JOURNAL OF LABELLED COMPOUNDS AND RADIOPHARMACEUTICALS
J Label Compd Radiopharm 2005; **48**: 337–352.
Published online in Wiley InterScience (www.interscience.wiley.com). DOI: 10.1002/jlcr.928

Research Article

Investigations into the *C*-deuteriation of enol acetates derived from aryl alkyl ketones

Svitlana Buksha, Gregory S. Coumbarides, Marco Dingjan, Jason Eames*, Michael J. Suggate and Neluka Weerasooriya
Department of Chemistry, Queen Mary, University of London, Mile End Road, London E1 4NS, UK

Summary

Results are reported on the regioselective *C*-deuteriation of a series of enol acetates (derived from the aryl alkyl ketones) using molecular deuterium as the D-source and palladium-on-barium sulphate as the mediator. The results presented highlight potential problems associated with the deuteriation of enol acetates. Copyright © 2005 John Wiley & Sons, Ltd.

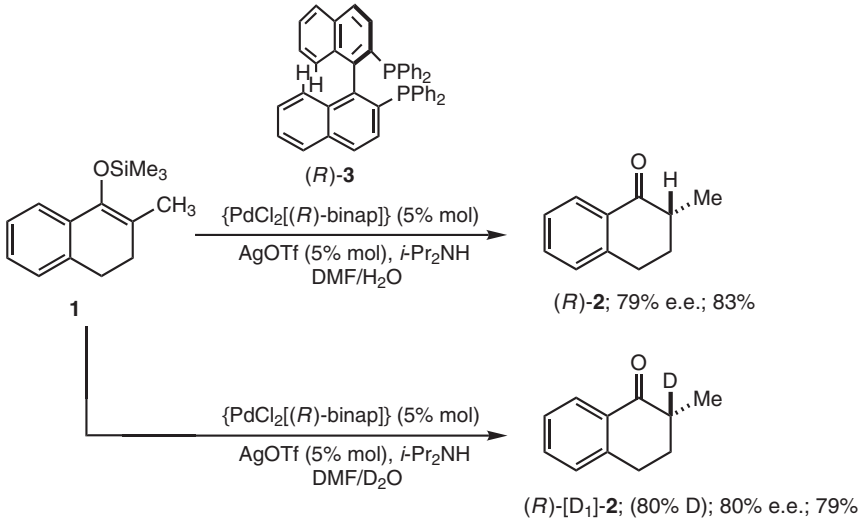
Key Words: deuteriation; deuterium; enol acetates; hydrogenation; palladium and reduction

Introduction

The use of molecular deuterium as a source of deuterium for selective metal-mediated deuteriation is very well documented.[1] These processes have been shown to be predictable giving good to excellent levels of deuterium incorporation.[2] Metal-mediated reduction of symmetrical and non-symmetrical carbon–carbon double bonds using molecular deuterium as the D-source is well known.[3] However, for activated enol equivalents,[4] such as enol acetates and silyl enol ethers, these processes are much less documented. Nakai has reported the enantioselective protonation and deuteriation of the silyl enol ether **1** using a chiral palladium (II) catalyst, (*R*)-**3**, to give access to the enantiomerically enriched 2-methyltetralones (*R*)-**2** and (*R*)-[D_1]-**2**, respectively (Scheme 1).[5] However, the associated level of deuterium incorporation at the *C*(2) position of 2-methyltetralone (*R*)-[D_1]-**2** was less than that expected for the level of enantiomeric excess. This evidently indicated that some background hydrogen atom transfer was partially responsible for lowering the

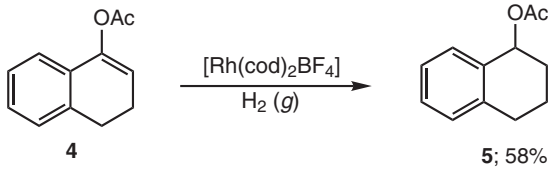
*Correspondence to: J. Eames, Department of Chemistry, Queen Mary, University of London, Mile End Road, London E1 4NS, UK. E-mail: j.eames@qmul.ac.uk

Received 9 October 2004
Revised 8 December 2004
Accepted 15 December 2004



Scheme 1.

level of deuterium incorporation and potential enantiomeric excess. By comparison, hydrogenation of the related enol acetate **4** (derived from tetralone) using an achiral rhodium (I) catalyst has been shown to give the reduced acetate **5** in good yield without loss of the acetate motif (Scheme 2).[6] This reduction is clearly an alternative process to ketone formation.

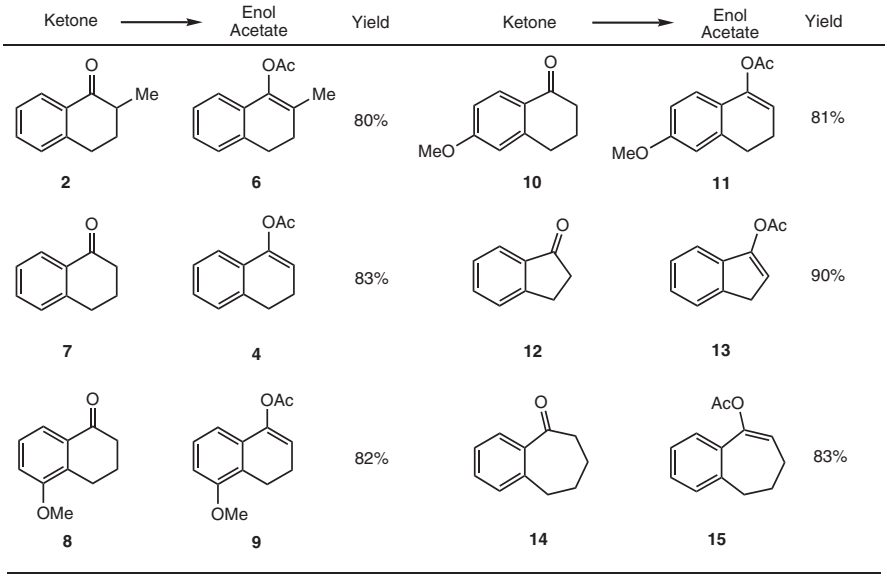


Scheme 2.

We now wish to report our study into the regioselective deuteriation of enol acetates derived from aryl alkyl ketones. We comment on factors such as the acceptable structural nature and substitution pattern for efficient deuteriation, and discuss the role they play towards regioselective *C*-deuteriation.

Results and discussion

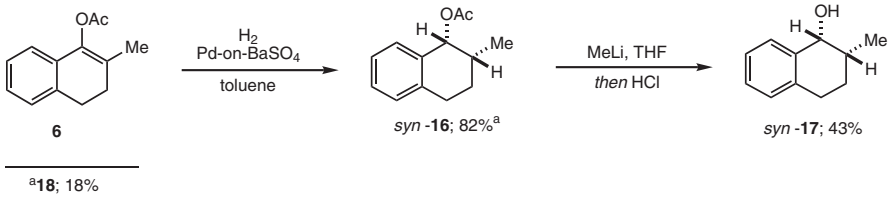
For this study, we were required to synthesize a series of related substituted enol acetates **4**, **6**, **9**, **11**, **13** and **15** (Scheme 3). These enol derivatives were synthesized from the parent phenyl ketones **2**, **7**, **8**, **10**, **12** and **14**, either by refluxing a solution of isopropenyl acetate[7] in the presence of a catalytic



Scheme 3.

amount of *p*-TsOH or by addition of perchloric acid to a stirred solution of acetic anhydride in carbon tetrachloride[8] to give the required enol acetates **4**, **6**, **9**, **11**, **13** and **15**, respectively, in good yield (Scheme 3).[9]

We initially investigated the hydrogenation of enol acetate **6** in an attempt to probe the stereochemical outcome of this reduction (Scheme 4). To prevent further reduction of the potential product (e.g. *syn*-**16**), we chose to use toluene as our reaction solvent and palladium-on-barium sulphate[10,†] as our mediator due to its low reactivity. Addition of the enol acetate **6** to a stirred solution of Pd-on-$BaSO_4$ (1–2 mol%) in toluene, under a hydrogen atmosphere, gave, after 48 h, the required *syn*-acetate **16** in good yield (Scheme 4). The stereochemistry of this adduct was confirmed[‡] by simple reduction of 2-methyltetralone **2** with sodium borohydride[11] to give the alcohol *anti*-**17**



[a]**18**; 18%

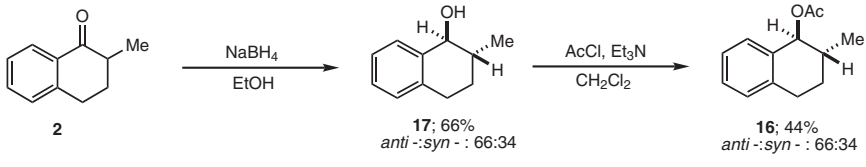
Scheme 4.

[†]This catalyst is commercially available from Aldrich (5% palladium-on-barium sulphate unreduced).
[‡]The relative stereochemistry has been determined by a 400 MHz NOESY spectrum.

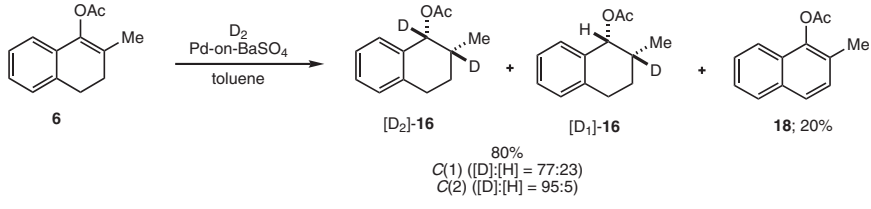
as the major diastereoisomer, followed by acetylation to give the required *anti*-acetate **16** (Scheme 5).

With this information in hand, we next chose to investigate the deuteriation of enol acetate **6** using our standard reduction protocol; addition of the enol acetate **6** to a stirred solution of Pd-on-$BaSO_4$ in toluene under a deuterium atmosphere gave the deuteriated *syn*-acetate [D_2]-**16** in good yield (Scheme 6). However, somewhat surprisingly, the levels and position of deuterium incorporation were found to be lower than initially anticipated. A higher level of deuterium incorporation had occurred at the more nucleophilic carbon, *C*(2), of the enol acetate **6** than the *C*(1) position. This was evident from the ^{1}H NMR spectrum of *syn*-[D_2]-**16** by the presence of the unlabelled *C*(1)H proton at 6.01 ppm (in [D_1]-**16**) and a singlet for the corresponding methyl group at 1.03 ppm (in [D_1]-**16**/[D_2]-**16**) (Scheme 6). In an attempt to get a better understanding of these processes, we re-investigated these reductions, and found the presence of a byproduct, naphthoxy acetate **18**, which was formed in approximately 20% yield. This byproduct was evidently derived from dehydrogenation of the parent enol acetate **6**. The loss and potential hydrogen transfer during this deuteriation process is clearly undesirable due to potential hydrogenation lowering the overall level of D-incorporation. To ensure that no background hydrogen transfer had occurred from the reaction solvent (toluene), we additionally performed the reaction in [D_8]-toluene which gave the acetate [D_2]-**16** with identical levels of hydrogen incorporation at both *C*(1) and *C*(2) positions.

We next probed whether the structural nature of the tetralone framework was responsible for the relative position and level of deuterium incorporation. Under our standard hydrogenation and deuteriation conditions, we screened a



Scheme 5.

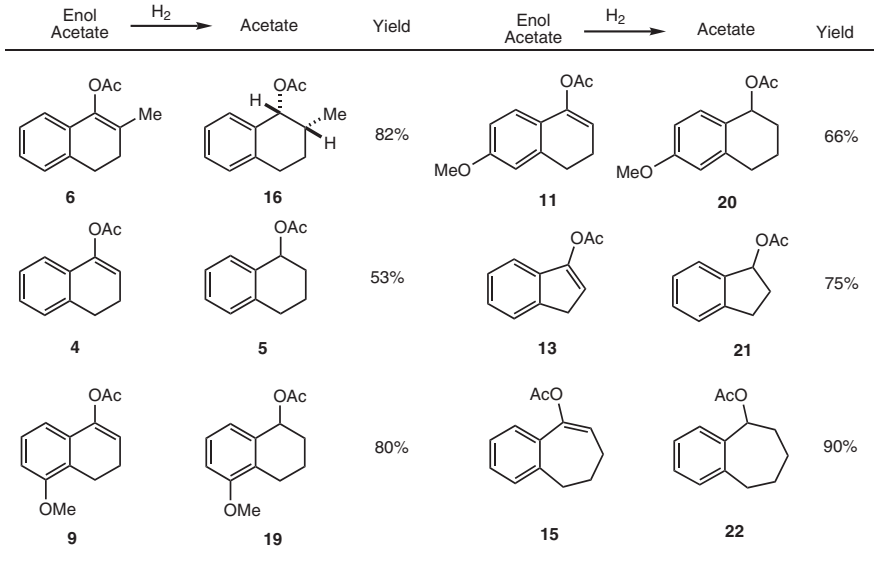


Scheme 6.

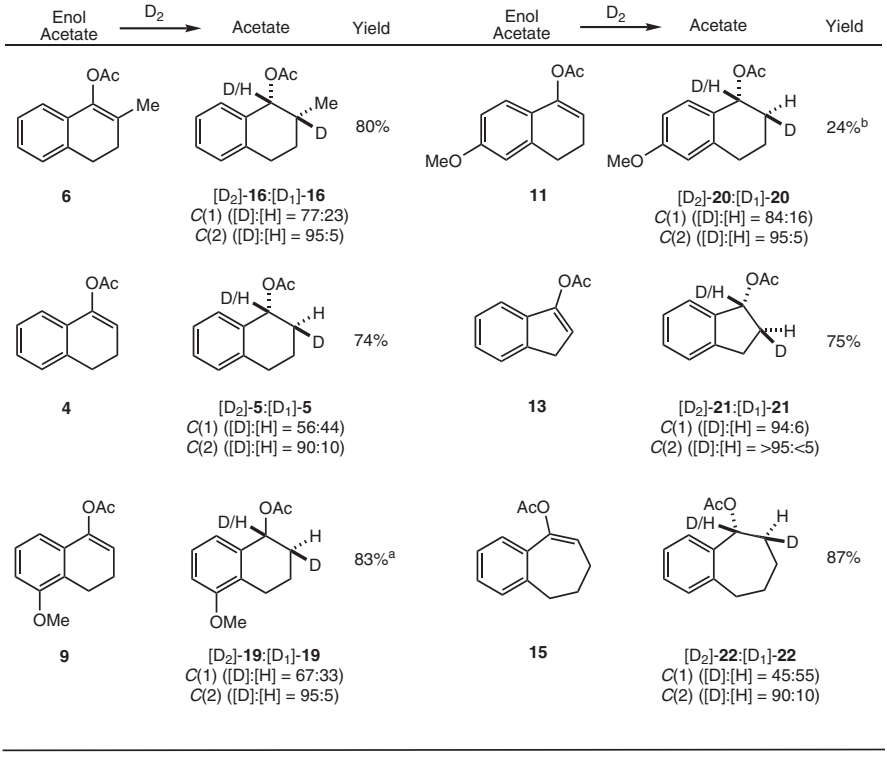
related series of enol acetates **4**, **9** and **11**, and found that these behaved similarly to the enol acetate **6** leading to the partially deuterium labelled acetates [D_2]-**5**, [D_2]-**19** and [D_2]-**20** (Schemes 7 and 8). The relative position and level of deuterium incorporation were characteristically higher at the more nucleophilic *C*(2) position than the neighbouring *C*(1) position (Scheme 8).

We next turned our attention to screening two related enol acetates **13** and **15** (derived from indanone **12** and benzosuberone **14**-see scheme 3) to examine whether the ring size of the cycloalkyl was responsible for this partial deuteriation (Schemes 7 and 8). Deuteriation of these enol acetates **13** and **15** under our standard conditions gave the partially deuteriated acetates [D_2]-**21** and [D_2]-**22** in good yield (Scheme 8). It appears that the indenyl skeleton in **13** promoted higher levels of D-incorporation at the *C*(1) position than both the tetralenyl and benzocycloheptenyl skeletons within the enol acetates **4** and **15**, respectively (Scheme 8). As expected, the levels of deuterium incorporation at the *C*(2) position were higher than those at the *C*(1) position.

In conclusion, we have shown that regioselective *C*-deuteriation of an enol acetate (e.g. **6**) can occur efficiently to give the corresponding acetate (e.g. *syn*-[D_2]-**16**) in good yield. The position and levels of deuterium incorporation were found to be dependent on the structural nature of the enol acetate precursor used; an indenyl acetate **13** gave higher levels of deuterium incorporation than related enol acetates tetralenylacetate **4** and benzocycloheptenylacetate **15**. For all the cases studied so far, it appears that deuterium



Scheme 7.



[a] **9**; 10%; [b] **11**; 60%.

Scheme 8.

incorporation was more positionally selective at the *C*(2) position of an enol acetate than at the corresponding *C*(1) position. We have yet to establish the exact nature of this mechanism for this apparent regioselective *C*-deuteriation process; however, progress towards this is currently under investigation in our laboratory.

Experimental

All solvents were distilled before use. Tetrahydrofuran (THF) and ether were freshly distilled from sodium wire. Benzophenone was used as the indicator for THF. All reactions were carried out under nitrogen using oven-dried glassware. Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography (TLC) was carried out on commercially available pre-coated plates (Merck Kieselgel 60F254 silica). Palladium-on-barium sulphate (5% unreduced) was purchased from Aldrich and used accordingly. Proton and carbon NMR spectra were recorded on a Bruker 270 and 400 MHz Fourier transform spectrometer using an internal deuterium lock. Chemical shifts are quoted in parts per million

downfield from tetramethylsilane. Carbon NMR spectra were recorded with broad proton decoupling. Infrared spectra were recorded on a Shimadzu 8300 FTIR instrument and mass spectra were recorded on a Kratos 50MSTC spectrometer using a DS503 data system for high-resolution analysis. The levels and positions of D-incorporation were determined by a combination of proton and carbon NMR spectroscopy.

3,4-Dihydro-naphthalen-1-yl acetate **4**

Tetralone **7** (0.65 g, 4.46 mmol) and *p*-toluenesulphonic acid (0.10 g, 0.58 mmol) were added to isopropenylacetate (9.09 g, 10.0 ml, 90.9 mmol). The resulting mixture was heated at 110°C for 12 h. The solution was cooled to room temperature, and extracted into ether (2 × 50 ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1) to give the enol acetate **4** (0.69 g, 83%) as a white crystalline solid; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.42; ν_{max}(film)/cm^{-1} 1758 (C═O); δ_H (270 MHz, $CDCl_3$) 7.15–7.10 (3 H, m, 3 × CH; Ar), 7.07–7.00 (1 H, m, CH; Ar), 5.70 (1 H, t, $J = 4.7$, CH), 2.90 (2 H, t, $J = 8.4$, CH_2), 2.40–2.43 (2 H, m, CH_2) and 2.25 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 169.3, 145.6, 136.3, 130.2, 127.8, 127.5, 126.3, 120.7, 115.1, 27.4, 22.0 and 20.5 (Found M^+ 188.2262, $C_{12}H_{12}O_2$, requires M, 188.2267).

1,2,3,4-Tetrahydro-naphthalen-1-yl acetate **5**

Hydrogen gas (250 ml) was gradually added to a stirred solution of 3,4-dihydronaphthalen-1-yl-acetate **4** (0.5 g, 2.7 mmol), toluene (3 ml) and Pd-on-$BaSO_4$ (0.1 g, 5% on $BaSO_4$ unreduced), and the resulting solution was stirred for 48 h. Ethyl acetate (5 ml) was added, and the mixture was filtered and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1) to give acetate **5** (0.27 g, 53%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.4; ν_{max}(film)/cm^{-1} 1730 (C═O); δ_H (270 MHz, $CDCl_3$) 7.52–7.05 (4 H, m, 4 × CH; Ar), 5.99 (1 H, br t, $J = 4.4$, CHOAc), 2.98–2.60 (2 H, m, CH_2), 2.01 (3 H, s, CH_3) and 2.00 (4 H, m, 2 × CH_2); δ_C (67 MHz, $CDCl_4$) 171.0 (C═O), 138.3 (*i*-C; Ar), 134.9 (*i*-C; Ar), 129.8, 129.4, 128.4 and 126.4 (4 × CH; Ar), 77.4 (CH–O), 29.4 (CH_2), 29.3 (CH_3), 21.8 (CH_3) and 19.2 (CH_2) (Found $(M + NH_4)^+$ 208.1329, $C_{12}H_{18}NO_2$, requires M, 208.1332); (*m*/*z*) 148.2 (100%, M−Ac + H).

*1,2-Dideutero-1,2,3,4-tetrahydro-naphthalen-1-yl acetate [D_2]-***5**

Under the same conditions as acetate **5**, 3,4-dihydronaphthalen-1-yl-acetate **4** (0.2 g, 1.1 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (43 mg, 5% on $BaSO_4$

unreduced) and deuterium gas (250 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), the acetate [D_2]-**5** (0.16 g, 74%) as a colourless oil; ν_{max}(film)/cm^{-1} 1730 (C═O); R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.40; δ_H (270 MHz, $CDCl_3$) 7.52–7.05 (4 H, m, 4 × CH; Ar), 5.99 (1 H, br d, J = 5.1, CHOAc),[§] 2.98–2.60 (2 H, m, CH_2), 2.01 (3 H, s, CH_3) and 2.00 (4 H, m, 2 × CH_2); δ_C (67 MHz, $CDCl_3$) 170.8 (C═O), 138.0 and 134.6 (2 × *i*-C; Ar), 129.5, 129.1, 128.1 and 126.1 (4 × CH; Ar), 69.8 (1 C, t, $^1J_{CD}$ = 22 Hz; CD–O), 29.0 (CH_2), 28.7 (1 C, t, $^1J_{CD}$ = 19 Hz at 100 MHz), 21.5 (CH_3) and 18.8 (CH_2). The isotopic shift at *C*(1) (69.1 ppm) was 0.36 ppm (24.1 Hz) and *C*(2) (28.7 ppm) was 0.23 ppm (15.4 Hz) (Found M_{D0} + NH_4^+ 208.1318, $C_{12}H_{18}NO_2$, requires M, 208.1317); (*m*/*z*) 210.1 (40%, M_{D2} + NH_4^+), 209.1 (10, M_{D1} + NH_4^+), 208.1 (3, M_{D0} + NH_4^+), 151.1 (50, M_{D2} + H − Ac + H), 150.1 (100, M_{D1} + H − Ac + H) and 149.1 (40, M_{D0} + H − Ac + H).

3,4-Dihydro-2-methyl-naphthalenyl acetate **6**

2-Methyltetralone **2** (0.51 g, 3.2 mmol) was added to a conical flask containing acetic anhydride (0.47 g, 0.43 ml, 4.6 mmol) and carbon tetrachloride (10 ml). Perchloric acid (2 drops) was slowly added, and the flask was left to stand for 10 h. The reaction mixture was then poured into a cooled solution of saturated aqueous sodium hydrogen carbonate (50 ml) and light petroleum (b.p. 40–60°C)–ether (50 ml). The resulting solution was stirred for 30 min and solid sodium hydrogen carbonate was added until the pH had reached 7. The organic layer was separated, and the aqueous layer was further extracted with light petroleum (b.p. 40–60°C)–ether (2 × 50 ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1) to give the enol acetate **6** (0.51 g, 80%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.32; ν_{max}(film)/cm^{-1} 1716 (C═O); δ_H (270 MHz, $CDCl_3$) 7.18–7.08 (3 H, m, 3 × CH; Ar), 7.00 (1 H, d, J = 7.5, CH; Ar) 2.85 (2 H, t, J = 7.8, CH_2), 2.36 (2 H, t, J = 7.8, CH_2), 2.32 (3 H, s, CH_3C═O) and 1.75 (3 H, s, CH_3CH); δ_C (100 MHz, $CDCl_3$) 168.8, 140.1, 135.2, 131.0, 127.3, 126.9, 126.4, 124.1, 120.1, 28.9, 27.5, 20.5 and 16.8 (Found MH^+ 202.2420, $C_{13}H_{15}O_2$, requires MH, 202.2425).

5-Methoxy-3,4-dihydro-naphthalenyl acetate **9**

5-Methoxytetralone **8** (1.0 g, 5.7 mmol) was added dropwise to a stirred solution of LDA [formed by addition of *n*-BuLi (2.5 ml, 2.5 M in

[§]Due to unlabelled position.

hexane, 6.2 mmol) to diisopropylamine (0.57 g, 0.76 ml, 5.7 mmol)] in THF (10 ml) at −78°C. The resulting solution was stirred for 20 min. Acetyl chloride (0.89 g, 0.80 ml, 11.4 mmol) was added dropwise and the resulting solution was stirred for 3 h. Saturated aqueous NH_4Cl (50 ml) was added, and the resulting mixture was extracted with ether (3×50 ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1) to give the enol acetate **9** (1.01 g, 82%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.25; ν_{max}(film)/cm^{-1} 1689 (C═O); δ_H (270 MHz, $CDCl_3$) 7.26–7.34 (2 H, m, $2 \times$ CH; Ar), 7.12 (1 H, t, $J = 8.4$, CH; Ar), 5.68 (1 H, t, $J = 4.7$, CH), 3.84 (3 H, s, OCH_3), 2.84 (2 H, t, $J = 8.6$, CH_2), 2.46–2.33 (2 H, m, CH_2) and 2.27 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 176.9, 169.3, 156.1, 145.4, 131.4, 126.6, 115.6, 113.5, 110.6, 55.5, 22.1, 20.8 and 19.5 (Found M^+ 218.0950, $C_{13}H_{14}O_3$, requires M, 218.0943).

6-Methoxy-3,4-dihydro-naphthalen-1-yl acetate **11**

Under the same conditions as enol acetate **4**, 6-methoxytetralone **10** (1.0 g, 5.70 mmol), isopropenylacetate (36.4 g, 40.0 ml, 0.36 mol) and *p*-toluenesulphonic acid (0.10 g, 0.58 mmol) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1), acetate **11** (1.00 g, 81%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.23; ν_{max}(film)/cm^{-1}1691 (C═O); δ_H (270 MHz, $CDCl_3$) 7.01 (1 H, d, $J = 8.1$, CH; Ar), 6.69–6.65 (2 H, m, $2 \times$ CH; Ar), 5.55 (1 H, t, $J = 4.6$, CH), 3.78 (3 H, s, OCH_3), 2.82 (2 H, t, $J = 7.9$, CH_2), 2.45–2.37 (2 H, m, CH_2) and 2.27 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 169.4, 158.0, 145.5, 138.3, 123.5, 122.8, 113.8, 112.7, 111.1, 74.3, 55.5, 27.9, 21.0 and 20.9 (Found M^+ 218.0950, $C_{13}H_{14}O_3$, requires M, 218.0943).

3H-Inden-1-yl acetate **13**

Under the same conditions as enol acetate **4**, indanone **12** (1.0 g, 7.6 mmol), isopropenylacetate (36.4 g, 40.0 ml, 0.36 mol) and *p*-toluenesulphonic acid (0.10 g, 0.58 mmol) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1), enol acetate **13** (1.2 g, 90%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (19:1)] 0.76; ν_{max}(film)/cm^{-1} 1760 (C═O); δ_H (270 MHz, $CDCl_3$) 7.31–7.24 (4 H, m, $4 \times$ CH; Ar), 6.32 (1 H, t, $J = 2.4$, CH), 3.41 (2 H, d, $J = 2.4$, CH_2) and 2.34 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 168.2, 149.1, 141.7, 139.0, 126.2, 125.6, 124.1, 118.0, 115.5, 35.0 and 21.1 (Found M^+ 174.1889, $C_{11}H_{10}O_2$, requires M, 174.1994).

8,9-Dihydro-7H-benzocyclohepten-5-yl acetate **15**

Under the same conditions as enol acetate **4**, benzosuberone **14** (1.3 g, 8.1 mmol), isopropenylacetate (36.4 g, 40.0 ml, 0.36 mol) and *p*-toluenesulphonic acid (0.13 g, 0.75 mmol) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1), the acetate **14** (1.35 g, 83%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.45; ν_{max}(film)/cm^{-1} 1747 (C═O); δ_H (270 MHz, $CDCl_3$) 7.25–7.17 (4 H, m, 4 × CH; Ar), 5.79 (1 H, t, $J = 5.9$, CH), 2.83–2.71 (2 H, m, CH_2), 2.13 (3 H, s, CH_3), 2.19–2.12 (2 H, m, CH_2) and 2.10–2.00 (2 H, m, CH_3); δ_C (100 MHz, $CDCl_3$) 169.8, 145.7, 141.8, 134.3, 129.1, 128.1, 126.0, 125.4, 119.7, 33.7, 31.0, 25.3 and 20.9 (Found MH^+ 203.2551, $C_{13}H_{15}O_2$, requires MH, 203.2556).

1,2,3,4-Tetrahydro-2 methylnaphthalen-1-yl acetate **16**

Under the same conditions as acetate **5**, 3,4-dihydro-2-methylnaphthalen-yl acetate **6** (0.2 g, 0.99 mmol) in toluene (3 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and hydrogen gas (250 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), the acetate **16** (0.17 g, 82%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.43; ν_{max}(film)/cm^{-1} 1078 (C–O); δ_H (270 MHz, $CDCl_3$) 7.35 (1 H, d, $J = 7.4$, CH; Ar), 7.25–7.14 (3 H, m, 3 × CH; Ar), 6.01 (1 H, d, $J = 3.2$, CH), 2.89–2.82 (2 H, m, CH_2), 2.06 (3 H, s, CH_3), 2.01–1.94 (1 H, m, CH), 1.72–1.71 (2 H, m, CH_2) and 1.03 (3 H, d, $J = 6.9$, CH_3); δ_C (100 MHz, $CDCl_3$) 170.9 (*C*OCH_3), 137.5 (*i*-CH; Ar), 135.1 (*i*-CH; Ar), 130.2, 128.9, 128.2 and 126.0 (4 × CH; Ar), 72.5 (CH–O), 33.0 (*C*HCH_3), 28.8 (CH_2C), 25.6 (CH_2), 21.2 (CH_3CO) and 16.9 (CHC*H*$_3$). (Found $(M + NH_4)^+$, 222.1491, $C_{13}H_{20}NO_2$ requires M, 222.1489); (*m*/*z*) 204.1 (100%, M^+); and napthoxyacetate **18** (35 mg, 18%) as an oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.25; ν_{max}(film)/cm^{-1} 1720 (C═O); δ_H (270 MHz, $CDCl_3$) 7.85 (1 H, d, $J = 7.2$, CH; Ar), 7.73 (1 H, d, $J = 7.6$, CH; Ar), 7.65 (1 H, d, $J = 8.2$, CH; Ar), 7.45 (2 H, qd, $J = 7.6$ and 1.9, 2 × CH; Ar) , 7.33 (1 H, d, $J = 8.2$, CH; Ar), 2.47 (3 H, s, CH_3; Ac) and 2.30 (3 H, s, CH_3); δ_C (67.5 MHz, $CDCl_3$) 169.0 (C═O), 144.3 (*i*-C; Ar), 133.2 (*i*-C; Ar), 128.7, 127.9, 127.0, 126.5, 126.4, 125.8, 125.5 and 120.7 (8 × CH; Ar), 20.6 and 16.4 (2 × CH_3) (Found $(M + NH_4)^+$ 218.1176, $C_{13}H_{16}NO_2$, requires $(M + NH_4)^+$, 218.1176).

*1,2-Dideutero-3,4-dihydro-2-methylnaphthalene-1-yl acetate [D_2]-***16**

Under the same conditions as acetate **5**, 3,4-dihydro-2-methyl-naphthalen-1-yl-acetate **6** (0.72 g, 3.6 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and deuterium gas (250 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether

(9:1), the acetate [D_2]-**16** (0.58 g, 80%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.50; ν_{max}(film)/cm^{-1} 2083 (CD); δ_H (270 MHz, $CDCl_3$) 7.31–7.14 (4 H, m, 4 × CH; Ar), 6.00 (1 H, s, CH) (see foonote §), 2.87–2.79 (2 H, m, CH_2), 2.05 (3 H, s, CO*C*H$_3$), 1.81–1.68 (2 H, m, CH_2) and 1.02 (3 H, s, CD*C*H$_3$); δ_C (100 MHz, $CDCl_4$) 170.9 (C═O), 137.3 and 135.1 (2 × *i*-C; Ar), 130.3, 128.9, 128.2 and 126.0 (4 × CH; Ar), 72.1 (CD–O), 32.4 (*C*DCH$_3$), 28.5 (OCO*C*H$_3$), 25.4 and 21.2 (2 × CH_2) and 16.9 (CH_3). (Found $M_{d0} + NH_4^+$ 222.1476, $C_{13}H_{14}O_2D_2 + NH_4^+$, requires M, 206.1473) and (Found $(M + NH_4^+)^+$ 224.1614, $C_{13}H_{18}NO_2D_2$, requires M, 224.1614); (*m*/*z*) 224.1 (25%, $M_{D2} + NH_4^+$), 223.1 (15, $M_{D1} + NH_4^+$), 222.1 (2, $M_{D0} + NH_4^+$), 165.2 (60, M_{D2} + H − Ac + H), 164.1 (100, M_{D1} + H − Ac + H) and 163.1 (50, M_{D0} + H − Ac + H); the isotopic shift at *C*(1) (72.1 ppm) was 0.37 ppm (1 C, t, $^1J_{CD} = 22$ Hz) and *C*(2) (32.4 ppm) was 0.48 ppm (1 C, t, $^1J_{CD} = 20$ Hz); and naphthoxyacetate **18** (0.14 g, 20%) as an oil, which was spectroscopically identical to that obtained previously.

1,2,3,4-Tetrahydro-2-methylnapthalen-1-ol syn-**17**

1,2,3,4-Tetrahydro-2-methylnapthalen-1-yl acetate **16** (0.1 g, 0.5 mmol) was added dropwise to a stirred solution of MeLi (1.2 ml, 1.5 M in diethyl ether, 1.8 mmol) in THF (4 ml) at −78°C. The resulting solution was stirred for 2 h. Saturated aqueous NH_4Cl (10 ml) was added, and the resulting mixture was extracted with ether (3 × 20 ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1) to give 1,2,3,4-tetrahydro-2-methylnapthalen-1-ol *syn*-**17** (44 mg, 43%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C); ether (9:1)] 0.12; ν_{max}(film)/cm^{-1} ν_{max}(film)/cm^{-1} 3500 (OH); δ_H (270 MHz, $CDCl_3$) 7.24–7.18 (4 H, m, 4 × CH; Ar), 4.56–4.50 (1 H, m, C*H*OH), 2.82–2.78 (2 H, m, CH_2), 1.88–1.80 (1 H, m, CH), 1.67–1.58 (2 H, m, CH_2) and 1.12 (3 H, d, $J = 6.7$, CH_3); δ_C (100 MHz, $CDCl_3$) 138.7 and 136.7 (2 × *i*-C; Ar), 129.8, 129.0, 128.2 and 126.2 (4 × CH; Ar), 71.5 (CH–O), 34.2 (*C*HCH$_3$), 28.9 and 24.8 (2 × CH_2) and 16.9 (CH_3).

Sodium borohydride reduction of 2-methyltetralone **2**

Sodium borohydride (0.37 g, 9.8 mmol) was added to a stirred solution of 2-methyltetralone **2** (0.51 g, 3.2 mmol) in ethanol (10 ml). The resulting solution was stirred for 2 h. HCl (10 ml, 3 M) was slowly added, followed by an aqueous solution of NaOH (10 ml, 10%). Water (50 ml) was added, and the resulting mixture was extracted with ether (3 × 50 ml). The combined organic layers were dried over $MgSO_4$, and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with

light petroleum (b.p. 40–60°C)–ether (9:1) to give a diastereoisomeric mixture of *anti*- and *syn*-2-methyltetralols **17** (0.34 g, 66%) (ratio 66:34: *anti*-:*syn*-) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (1:1)] 0.44; ν_{max}(film)/cm^{-1} 3500 (OH); δ_H (270 MHz, $CDCl_3$) 7.51 (1 H, m, CH; Ar_a), 7.34 (1 H, m, CH; Ar_s), 7.22–7.05 (6 H, m, 6 × CH; Ar_{a+s}), 4.56 (1 H, d, $J = 3.2$, CH–O_s), 4.31 (1 H, d, $J = 7.6$, CH–O_a), 2.90–2.70 (4 H, m, CH_{2a} and CH_{2s}), 1.94–1.50 (6 H, m, CH_{2a}, CH_{2s}, C*H*CH_{3a} and C*H*CH_{3s}) and 1.10 (6 H, d, $J = 6.5$, CH_{3a} and CH_{3s}); δ_C (67 MHz, $CDCl_3$) 139.3, 139.11, 137.1 and 137.0 (4 × *i*-C; Ar_{a+s}), 130.3, 130.2, 129.4, 129.0, 128.2, 127.6, 126.6 and 126.5 (8 × CH; Ar_{a+s}), 75.5 (CH–O_a), 71.9 (CH–O_s), 37.7 (*C*HCH_{3a}), 34.6 (*C*HCH_{3s}), 29.3 (CH_{2s}), 28.5 (CH_{2a}), 28.3 (CH_{2a}), 25.1 (CH_{2s}), 18.5 (CH_{3a}) and 17.3 (CH_{3s}); (*m*/*z*) 162.2 (100%, M).

Acetylation of 2-methyltetralol **17**

Acetyl chloride (0.17 g, 0.15 ml, 2.2 mmol) was added to a stirred solution of *anti*- and *syn*-tetralols **17** (0.31 g, 1.9 mmol) and Et_3N (0.22 g, 0.30 ml, 2.2 mmol) in dichloromethane (10 ml). The resulting solution was stirred for 24 h. Saturated aqueous NH_4Cl (30 ml) was added, and the resulting mixture was extracted with ether (3 × 20 ml). The combined organic layers were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1) to give a diastereoisomeric mixture of *anti*- and *syn*-1,2,3,4-tetrahydro-2-methylnaphthalen-1-yl acetate **16** (0.17 g, 44%) (ratio 66:34: *anti*-:*syn*-) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.50; ν_{max}(film)/cm^{-1} 1715 (C═O); δ_H (270 MHz, $CDCl_3$) 7.46–7.05 (8 H, m, Ar_a and Ar_s), 6.02 (1 H, d, $J = 3.4$, CH–O_s), 5.74 (1 H, d, $J = 6.7$, CH–O_a), 2.88–2.70 (4 H, m, CH_{2a} and CH_{2s}), 2.25–1.50 (6 H, m, CH_a, CH_s, CH_{2a} and CH_{2s}), 2.10 (3 H, s, CH_3; Ac_a), 2.05 (3 H, s, CH_3; Ac_s), 1.10 (3 H, d, $J = 7.0$, CH_3; Ac_s) and 1.00 (3 H, d, $J = 7.1$, CH_3; Ac_a) (Found $(M + NH_4)^+$ 222.1493, $C_{13}H_{20}NO_2$, requires $(M + NH_4)^+$, 222.1489).

5-Methoxy-1,2,3,4-tetrahydronaphthalen-1-yl acetate **19**

Under the same conditions as acetate **5**, 5-methoxy-3,4-dihydronaphthalen-1-yl acetate **9** (0.23 g, 1.06 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and hydrogen gas (500 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), acetate **19** (0.18 g, 80%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.49; ν_{max}(film)/cm^{-1} 1718 (C═O); δ_H (270 MHz, $CDCl_3$) 7.15 (1 H, t, $J = 7.7$, CH; Ar), 6.90 (1 H, d, $J = 7.7$, CH; Ar), 6.75 (1 H, d, $J = 7.7$, CH; Ar), 5.97 (1 H, t, $J = 4.8$, CHO), 3.81 (3 H, s, OCH_3), 2.88–2.78 (2 H, m, CH_2), 2.60–2.54 (2 H, m, CH_2), 2.09 (3 H, s, $COCH_3$) and 1.92–1.86

(2 H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 171.1 ($OCOCH_3$), 157.4 ($COCH_3$), 136.0 and 127.4 (2 × *i*-C; Ar), 126.8, 121.7 and 109.5 (3 × CH; Ar), 70.3 (CH–O), 55.7 ($COCH_3$), 39.2 (CH_2), 28.9 (CH_2), 20.8 ($OCOCH_3$) and 18.4 (CH_2).

5-Methoxy-1,2-dideutero-3,4-dihydro-naphthalen-1-yl acetate [D_2]-**19**

Under the same conditions as acetate **5**, 5-methoxy-3,4-dihydro-naphthalen-1-yl acetate **9** (0.20 g, 1.06 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and deuterium gas (250 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), the acetate [D_2]-**19** (0.19 g, 83%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.70; ν_{max}(film)/cm^{-1} 2071 (C–D); δ_H (270 MHz, $CDCl_3$) 7.15 (1 H, t, $J = 7.6$, CH; Ar), 6.89 (1 H, d, $J = 7.6$, CH; Ar), 6.77 (1 H, d, $J = 7.6$, CH; Ar), 5.95 (1 H, br d, $J = 4.6$, CHO) (see footnote §), 3.81 (3 H, s, OCH_3; Ar), 2.85–2.78 (2 H, m, CH_2), 2.06 (3 H, s, $COCH_3$) and 1.92–1.81 (3 H, m, CDH and CH_2); δ_C (100 MHz, $CDCl_3$) 170.8 ($OCOCH_3$), 159.0, 139.6, 131.0, 126.9, 113.4, 112.5, 69.7 (1 C, t, $^1J_{CD} = 20$ Hz; CD–O), 55.3 ($OCOCH_3$), 30.9 (1 C, t, $^1J_{CD} = 20$ Hz; CD), 28.7 (CH_2), 21.5 ($COCH_3$) and 18.5 (CH_2) (Found M^+ 222.1221, $C_{13}H_{14}O_3D_2$, requires M, 222.1219). The isotopic shift at *C*(1) (69.7 ppm) was 0.22 ppm.

6-Methoxy-1,2,3,4-tetrahydro-naphthalen-1-yl acetate **20**

Under the same conditions as acetate **5**, 6-methoxy-3,4-dihydro-naphthalen-1-yl acetate **11** (0.20 g, 1.06 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and H_2 (500 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), acetate **20** (0.15 g, 66%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.59; ν_{max}(film)/cm^{-1} 1719 (C═O); δ_H (270 MHz, $CDCl_3$) 7.25–7.20 (1 H, m, CH; Ar), 6.74–6.71 (1 H, m, CH; Ar), 6.62 (1 H, s, CH; Ar), 5.95–5.93 (1 H, m, CHOAc), 3.77 (3 H, s, OCH_3), 2.85–2.73 (2 H, m, CH_2), 2.10 (3 H, s, CH_3) and 1.96–1.89 (4 H, m, 2 × CH_2); δ_C (100 MHz, $CDCl_3$) 171.2 ($OCOCH_3$), 159.6 ($COCH_3$), 139.9 and 131.4 (2 × *i*-C; Ar), 126.5, 116.2 and 112.8 (3 × CH; Ar), 70.1 (CH–O), 55.7 ($COCH_3$), 29.7 (CH_2), 29.6 (CH), 21.4 (CH_3) and 18.9 (CH_2).

6-Methoxy-1,2-dideutero-3,4-dihydro-naphthalen-1-yl acetate [D_2]-**20**

Under the same conditions as acetate **5**, 6-methoxy-3,4-dihydro-naphthalen-1-yl acetate **11** (0.20 g, 1.06 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and deuterium gas (250 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), acetate [D_2]-**20** (56 mg, 24%) as a colourless oil; R_F [light petroleum (40–60°C)–ether (9:1)] 0.40; ν_{max}(film)/cm^{-1} 2197 (C–D); δ_H (270 MHz, $CDCl_3$) 7.25–

7.15 (2 H, m, 2 × CH; Ar), 6.75 (1 H, dd, $J = 8.6$ and 2.7, CH; Ar), 5.95 (1 H, br d, $J = 3.4$ Hz, CHOAc) (see footnote §), 3.78 (3 H, s, OCH_3), 2.80–2.71 (2 H, m, CH_2), 2.10 (3 H, s, CH_3) and 2.05–1.81 (3 H, m, CH_2 and CHD); δ_C (100 MHz, $CDCl_3$) 170.0 ($OCOCH_3$), 159.3 ($COCH_3$), 139.5 and 131.0 (2 × *i*-C; Ar), 126.1, 113.4 and 112.5 (3 × CH; Ar), 69.6 (CD–O), 55.3 ($COCH_3$), 30.9 (CH_2), 28.7 (CD), 21.0 (CH_3) and 18.4 (CH_2) (Found M^+ 222.1216, $C_{13}H_{14}O_3D_2$, requires M, 222.1219). The isotopic shift at *C*(1) (69.6 ppm) was 0.20 ppm (1 C, t, $^1J_{CD} = 23$ Hz) and *C*(2) (28.7 ppm) was 0.58 ppm (1 C, t, $^1J_{CD} = 20$ Hz).

Indan-1-yl acetate **21**

Under the same conditions as acetate **5**, 3*H*-inden-1-yl acetate **13** (0.20 g, 1.15 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and hydrogen gas (500 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), acetate **21** (0.15 g, 75%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.39; ν_{max}(film)/cm^{-1} 1732 (C═O); δ_H (270 MHz, $CDCl_3$) 7.39 (1 H, d, $J = 2.0$, CH; Ar), 7.28–7.21 (3 H, m, 3 × CH; Ar), 6.18 (1 H, dd, $J = 6.9$, CHCO), 3.10–3.07 (1 H, m, CH_AH_B), 2.90–2.78 (1 H, m, CH_AH_B), 2.50–2.45 (1 H, m, CH_AH_B), 2.11–2.07 (1 H, m, CH_AH_B) and 2.05 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.0 ($COCH_3$), 143.4 and 140.0 (2 × *i*-C; Ar), 127.9, 125.6, 124.5 and 123.7 (4 × CH; Ar), 77.3 (CH–O), 31.2 (CH_2), 29.1 (CH_2) and 20.3 (CH_3).

*1,2-Dideutero-inden-1-yl acetate [D_2]-***21**

Under the same conditions as acetate **5**, 3*H*-inden-1-yl acetate **13** (0.20 g, 1.15 mmol) in toluene (2 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and deuterium gas (250 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), acetate [D_2]-**21** (0.15 g, 75%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.43; ν_{max}(film)/cm^{-1} 2123 (C–D); δ_H (270 MHz, $CDCl_3$) 7.39 (1 H, d, $J = 8.2$, CH; Ar), 7.28–7.21 (3 H, m, 3 × CH; Ar), 6.18 (1 H, br d, $J = 3.9$, CHCO) (see footnote §), 3.08 (1 H, dd, $J = 16.1$ and 8.4, CH_AH_B), 2.90 (1 H, dd, $J = 16.1$ and 5.7, CH_AH_B), 2.09–2.06 (1 H, dd, 8.4 and 5.7, CHD) and 2.06 (3 H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 170.0 (C═O), 143.4 and 139.9 (2 × *i*-C; Ar), 127.9, 125.6, 124.5 and 123.9 (4 × CH; Ar), 76.9 (CD–O), 31.0 (CD), 29.1 (CH_2) and 20.3 ($COCH_3$). (Found $(M + NH_4)^+$ 196.1299, $C_{11}H_{14}NO_2D_2$, requires M, 196.1301). The isotopic shift at *C*(1) (76.9 ppm) was 0.31 ppm (1 C, t, $^1J_{CD} = 23$ Hz) and *C*(2) (31.0 ppm) was 0.24 ppm (1 C, t, $^1J_{CD} = 20$ Hz).

6,7,8,9-Tetrahydro-5H-benzocyclohepten-5-yl acetate **22**

Under the same conditions as acetate **5**, 8,9-dihydro-7*H*-benzocyclohepten-5-yl acetate **15** (0.16 g, 0.8 mmol) in toluene (1.5 ml), Pd-on-$BaSO_4$ (40 mg, 5%

on $BaSO_4$ unreduced) and hydrogen gas (500 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (19:1), acetate **22** (0.15 g, 90%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (19:1)] 0.37; ν_{max}(film)/cm^{-1} 1732 (C═O); δ_H (270 MHz, $CDCl_3$) 7.30–7.26 (1 H, m, CH; Ar), 7.17–7.13 (3 H, m, 3 × CH; Ar), 5.94 (1 H, dd, $J = 7.7$ and 1.9, CHOAc), 3.01–2.92 (1 H, m, CH_AH_B), 2.79–2.70 (1 H, m, CH_AH_B), 2.13 (3 H, s, CH_3), 1.96–1.52 (4 H, m, 2 × CH_2) and 1.82–1.69 (2 H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 170.0 (*C*OCH_3), 141.4 and 140.2 (2 × *i*-C; Ar), 135.7, 129.7, 127.5 and 126.0 (4 × CH; Ar), 75.9 (CH–O), 33.4, 27.6 and 27.2 (3 × CH_2), and 21.3 (CO*C*H_2).

*6,7-Dideutero-8,9-dihydro-5H-benzocyclohepten-5-yl acetate [D_2]-***22**

Under the same conditions as acetate **5**, 8,9-dihydro-7*H*-benzocyclohepten-5-yl acetate **15** (0.16 g, 0.8 mmol) in toluene (1.5 ml), Pd-on-$BaSO_4$ (40 mg, 5% on $BaSO_4$ unreduced) and deuterium gas (250 ml) gave, after flash column chromatography on silica gel eluting with light petroleum (b.p. 40–60°C)–ether (9:1), acetate [D_2]-**22** (0.14 g, 87%) as a colourless oil; R_F [light petroleum (b.p. 40–60°C)–ether (9:1)] 0.37; ν_{max}(film)/cm^{-1} 2130 (C–D) and 1732 (C═O); δ_H (270 MHz, $CDCl_3$) 7.24–7.16 (1 H, m, CH; Ar), 7.17–7.11 (3 H, m, 3 × CH; Ar), 5.94 (1 H, d, $J = 8.1$, CHOAc) (see footnote §), 2.97 (1 H, dd, $J = 4.7$ and 13.9, CH_AH_B), 2.76 (1 H, dd, $J = 13.9$ and 1.9, CH_AH_B), 2.13 (3 H, s, CH_3), 1.93–1.81 (3 H, m, CH_2 and CHD), 1.73–1.53 (2 H, m, CH_2); δ_C (100 MHz, $CDCl_3$) 170.0 (*C*OCH_3), 141.3 and 140.2 (2 × *i*-C; Ar), 129.7, 127.5 and 126.0 (3 × CH; Ar), 75.9 (CD–O), 35.7 (CH_2), 33.7 (1 C, quintet, $^1J_{CD} = 20$ Hz, CDH), 27.2 (CH_2), 17.1 (CHD) and 21.3 (CO*C*H_3); (*m*/*z*) 224.1 (30%, $M_{D2} + NH_4^+$), 223.1 (50, $M_{D1} + NH_4^+$), 222.1 (30, $M_{D0} + NH_4^+$), 164.2 (60, M_{D2} + H – Ac + H), 163.1 (100, M_{D1} + H – Ac + H) and 162.1 (60, M_{D0} + H – Ac + H). The isotopic shift at *C*(1) (75.9 ppm) was 0.40 ppm (1 C, t, $^1J_{CD} = 20$ Hz).

Acknowledgements

We thank GOSS Scientific Instruments Ltd and AstraZeneca (David J. Wilkinson, Loughborough, UK) for their interest and generous support. We are also grateful to the EPRSC National Mass Spectrometry Service (Swansea) for mass determination.

References

1. (a) Chappelle MR, Harding JR, Kent BB, Jones JR, Lu S-Y, Morgan AD. *J Label Compd Radiopharm* 2003; **46**: 567; (b) Lei H, Atkinson J. *J Label Compd Radiopharm* 2001; **44**: 215; (c) Anet FAL, Leyendecker F. *J Am Chem Soc* 1973; **95**: 156; (d) McDonald RN, Schell PL, Chowdhury AK. *J Am Chem Soc* 1985;

107: 5579; (e) Makoto O, Ishihara T, Satake H, Nishiyama K. *J Label Compd Radiopharm* 2002; **45**: 619.
2. Ellames GJ, Gibson JS, Herbert JM, Kerr WJ, McNeill AH. *J Label Compd Radiopharm* 2004; **47**: 1.
3. (a) Conner WC, Kokes RJ. *J Phys Chem* 1968; **72**: 2436; (b) Salter R, Bosser I. *J Label Compd Radiopharm* 2003; **46**: 489; (c) Lei H, Atkinson J. *J Label Compd Radiopharm* 2001; **44**: 215.
4. Oba M, Ishihara T, Satake H, Nishiyama K. *J Label Compd Radiopharm* 2002; **45**: 619.
5. Sugiura M, Nakai T. *Angew Chem Int Ed* 1997; **36**: 2366.
6. Jung HM, Koh JN, Kim MJ, Park J. *Org Lett* 2000; **2**: 2487.
7. House HO, Trost BM. *J Org Chem* 1965; **30**: 2502.
8. (a) Cuneca A, Medio-Simon M, Aguilar GA, Weibel D, Beck AK, Dieter S. *Helv Chim Acta* 2000; **83**: 3153; (b) Takahashi T, Nakao N, Koizumi T. *Tetrahedron: Asymmetry* 1997; **8**: 3293; (c) Fuji K, Tanaka K, Miyamoto H. *Tetrahedron: Asymmetry* 1993; **4**: 247.
9. (a) Eames J, Coumbarides GS, Weerasooriya N. *Eur J Org Chem* 2003; 634; (b) Eames J, Coumbarides GS, Weerasooriya N. *J Label Compd Radiopharm* 2001; **44**: 871.
10. (a) Shevchenko VP, Nagaev IY, Myasoedov NF, Andres H, Moenius T, Susan A. *J Label Compd Radiopharm* 2004; **47**: 407; (b) Shevchenko VP, Nagaev IY, Myasoedov NF, Susan A. *J Label Compd Radiopharm* 2002; **45**: 911.
11. Kabuto K, Imuta M, Kempner ES, Ziffer H. *J Org Chem* 1978; **43**: 2357.

