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X-ray structure and conformation of some enol acetates derived from simple ketones

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The conformational arrangements of a series of enol acetates derived from simple ketones have been examined by X-ray crystallography. For this series, the carbonyl enol motif was found to adopt a similar conformation.

KEY WORDS: enolacetate; conformation; ketones.

Introduction

The synthesis of substituted enol acetates derived from carbonyl-based substrates is very well documented.[1] These enol derivatives have played an important role in organic synthesis as protected enol(ate) equivalents.[2] Recently, we became interested in the use of enol acetate **1**[3] (derived from the parent ketone, (±)-2-methyltetralone (**3**), and acetic anhydride)[4] as a precursor to the prostereogenic lithium enolate **4** because of its improved stability over other related enol derivatives (Scheme 1).[5] This lithium enolate **4** has been shown to be synthetically important[6] within the field of enantioselective C-protonation[7] as simple addition of a chiral proton source[8] [e.g., (*R*,*R*)-**2**][9] leads to the required enantiomerically enriched parent ketone 2-methyltetralone (*R*)-**3** with 64% e.e. in good yield (Scheme 1).

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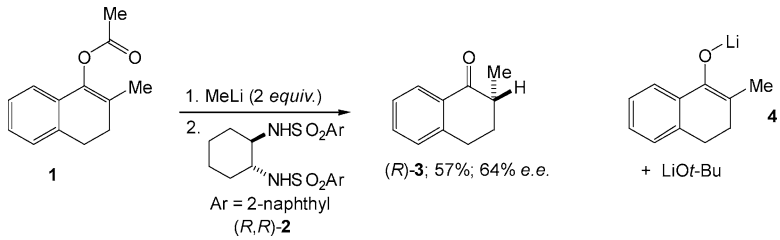
Results and discussion

Very little attention has been paid to the structural and stereochemical arrangement of prostereogenic enol acetates. In an attempt to gain some insight and comprehension for their structural arrangements, we have decided to focus our attention on the structural arrangement of enol acetates, like **1**, using X-ray crystallography (Scheme 1). Reports into the structural arrangement of enol acetates are common,[10] but these generally deal with the derivatives which are intrinsically chiral[11] because of the presence of one or more stereocenters. By comparison, reports into the synthesis of conformationally chiral enol acetates are rare.[12]

For our study, we chose to synthesize a variety of structurally diverse enol acetates **1**, **5**, **7**, and **9**, which were derived from the corresponding ketones 2-methyltetralone **3**, 2'-acetonaphthone

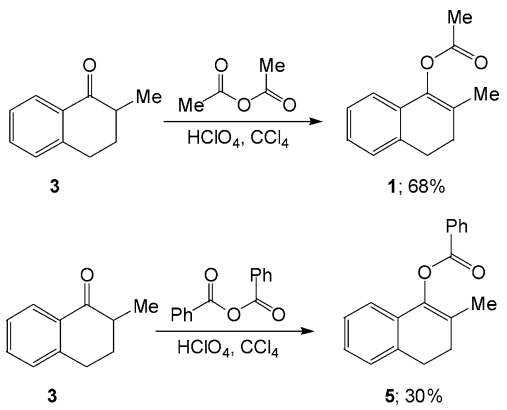


Scheme 1. Enantioselective C-protonation of enolate **4** using bissulfonamide (*R*,*R*)-**2**.

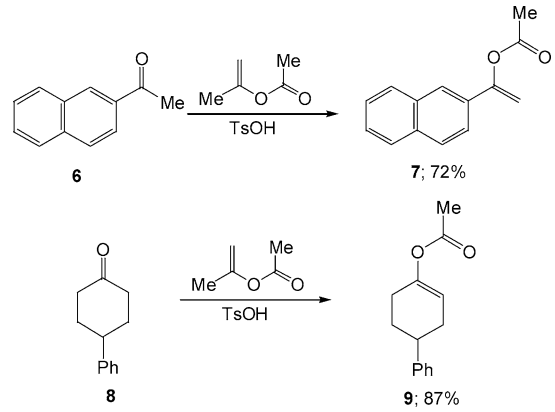
6, and 4-phenylcyclohexanone **8** using well-established methodology (Schemes 2 and 3).[13] For simplicity, we chose to use X-ray crystallography to determine the relative conformation of these enol acetates within their crystalline state.

Enol acetate **1**[15] revealed a rotational isomer about the C4–O1 axis (dihedral angle C(13)C(4)–O(1)C(1) = 100.74°) and evidently the acetate motif was twisted out of plane (with the rest of the molecule) and adopts an almost orthogonal arrangement with the neighboring enolic carbon–carbon double bond (Fig. 1). This acetate motif has a well-documented *S-cis* conformation due to its anomeric effect[16] and is virtually coplanar around C(4)O(1)–C(1)O(2) (dihedral angle = 0.80°). Closer examination of bond lengths revealed that the carbon–carbon double bond C(4)–C(5) [1.446 Å] was marginally shorter, and the carbon–oxygen single bond O(1)–C(4) [1.362(2) Å] was significantly longer than those of the related enol ethers.[17] This apparent change in bond length is presumably due to the lower conjugation present between the enol oxygen O(1) and the adjacent carbon–carbon double bond C(4)C(5) through increased conjugation with the more electron deficient carbonyl group C(1)O(2). This competitive conjugation is presumably responsible for its reduced basicity and nucleophilicity compared with other enol ether derivatives.[5] The unit cell of **1** contains four molecules ($Z = 4$), consisting of two pairs of enantiomeric enol acetates (Fig. 2). Somewhat surprisingly, the unit cell does not contain a center of symmetry (space group *Pc21b*).

Within the crystal phase, these conformeric enol acetates were oriented in parallel layers (*R-R-R-R*, *S-S-S-S*, *R-R-R-R*), presumably because of crystal packing effects, creating a herringbone



Scheme 2. Synthesis of enol acetate **1** and enol benzoate **5**.



Scheme 3. Synthesis of enol acetate **7** and enol benzoate **9**.

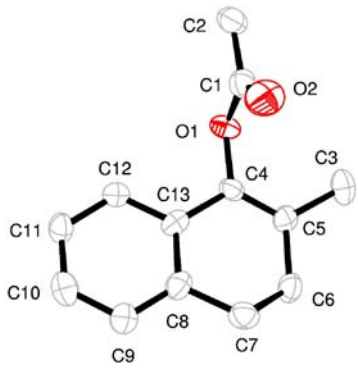


Fig. 1. ORTEP diagram of 3,4-dihydro-2-methylnaphthal-1-enyl acetate **1**.[14]

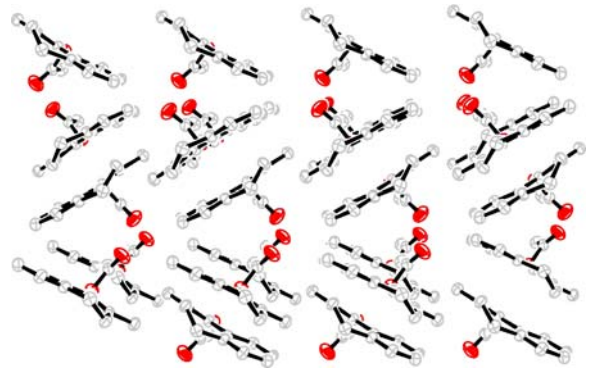


Fig. 3. Crystal packing of 3,4-dihydro-2-methylnaphthal-1-enyl acetate **1**.[14]

arrangement (Fig. 3). The structural nature of the enol motif appears to be unimportant for the overall conformation of these enol derivatives; the related enol benzoate **5** appears to adopt a similar chiral conformer (Fig. 4). Closer examination has revealed the dihedral angle of C(9)C(8)–O(2)C(7) (83.27°) was slightly lower, but nearer to 90°, than that of the corresponding acetate **1** causing this motif to be positioned in a near orthogonal arrangement with the aryl framework (Table 1). The unit cell of **5** consists of two pairs of enantiomeric enol benzoates ($Z = 4$) oriented in a *R-S-R-S* arrangement which contains a point of symmetry (space group *P-1*) (Fig. 5). This crystal packing is slightly different and consists of *anti*-parallel layers (*R-R-R-R*, *S-S-S-S*, *R-R-R-R*) of enantiomeric enol benzoate molecules (Fig. 6).

Our attention next turned to the structural arrangement of acyclic enol acetate **7** derived from 2'-acetonaphthone **6** (Fig. 7). The conformation of this acetate motif [dihedral angle C(5)C(1)–O(1)C(3) = 90.87°] was found to be similar to that of the related cyclic enol derivatives **1** and **5** (Table 1). The acetate motif was oriented orthogonal to the naphthyl skeleton, to presumably maximize the interaction between the

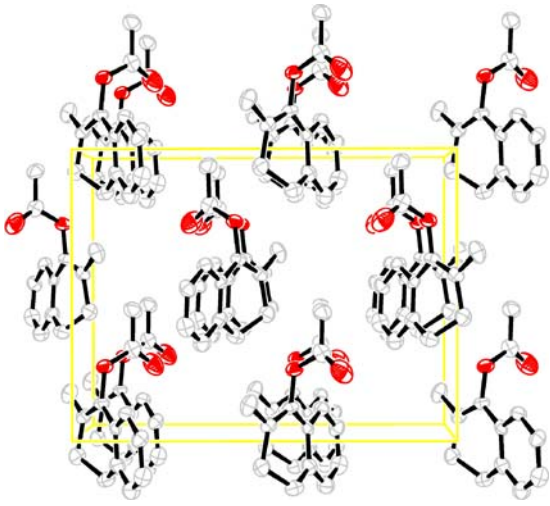


Fig. 2. Unit cell of 3,4-dihydro-2-methylnaphthal-1-enyl acetate **1**.[14]

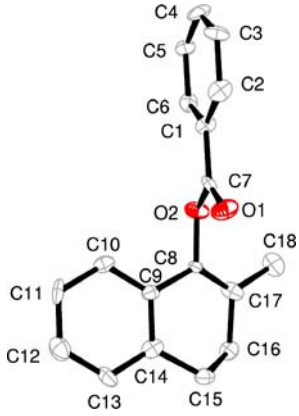


Fig. 4. ORTEP diagram of 3,4-dihydro-2-methylnapthal-1-enyl benzoate **5**.[14]

Table 1. Torsion Angles for Enol Acetates **1**, **5**, **7**, and **9**

Enol derivatives	Torsion angles (°)
1 (C13–C4–O1–C1)	100.74
5 (C9–C9–O9–O7)	83.27
7 (C5–C1–O1–C3)	90.87
9 (C8–C3–O1–C2)	90.34

lone pair of electrons on O(1) and the neighboring C(1)=C(2) and C(3)=O(2) double bonds. The unit cell of **7** contains four molecules ($Z = 4$), comprising two pairs of enantiomeric enol acetates oriented in a *R-R-S-S* arrangement and contains a center of symmetry (space group *P21/n*) (Fig. 8). This slight change in relative orientation from *R*,*S*,*R*,*S* in **5** to *R*,*R*,*S*,*S* in **7** has a dramatic effect on the overall crystal packing; each layer now consists of an alternating enantiomeric enol acetate **7** (*R-S-R-S*, *S-R-S-R*, *R-S-R-S*) (Fig. 9).

With this information in hand, we next focused our attention on the cyclic enol acetate **9** derived from 4-phenylcyclohexanone **8** (Fig. 10). We were particularly interested in this enol acetate because of the absence of substitution at C(8), C(7), and C(4). However, the conformation of this acetate motif in **9** was found to contain a similar rotational isomer around the C(3)–O(1) bond [dihedral angle C(8)C(3)–O(1)C(2) = 90.34°, Table 1]. It is interesting to note that the acetate motif on C(3) and the 4-phenyl substituent on C(6) were oriented in a less sterically demanding *anti*-relationship (Fig. 10). The unit cell evidently contains two molecules of enol acetate **9** ($Z = 2$), comprising a pair of enantiomeric conformers (*R-S*) oriented in an *anti*-parallel (*R-R-R-R*, *S-S-S-S*, *R-R-R-R*) arrangement (space group *P-1*) (Figs. 11 and 12).

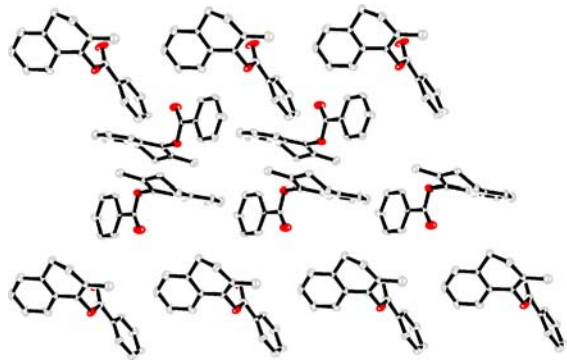


Fig. 6. Crystal packing of 3,4-dihydro-2-methylnapthal-1-enyl benzoate **5**.[14]

In conclusion, we report the conformational arrangement of a series of crystalline enol derivatives **1**, **5**, **7**, and **9**. We have shown the structural arrangement of the enol motif to be similar. For all cases studied, the acetate/benzoate motif prefers to be oriented near-orthogonal to carbon–carbon double bond of the enol component. This results in rotational isomers being present within these derivatives. These enol derivatives evidently exist as a racemate in the crystal phase and are not

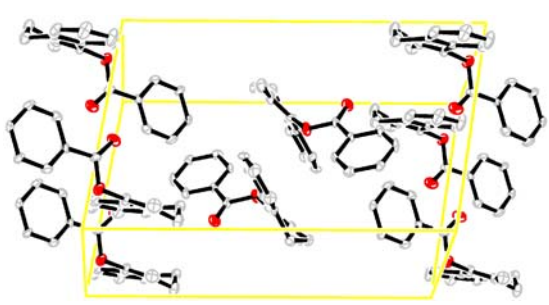


Fig. 5. Unit cell of 3,4-dihydro-2-methylnapthal-1-enyl benzoate **5**.[14]

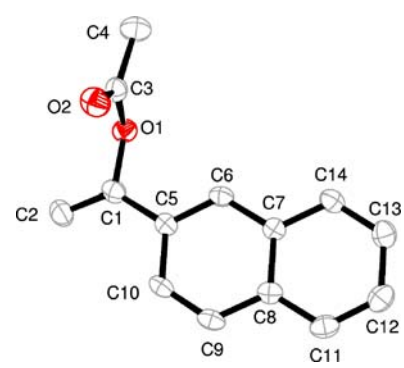


Fig. 7. ORTEP diagrams of 1-naphthylene-2-yl vinyl acetate **7**.[14]

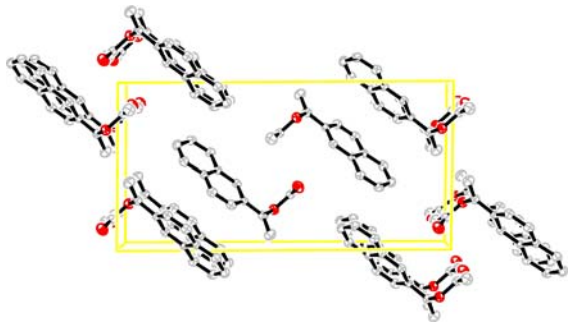


Fig. 8. Unit cell of 1-naphthylene-2-yl vinyl acetate **7**.[14]

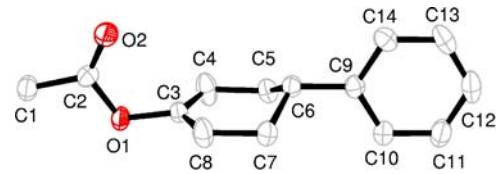


Fig. 10. ORTEP diagrams of (4-phenyl-cyclohex-1-enyloxy)-acetate **9**.[14]

achiral as originally thought. Even though the conformation appears to be predictable; the relative orientation of these derivatives within their unit cell, and their associated crystal packing was highly dependent on the structural nature of the enol derivative. We believe this study will assist in the understanding and structural consequences of related enol precursors and their application[18] towards enantioselective addition processes within asymmetric synthesis.

Experimental

*3,4-Dihydro-2-methylnaphthal-1-enyl acetate **1***

2-Methyl-tetralone **3** (0.26 g, 1.67 mmol), acetic anhyride (90.6 mg, 0.88 mmol, 80 μL) in carbon tetrachloride (10 mL) was placed in a conical flask with perchloric acid (10 drops) and left to stand for 3 h. The reaction mixture was then poured into a cooled solution of sodium hydrogen carbonate (50 mL) and light petroleum (40–60°C):ether (50 mL). The solution was stirred for 30 min and solid sodium hydrogen carbonate was added until pH 7. The organic layer was separated and the water layer was further extracted with light petroleum (40–60°C):ether (2 × 50 mL). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel eluting with light petroleum ether–ether (19:1) to give the enol acetate **1** (0.23 g, 68%) as an oil; R_f [light petroleum (40–60°C):ether (9:1)] 0.43; mp 46°C; ν_{max} (film)/cm^{-1} 1716 (C=O); δ_H (250 MHz, $CDCl_3$) 7.18–7.08 (4 H, m, 4 × CH; Ar), 2.86 (2 H, t, *J* 8.3, CH_2), 2.40 (2 H, t, *J* 8.3, CH_2), 2.32 (3 H, s, CH_3), and 1.76 (3 H, s, CH_3); δ_C (62.5 MHz, $CDCl_3$) 168.6, 135.2, 129.9, 128.6, 127.3, 126.9, 126.4, 124.1, 120.1, 28.9, 27.5, 20.5, and 16.8 (found M^+ 202.2420, $C_{13}H_{14}O_2$, requires 202.2425).

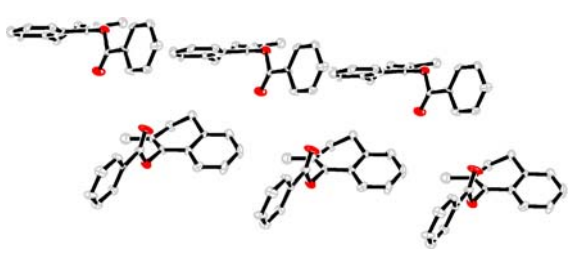


Fig. 9. Crystal packing of 3,4-dihydro-2-methylnapthal-1-enyl benzoate **7**.[14]

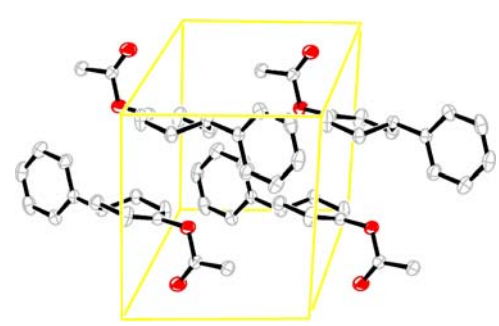


Fig. 11. Unit cell of (4-phenyl-cyclohex-1-enyloxy)-acetate **9**.[14]

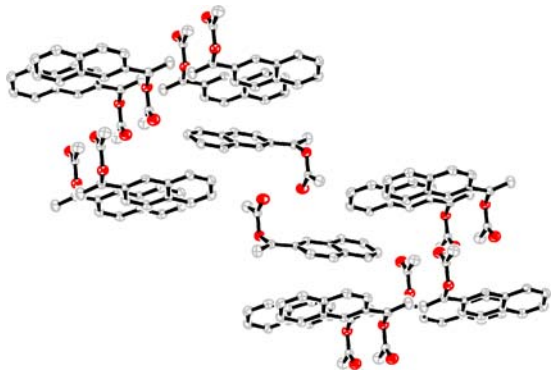


Fig. 12. Crystal packing of 1-naphthylene-2-yl vinyl acetate **9**.[14]

3,4-Dihydro-2-methylnapthal-1-enyl benzoate ***5***

2-Methyl-tetralone **3** (0.44 g, 2.8 mmol), benzoic anhydride (0.78 g, 3.4 mmol) in carbon tetrachloride (5 mL) was placed in a conical flask with perchloric acid (10 drops) and left to stand for 1 day. The reaction was quenched with saturated bicarbonate (10 mL) and the organic layer partitioned with dichloromethane (10 mL). The crude mixture was dried (over $MgSO_4$) and solvent removed under reduced pressure. Because of the inseparability of the benzyl derivative from the starting precursor by flash chromatography, the crude mixture (0.46 g) was reduced using sodium borohydride (55 mg, 1.45 mmol) in ethanol (5 mL). The resulting solution was stirred overnight. The solvent was removed under reduced pressure and the crude residue was washed with water (10 mL) and extracted into diethylether (10 mL). The organic solvent was dried (using $MgSO_4$) and concentrated under reduced pressure. The residue was purified by column chromatography eluting with petroleum spirit (40–60°C):diethyl ether (19:1) to give 3,4-dihydro-2-methylnapthal-1-enyl benzoate **5** (0.23 g, 30%) as an cystalline solid; R_f [light petroleum (40–60°C):ether (9:1)] 0.43; mp 75°C; ν_{max} (film)/cm^{-1} 1755 (C=O); δ_H (250 MHz, $CDCl_3$) 8.26 (2H, d, *J* 7.1, 2 × CH; Bz), 7.64 (1H, m, CH; Bz), 7.52 (2H, t, *J* 7.1, 2 × CH; Bz), 7.10–7.10 (4H, m, 4 × CH; Ar), 2.95 (2H, t, *J* 7.5, CH_2), 2.49 (2H, t, *J* 7.5, CH_2), and 1.81 (3H, s, CH_3); δ_H (67.5MHz, $CDCl_3$) 164.2, 140.1, 135.4, 133.5, 131.3, 130.2, 129.4, 128.7, 127.3, 127.0, 126.4, 124.4, 120.3, 29.1, 27.7, and 17.0; and *anti*- and *syn*-2-methyltetralols (0.34 g, 66%) (ratio 66:34: *anti*-:*syn*-) as a colorless oil; R_F [light petroleum (40–60°C)–ether (9:1)] 0.34; ν_{max} (film)/cm^{-1} 3500 (OH); δ_H (270 MHz, $CDCl_3$) 7.51 (1H, m, CH; Ar_a), 7.34 (1H, m, CH; Ar_s), 7.22–7.05 (6H, m, 6 × CH; Ar_{a+s}), 4.56 (1H, d, *J* 3.2, CH–O_s), 4.31 (1H, d, *J* 7.6, CH–O_a), 2.90–2.70 (4H, m, CH_{2a}, and CH_{2s}), 1.94–1.50 (6H, m, CH_{2a}, CH_{2s}, C*H*CH_{3a} and $CHCH_{3s}$) and 1.10 (6H, br 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 (CHO_a), 71.9 (CHO_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).

1-Naphthylene-2-yl vinyl acetate ***7***

2′-Acetonaphthone **6** (1.0 g, 5.88 mmol) and toluene-*p*-sulphonic acid (0.10 g, 0.58 mmol) was added to a neat solution of isoprenylacetate (30 mL, 0.26 mol). The resulting reaction mixture was refluxed at 110°C for 12 h. The solution was cooled to room temperature and extracted into ether (2 × 50 mL), washed with water (3 × 50 mL), and concentrated, under reduced pressure. The residue was purified by flash chromatography (light petroleum 40–60°C/diethyl ether 19:1) to give the enolate acetate **7** (1.01 g, 72%) as white needle-like crystals; R_F [light petroleum (40–60°C):ether (19:1)] 0.75; mp 82°C; ν_{max} (film)/cm^{-1} 1730 (C=O); δ_H(270 MHz, $CDCl_3$) 7.85–7.79 (4H, m, 4 × CH; Ar), 7.61 (1H, dd, *J* 1.9 and 8.7, CH; Ar), 7.49–7.45 (2H, m, 2 × CH; Ar), 5.61 (1H, d, *J* 2.2, CH_AH_B), 5.11 (1H, d, *J* 2.2, CH_AH_B), and 2.35 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) 169.1 (C=O), 152.9 (*C*OCH_2), 133.4 ($COCH_2$), 133.0, 131.5, 128.4, 128.3, 127.6, 126.6, 126.5, 124.0, 122.6,

102.7, and 21.0 (CH_3) (found MH^+ 212.2482, $C_{14}H_{13}O_2$, requires MH, 212.2887).

(4-Phenyl-cyclohex-1-enyloxy) acetate ***9***

Using the above-mentioned method, 4-phenylcyclohexanone **8** (2.00 g, 11.5 mmol) and toluene-*p*-sulphonic acid (0.22 g, 1.16 mmol) in isoproprenylacetate (60 mL, 0.52 mol) gave, after purification by flash chromatography, the 4-phenylcyclohex-1-enyloxy acetate **9** (2.16 g, 87%) as white needles; R_F [light petroleum (40–60°C):ether (9:1)] 0.40; mp 69°C; ν_{max} (film)/cm^{-1} 1751 (C=O); δ_H (250 MHz, $CDCl_3$) 7.36–7.18 (5H, m, 5 × CH; Ph), 5.49 (1H, t, *J* 2.9, CH), 2.98–2.86 (1H, m, CH), 2.48–2.18 (4H, m, 2 × CH_2), 2.15 (3H, br s, CH_3), and 2.09–1.96 (2H, m, CH_2); δ_C (62.5 MHz, $CDCl_3$) 169.5, 148.2, 145.9, 128.4, 126.8, 126.2, 113.7, 39.4, 31.6, 29.6, 27.2, and 21.1 (found MH^+ 217.1220, $C_{14}H_{17}O_2$, requires 217.1224).

X-ray crystallographic data and structure determinations

For **1**, **7**, and **9**, the intensity data were collected at 160(2) K on a CAD-4 diffractometer using MoKα radiation (λ 0.71069 Å) with $\omega - 2\theta$ scans. All data were corrected for absorption by empirical methods (ψ scan)[19] and for Lorentz-polarization effects by XCAD4.[20] For **5**, data were collected at 120(2) K using a Nonius Kappa CCD area detector diffractometer mounted at the window of molybdenum rotating anode (50 kV, 90 mA, $\lambda = 0.71069$ Å). The crystal-to-detector distance was 30 mm and Ω scans (2.0° increments, 12 s exposure time) were carried out to fill the Ewald sphere. Data collection and processing were carried out using the COLLECT,[21] DENZO[22] and maXus[23] and empirical absorption correction was applied using SORTAV.[24] The structures were solved by the direct method using the program SHELXS-97,[25] and refined anisotropically (non-hydrogen atoms) by full-matrix least-squares on F^2 using SHELXL-97.[25] The H atom positions were calculated geometrically and refined using a riding model. The program, ORTEP-3,[26] was used for drawing the molecules and WINGX[27] was used to prepare material for publication. All data relating to these single crystal X-ray structures have been deposited at the Cambridge Crystallographic Database: reference numbers CCDC 262158 (for **1**), 262159 (for **7**), 262160 (for **9**), and 262161 (for **5**).

3,4-Dihydro-2-methylnaphthal-1-enyl acetate ***1***

$C_{13}H_{14}O_2$, M_r 202.24, orthorhombic, space group *Pc21b*, $a = 7.271(6)$, $b = 10.526(8)$, $c = 13.885(9)$ Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V = 1062.7(14)$ Å^3, $Z = 4$, $D_{ca} = 1.264$ Mg m^{-3}, $\mu = 0.084$ mm^{-1}, F (0 0 0) = 432. There were 1866 independent reflections [$R_{int} = 0.0181$]. The final R indices were [$I > 2\sigma(I)$] $R_1 = 0.0575$, $wR_2 = 0.1221$ (all data) $R_1 = 0.2130$, $wR_2 = 0.1706$. The largest difference peak and hole was 0.237 and -0.264 e Å^{-3}.

3,4-Dihydro-2-methylnaphthal-1-enyl benzoate ***5***

$C_{17}H_{14}O_2$, M_r 264.31, triclinic, space group *P-1* = 8.929(4), b = 9.742(10), c = 16.143(7) Å, α = 80.98(8)°, β = 87.46(5)°, γ = 84.81(5)°, V = 1380.5(17) Å^3, Z = 4, D_{ca} = 1.272 Mg m^{-3}, μ = 0.082 mm^{-1}, F(0 0 0) = 560. There were 4019 independent reflections [R_{int} = 0.2511]. The final R indices were [$I > 2\sigma(I)$] R_1 = 0.1217, wR_2 = 0.1999 (all data) $R_1 = 0.3074$, $wR_2 =$ 0.2795. The largest difference peak and hole was 0.338 and -0.312 e Å^{-3}.

1-Naphthylene-2-yl vinyl acetate ***7***

$C_{14}H_{12}O_2$, M_r 212.24, monoclinic, space group *P21/n*, $a = 19.296(10)$, $b = 5.837(5)$, $c = 9.715(7)$ Å, $\alpha = 90°$, $\beta = 90.92(4)°$, $\gamma = 90°$, $V = 1094.1(13)$ Å^3, $Z = 4$, $D_{ca} = 1.289$ Mg m^{-3},

$\mu = 0.085$ mm^{-1}, $F(0\ 0\ 0) = 448$. There were 1903 independent reflections [$R_{int} = 0.0099$]. The final R indices were [$I > 2\sigma(I)$] $R_1 = 0.0460$, $wR_2 = 0.0975$ (all data) $R_1 = 0.1290$, $wR_2 = 0.1202$. The largest difference peak and hole was 0.180 and -0.211 e Å^{-3}.

4-Phenyl cyclohexenyl acetate ***9***

$C_{14}H_{16}O_2$, M_r 216.27, triclinic, space group *P-1*, $a = 7.146(4)$ Å, $b = 9.018(6)$ Å, $c = 9.560(8)$ Å, $\alpha = 92.38(8)^\circ$, $\beta = 71.77(7)^\circ$, $\gamma = 87.27(10)^\circ$, $V = 580.0(7)$ Å^3, $Z = 2$, $D_{ca} = 1.238$ Mg m^{-3}, $\mu = 0.081$ mm^{-1}, $F(0\ 0\ 0) = 232$. There were 2035 independent reflections [$R_{int} = 0.0098$]. The final R indices were [$I > 2\sigma(I)$] $R_1 = 0.0497$, $wR_2 = 0.1264$ (all data) $R_1 = 0.0851$, $wR_2 = 0.1430$. The largest difference peak and hole was 0.315 and -0.258 e Å^{-3}.

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