13}C NMR: 19.05, 19.1 (C(2)*, C(6)*); 23.9 (C(7)); 25.5 (C(20)); 27.4 ($ArCH_2$); 27.55 (C(18)); 32.5 ($COCH_3$); 35.7 (C(3)); 37.9 (C(10)); 38.6 (C(4)); 39.3 (C(1)); 40.4 (SO_2CH_3); 50.5 (C(5)); 54.65 (CH_2SO_2); 55.4 (12-OMe); 59.35 (19-OMe); 75.8 (C(19)); 106.6 (C(11)); 126.05 (C(13)); 129.25 (C(8)); 133.0 (C(14)); 153.6 (C(9)); 154.8 (C(12)); 206.0 (COMe) ppm.

Repetition of this reaction, but using only 1.2 molar equivalent of methyl vinyl sulfone and then photolysis (10 h)-oxidation gave **16** (7%) and **14** (14%).

3.6.2. Trifluoroacetic acid work-up

A solution of the complex **10** (0.1 g, 0.2 mmol) in benzene (10 mL) was added during 30 min to a solution of methyl vinyl sulfone (29 mg, 0.27 mmol) in benzene (8 mL). After a further 1.5 h trifluoroacetic acid (0.5 mL) was added and the deep orange solution was refluxed for 15 min. Removal of the solvents and

flash chromatography (silica gel, hexanes: Et_2O, 1:1) gave **14** (69 mg, 79%).

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