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Research Article

Probing the regioselective *C*-deuteriation of lithium enolates derived from 2-methyl-tetralone in the presence of substituted tertiary amines

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Summary

Results are reported on the regioselective *C*-deuteriation of 2-methyl-tetralone using a series of *D*-sources and tertiary amines as potential mediators. The results presented further aid the understanding of kinetic deuteriation of both 'base-containing' and 'base-free' enolates. Copyright © 2006 John Wiley & Sons, Ltd.

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Introduction

The understanding of proton transfer in chemical and biological systems is becoming an increasingly important area.[1] The absolute rates of many proton transfer processes are well known,[2] but the chemical significance of these processes are less documented.[3] Over the last 20 years,[4] an enormous amount of attention has focused on the synthetic applicability of enolates within organic chemistry, and these studies have unequivocally shown them to be highly valued synthetic intermediates. Within this domain, numerous groups[5,†] have focused their attention on controlling enantio-,[7] diastereo-[6] and regioselective[8] protonation of enol(ate)s with some notable successes. From

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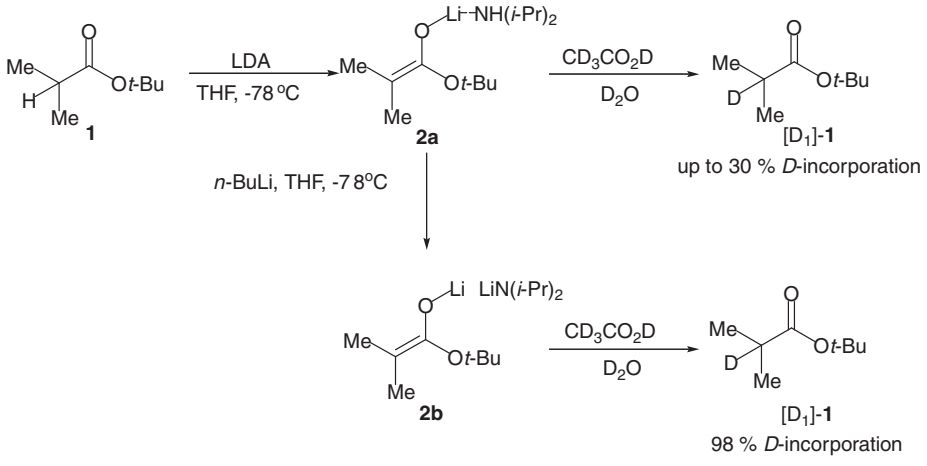
† For additional information see Zimmerman.[6]



Scheme 1.

these studies, it is somewhat surprising to find only a limited amount of attention has been paid to elemental protonation processes using traditional synthetic methodology.[9] Most importantly within this area, Seebach and co-workers have reported within their seminal paper[10] the concept of *internal proton return*. They have shown that simple deprotonation of an ester (e.g. **1**) with lithium diisopropylamide (LDA), followed by addition (of a solution) of acetic acid-d_4 in D_2O (to this intermediate lithium enolate diisopropylamine complex **2a**) gave moderate *D*-incorporation (of up to 30%) (Scheme 1).[10] By comparison, the levels of deuterium incorporation could be increased dramatically to greater than 98% by sequential deprotonation of the intermediate complex, **2a**, using *n*-butyl lithium to give the lithium enolate-lithium amide complex **2b** (Scheme 1). The removal of the unwanted and problematic NH proton (from the residue diisopropylamine in **2a** to give **2b**) has lead to the concept of *internal proton return*[10] in which the NH proton of the intermediate amine (in **2a**) can be re-delivered back to the enolate (during the deuterium quench) to give the unlabelled ester **1** (Scheme 1). Additional evidence for this proton return has come from a complementary *internal deuterium return*; de-deuteriation of the related ester [D_1]-**1** with lithium diisopropylamide, followed by attempted protonation with acetic acid (in H_2O) simply re-formed the original ester [D_1]-**1** with moderate levels of *D*-incorporation (70%) (Scheme 2).[10] This reaction must proceed via the related lithium enolate-diisopropylamine complex [D_1]-**2a**, which evidently must allow efficient internal deuterium return (back to the lithium enolate to give [D_1]-**1**) in the presence of acetic acid (Scheme 2).[10]

Over the last few years, whilst attempting to get a better understanding of related enantioselective processes,[11] we have probed the mechanism of

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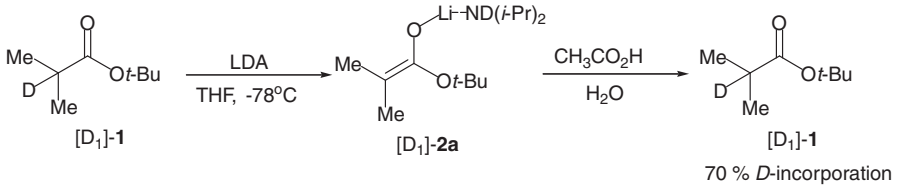
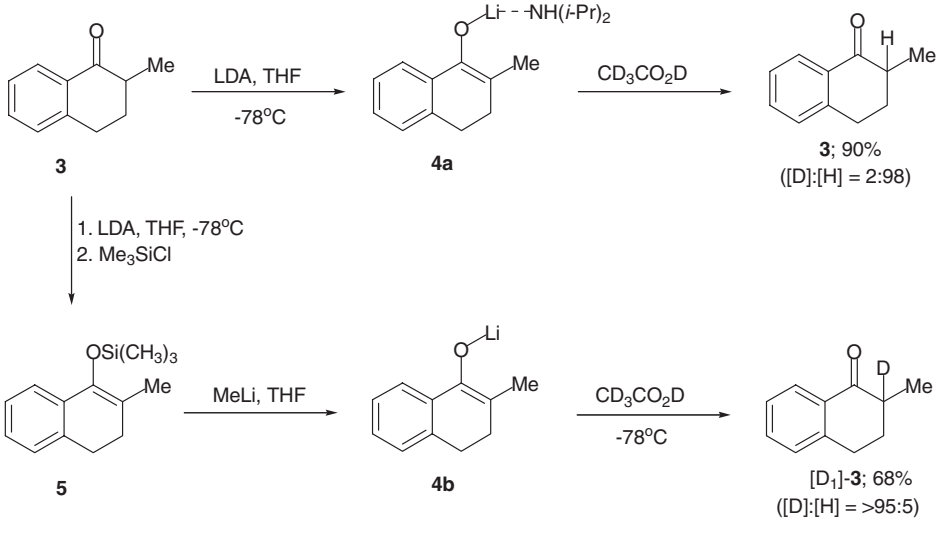


Scheme 2.



Scheme 3.

C-deuteriation of 2-methyl-tetralone **3**‡ with some success.[12] We have shown, as predicted from Seebach's studies,[10] simple deprotonation of 2-methyl-tetralone **3** with LDA, followed by addition of CD_3CO_2D to the corresponding lithium enolate complex **4a**, gave the recovered 2-methyl-tetralone **3** with no deuterium incorporation ([D]:[H] = 2:98) (Scheme 3). However, by simple removal of the unwanted residual diisopropylamne from the enolate complex **4a** (via formation of the corresponding silyl enol ether **5** and addition of MeLi) to re-form the 'residual base-free' enolate **4b** does increase the levels of deuterium incorporation to greater than 95% (Scheme 3).[12]

We have probed the deuteriation of related lithium enolate-amine complexes, like [D_{11}]-**4c** (formed by addition of a secondary amine, deuteriated

‡Many of these reports have focused their attention on the use of the commercially available ketone, 2-methyl tetralone **3**, as their substrate of choice due to its predictable enol(ate) configuration, UV activity and non-volatile nature.

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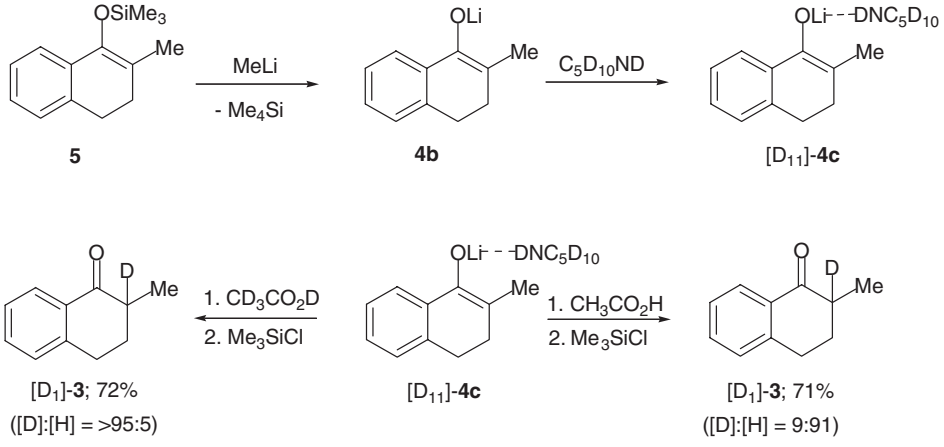
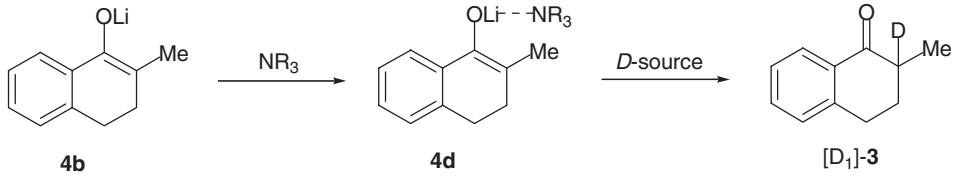
piperidine ($C_5D_{10}ND$), to a solution of the pre-formed 'residual base-free' enolate **4b** in THF), and have shown that internal deuterium transfer {from the *D*-labelled amine to the 2-methyl-tetralone [D_1]-**3** ([D]:[H] = 9:91)} can occur in the presence of unlabelled acetic acid and Me_3SiCl (Scheme 4). Near perfect levels of *D*-incorporation can be achieved by quenching the lithium enolate-amine complex [D_{11}]-**4c** with CD_3CO_2D to give the corresponding 2-deuterio-2-methyl-tetralone [D_1]-**3** ([D]:[H] = > 95:5) (Scheme 4). By comparison, similar levels of deuterium incorporation were found to occur by addition of CD_3CO_2D to the corresponding 'base-free' enolate **4b** (Scheme 3).

In an attempt to get a better understanding of the role the 'residual amine' itself, we chose to investigate the deuteriation of lithium enolate-amine complexes containing non-protic amines, like tertiary amines (NR_3), using a variety of *D*-sources (e.g. [D_4]-acetic acid, [D_4]-MeOH and D_2O) (Scheme 5). For our study, we chose to focus our attention on the use of simple amines such as triethylamine **6** and dimethylbenzylamine **7**, and 1,2-diamines, like 1,4-diazabicyclo[2.2.2]octane (DABCO) **8** and *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) **9** (Scheme 6).



Scheme 4.



Scheme 5.

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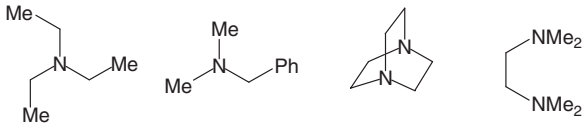

6 **7** **8** **9**

Scheme 6.

The required lithium enolate-amine complexes were formed using our standard approach by direct addition of the amines **6** and **7**, and diamines **8** and **9**, to a solution of related enolates **4b** and **4f** in THF – formed by addition of MeLi•LiBr to the corresponding silyl enol ether **5** and the related enol acetate **10**, respectively (Schemes 7–10) as outlined in Scheme 5. These enolate complexes were in turn deuteriated by the addition of one equivalent and three equivalents of D_2O, [D_4]-MeOH and [D_4]-acetic acid to give the partially deuteriated 2-deuterio-2-methyl-tetralone [D_1]-**3** (Schemes 7 and 8). The levels of deuterium incorporation were determined by integration of the 270 MHz ^{1}H NMR spectrum of the corresponding methyl doublet (CH_3CH) at 1.30 ppm (for 3) versus the methyl singlet (CH_3CD) at 1.30 ppm (for [D_1]-**3**) (see Figure 1). From these results, it is evident that *C*-deuteriation of a lithium enolate-tertiary amine complex, such as **4d** was significantly less regioselective than the corresponding 'base-free' enolate **4b**, but moderately more selective than the related lithium enolate-secondary amine complex (e.g. **4a** or [D_{11}]-**4c**) (Schemes 3–5). The levels of *D*-incorporation were found to be highly dependent on the structural nature of the enol precursor, amine and deuterium donor used. With this information in hand, it appears the enol acetate **10** gave higher levels of *D*-incorporation than the corresponding silyl enol ether **5**, and mild deuterium donors, like D_2O and [D_4]-MeOH gave better *D*-incorporation (Schemes 7 and 8). The optimum conditions appear to favour the use of enol acetate **10**, dimethylbenzylamine **7** as the amine mediator and D_2O (3 equivalents) as the deuterium source (Scheme 7: Entry 8). The low levels of *D*-incorporation for mildly acidic deuterium donors (e.g. [D_4]-acetic acid) can be accounted for by competitive *N*- and *O*-deuteriation of the lithium enolate-amine complex **4d** to give the corresponding lithium enolate-ammonium salt complex **4e** and *D*-enol **11**, respectively (Scheme 9). Competitive *O*-deuteriation has been shown to lead to loss of the deuterium label[§] through random tautomerization on aqueous work-up to give unlabelled 2-methyl-tetralone **3**.[¶] By comparison, using a *D*-labelled ammonium salt itself as a

[§]This washing out of a deuterium label (from a *D*-enol) to give an unlabelled carbonyl derivative has previously been responsible for the lack of deuteriation for sterically hindered enolates.[13]
[¶]We have observed similar behaviour – Eames *et al.*[9] and Coumbarides *et al.* [12,14,15]

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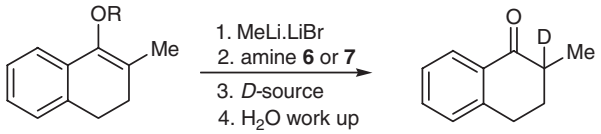
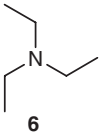


5; R = Me_3Si-
10; R = MeCO-

[D_1]-**3**



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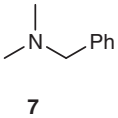

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Entry	*D*- source	silyl enol ether **5**; R = Me_3Si- [D]:[H]	Yield (%)	enol acetate **10**; R = MeCO- [D]:[H]	Yield (%)
1	D_2O (1 *equiv.*)	8:92	61	55:45	24
2	D_2O (3 *equiv.*)	55:45	61	66:34	53
3	[D_4]-MeOH (1 *equiv.*)	9:91	71	45:55	59
4	[D_4]-MeOH (3 *equiv.*)	35:65	63	62:38	52
5	[D_4]-acetic acid (1 *equiv.*)	1:99	77	50:50	29
6	[D_4]-acetic acid (3 *equiv.*)	22:78	74	46:54	68
7	D_2O (1 *equiv.*)	12:88	40	66:34	49
8	D_2O (3 *equiv.*)	13:87	54	81:19	54
9	[D_4]-MeOH (1 *equiv.*)	3:97	83	57:43	68
10	[D_4]-MeOH (3 *equiv.*)	7:93	66	67:33	56
11	[D_4]-acetic acid (1 *equiv.*)	3:97	46	26:74	80
12	[D_4]-acetic acid (3 *equiv.*)	8:92	43	56:44	42

Scheme 7.

deuterium donor has been shown to lead to moderate *D*-incorporation.[14] For less *D*-acidic donors, like D_2O and [D_4]-MeOH, competitive *N*-deuteriation appears to be less problematic. The increase in *D*-incorporation for enolate **4f** (derived from **10**) than enolate **4d** (derived from **5**) is more intriguing (Schemes 9 and 10). The only obvious difference between these two enolates is the presence of an additional basic species, lithium *tert*-butoxide **12** (within the enolate complex **4f**), formed by the addition of two equivalents of MeLi•LiBr to the acetate motif in **10** (Scheme 10). The presence of this additional additive appears to play an important role for mediating this regioselective *C*-deuteriation process. Kinetic formation of the additional deuterium source, *tert*-butyl alcohol [D_1]-**13**, could also in principle promote *C*-deuteriation (Scheme 10).[15]

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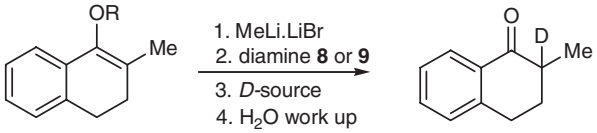
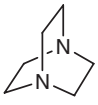


5; R = Me_3Si-
10; R = MeCO-

[D_1]-**3**



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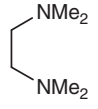

9

Entry	*D*- source	silyl enol ether **5**; R = Me_3Si- [D]:[H]	Yield (%)	enol acetate **10**; R = MeCO- [D]:[H]	Yield (%)
1	D_2O (1 *equiv.*)	6:94	63	47:53	67
2	D_2O (3 *equiv.*)	5:95	31	75:25	68
3	[D_4]-MeOH (1 *equiv.*)	5:95	77	31:69	39
4	[D_4]-MeOH (3 *equiv.*)	5:95	63	33:67	32
5	[D_4]-acetic acid (1 *equiv.*)	1:99	60	37:63	37
6	[D_4]-acetic acid (3 *equiv.*)	12:88	71	34:67	50
7	D_2O (1 *equiv.*)	12:88	83	61:39	37
8	D_2O (3 *equiv.*)	32:68	66	72:28	29
9	[D_4]-MeOH (1 *equiv.*)	1:99	83	55:45	60
10	[D_4]-MeOH (3 *equiv.*)	20:80	94	67:33	60
11	[D_4]-acetic acid (1 *equiv.*)	1:99	31	31:69	49
12	[D_4]-acetic acid (3 *equiv.*)	5:95	37	35:65	34

Scheme 8.

We next turned out attention towards a new class of conformationally restricted 1,2-diamine, such as (*rac*)-**14**, as a potential deuterium-enolate mediator (Scheme 11). This 1,2-diamine proved moderately successful for the lithium enolate-lithium *tert*-butoxide complex **4f** (derived from enol acetate **10**) allowing the required 2-deuterio-2-methyl-tetralone [D_1]-**3** to be formed with good levels of deuterium incorporation (from 84% using D_2O to 88% using [D_4]-acetic acid, respectively) (Scheme 11). By comparison, the related silyl enol ether **5** gave little *D*-incorporation (Scheme 11). In an attempt to extend this area, we next focused our attention on the enantioselective protonation of the enolates **4b** and **4f** (derived from **5** and **10** respectively) using an enantiomerically pure 1,2-diamine (*R*,*R*)-**15** as the chiral mediator (Scheme 12). Interestingly, the levels of differential facial protonation appear

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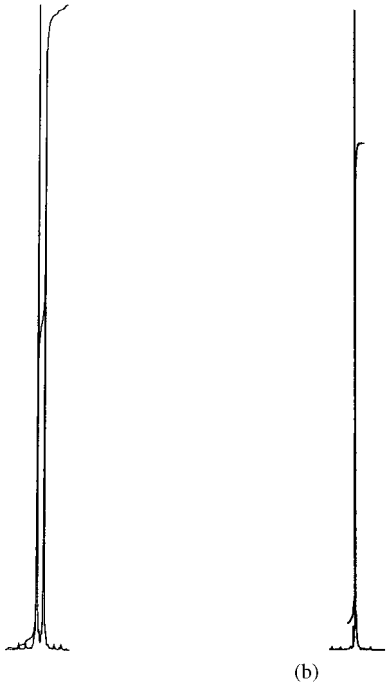

Figure 1. (a) Methyl doublet for 3, at 1.30 ppm ($^3J_{C,H} = 7.3$ Hz); (b) Methyl singlet for [D_1]-3, at 1.30 ppm.

to be better for the lithium enolate **4b** derived from the silyl enol ether **5** than the related enol acetate **10** even though the levels of deuterium transfer for related amines were much worse (Scheme 12).[‖] We are currently probing the mechanistic outcome of this type of enantioselective protonation/deuteriation versus regioselective *C*-deuteriation/protonation, and this study will be published in due course.

In conclusion, we have shown that efficient *C*-deuteriation of a given enolate was dependent on the structural nature of the deuterium donor (*D*-acidity and charge) and the structural nature of the residual base. *C*-Deuteriation in the presence of a residual amine can be improved by disfavouring competitive deuteriation using a weakly *D*-acidic deuterium source.** The deuterium donor must naturally favour *C*-deuteriation to give directly the required 2-deuterio-carbonyl derivative rather than *O*-deuteriation to form the related *D*-enol. This can be partially controlled by ensuring that the deuterium donor is weakly *D*-acidic (to prevent *D*-enol formation) and by using a *C*-directing

[‖] For enantioselective protonation of lithium enolates with reduced deuterium incorporation Yanagisawa *et al.*[18]

[**] Or by formation of a weakly *D*-basic amine to prevent internal proton return.[17] For further information see Eames *et al.*[9]

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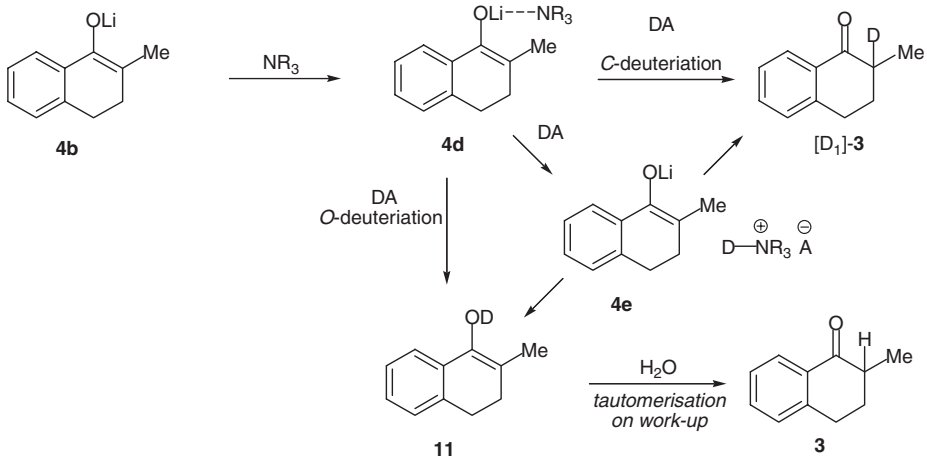
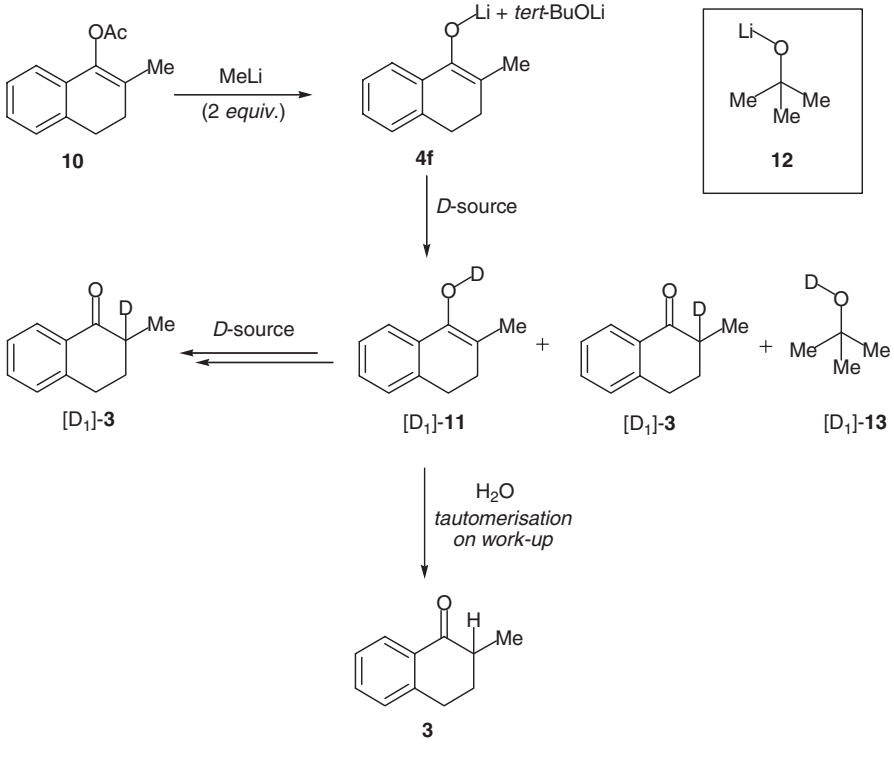


Scheme 9.



Scheme 10.

deuterium donor. The affect of *O*-deuteriation can be particularly problematic since this can lead to the unlabelled carbonyl derivative by 'washing-out' the deuterium label (from the *D*-enol) through tautomerization under aqueous work-up.

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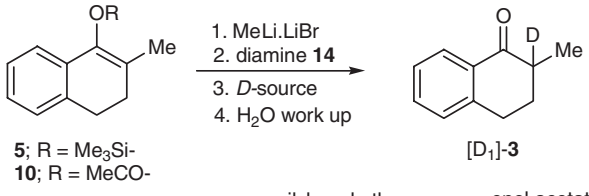
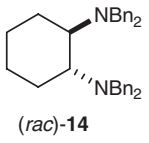


5; R = Me_3Si-
10; R = MeCO-

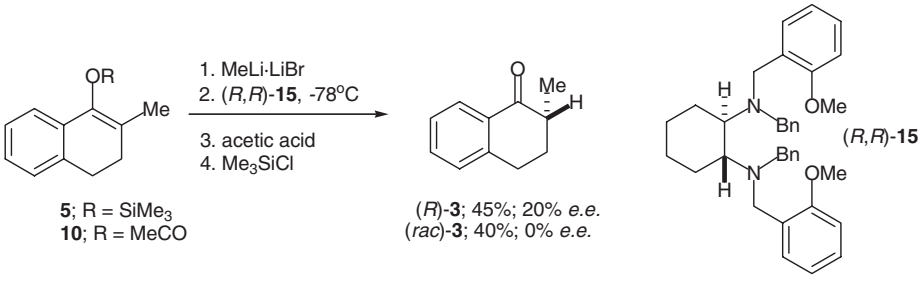
[D_1]-**3**



(*rac*)-**14**

Entry	*D*-source	silyl enol ether **5**; R = Me_3Si- [D]:[H]	Yield (%)	enol acetate **10**; R = MeCO- [D]:[H]	Yield (%)
1	D_2O (3 *equiv.*)	12:88	83	84:16	37
2	acetic acid-d_4 (3 *equiv.*)	6:94	77	88:12	36

Scheme 11.



5; R = $SiMe_3$
10; R = MeCO

(*R*)-**3**; 45%; 20% *e.e.*
(*rac*)-**3**; 40%; 0% *e.e.*

Scheme 12.

Experimental

All reactions were carried out under nitrogen using oven-dried glassware. Proton and carbon NMR spectra were recorded on a Bruker 250, 270 and 400 Fourier transform spectrometers 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 spectrometer and mass spectra were recorded on a Kratos 50MSTC spectrometer using a DS503 data system for high-resolution analysis. The levels of *D*-incorporation were determined by a combination of mass and proton NMR spectra.

Synthesis of 1-trimethylsilyloxy-2-methyl-tetral-1-ene **5**

2-Methyl-tetralone **3** (1.0 g, 6.25 mmol) was slowly added dropwise to a stirred solution of LDA (4.2 ml, 1.5 M in THF, 6.25 mmol) in THF (50 ml) at −78°C

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and stirred for 20 min. Trimethylsilyl chloride (0.70 g, 0.82 ml, 6.25 mmol) was added and this solution was stirred for 3 h. A solution of NH_4Cl (50 ml) was added and the mixture was extracted with diethyl ether (3×50 ml). The combined organic layers were dried ($MgSO_4$) 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):diethyl ether (19:1) to give the trimethylsilyloxy-2-methyl-tetral-1-ene **5**[9a] (1.23 g, 84%) as a colourless oil; R_F [light petroleum (40–60°C):diethyl ether (9:1)] 0.9; ν_{max}(film)/cm^{-1} 1657 (C═CO); 7.28 (1 H, d, $J = 6.8$, CH; Ar), 7.13–7.06 (3 H, m, $3 \times$ CH; Ar), 2.72 (2 H, t, $J = 7.7$, CH_2), 2.26 (2 H, t, $J = 7.7$, CH_2), 1.83 (3 H, s, CH_3) and 0.17 (9 H, s, (Si−$(CH_3)_3$); δ_C(100 MHz, $CDCl_3$) 141.8 (*i*-C; Ar), 135.3 (C═C–O), 133.7 (*i*-C; Ar), 126.4, 125.5, 125.0 and 120.9 ($4 \times$ CH; Ar), 116.3 (C═C–O), 29.8 (CH_2), 27.6 (CH_2), 16.7 (C═CCH_3) and 0.3 (Si−$(CH_3)_3$) (found M^+, 232.1274. $C_{14}H_{20}OSi$, requires M^+ 232.1283).

Synthesis of 3,4-dihydro-2-methylnapthal-1-enyl acetate **10**

2-Methyl-tetralone **3** (2.00 g, 12.5 mmol) was added to a solution of acetic anhydride (1.28 g, 12.5 mmol) and perchloric acid (2 drops) in dry carbon tetrachloride (30 ml) under nitrogen. The vessel was left at room temperature for 24 h, by which time a black oil had formed upon the surface. The mixture was cooled in ice and treated with saturated sodium hydrogen carbonate solution (20 ml) then fully neutralized with solid $NaHCO_3$ (circa 3 g) with vigorous stirring. The organic layer was extracted into diethyl ether (3×30 ml), washed with aqueous ammonium chloride dried over magnesium sulfphate and concentrated under reduced pressure. The residue was subject to column chromatography (light petroleum 40–60°C:diethyl ether 19:1) to give 3,4-dihydro-2-methylnapthal-1-enyl acetate **10**[9a] (2.36 g, 93%) as pale yellow plate like crystals; R_F [light petroleum 40–60°C:diethyl ether (9:1)] 0.33; ν_{max}(NaCl)/cm^{-1} 1734 (C = O); δ_H(270 MHz, $CDCl_3$) 7.15–7.00 (4 H, m, $4 \times$ CH; Ar), 2.85 (2 H, t, $J = 7.5$, CH_2), 2.39 (2 H, t, $J = 7.5$, CH_2) and 2.31 (3 H, s, CH_3C = O), 1.54 (3 H, s, CH_3C); δ_C(100 MHz, $CDCl_3$) 169.0 (C = O), 140.2 (*i*-C; Ar), 135.4 (O*C*═C), 131.1 (*i*-C; Ar), 127.1, 126.5, 126.0 and 124.3 ($4 \times$ CH; Ar), 120.2 (OC═*C*), 29.0 (CH_2) and 27.6 (CH_2), 20.7 (*C*H_3C═O) and 17.0 (CH_3C═C) (found MH^+, 203.1073. $C_{13}H_{15}O_2$ requires MH^+ 203.1072).

Representative procedure for deuteriation of enolate **4b** *derived from the silyl enol ether* **5**

A solution of MeLi (0.43 ml, 1 M in diethyl ether, 0.43 mmol) was added dropwise to the silyl enol ether **5** (0.1 g, 0.43 mmol) at room temperature. The resulting solution was stirred for 1 h. THF (3 ml) was then added and the

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solution cooled to −78°C. The chosen deuterium source {e.g. [D_4]-acetic acid (64 mg, 1 mmol)} was then added and the solution stirred for 30 min. A solution of NH_4Cl (saturated, 10 ml) was added and the mixture was extracted with diethyl ether (3 × 20 ml). The combined organic layers were dried ($MgSO_4$) 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):diethyl ether (19:1) to give 2-deuterio-2-methyl-tetralone [D_1]-**3** (47 mg, 68%) ([D]:[H] = >95:<5) as an oil; R_F [light petroleum (40–60°C):diethyl ether (9:1)] 0.5; ν_{max}(film)/cm^{-1} 2106 (C-D) and 1683 (CO); δ_H (250 MHz, $CDCl_3$) 8.00 (1 H, d, J = 7.7, CH; Ar), 7.47 (1 H, d, J = 7.7, CH; Ar), 7.25 (1 H, t, J = 7.7, CH; Ar), 7.22 (1 H, d, J = 7.7, CH; Ar), 3.00 (2 H, m, CH_2CH = C), 2.20 (1 H, dt, J = 13.2 and 4.4, CH_AH$_B$), 1.87 (1 H, m, CH$_A$H$_B$) and 1.28 (3 H, s, CH_3CD); δ_C (62.5 MHz, $CDCl_3$) 200.8 (C = O), 144.2 (*i*-C; Ar), 133.1 (*i*-C; Ar), 132.4, 128.7, 127.4 and 126.6 (4 × CH; Ar), 42.0 (1 C, t [1:1:1], $J_{C\text{-}D}$ = 19.0, CDMe), 31.3 (CH_2), 28.8 (CH_2) and 15.3 (CH_3) (found MH$^+$, 162.1034. $C_{11}H_{12}DO$ requires MH, 162.1029); m/z 162 (100%, M). The isotopic shift was 0.5 ppm (75.4 Hz at 150 MHz).

Representative procedure for deuteriation of enolate **4f** *derived from the enol acetate* **10**

A solution of MeLi (0.61 ml, 1.6 M in diethyl ether, 0.99 mmol) was added dropwise to the enol acetate **10** (0.1 g, 0.49 mmol) at room temperature. This resulting solution was stirred for 1 h at room temperature and cooled to −78°C. The chosen deuterium source {e.g. [D_4]-acetic acid (90 mg, 0.08 ml, 1.44 mmol)} in THF (1 ml) was added dropwise to this solution and the mixture stirred for a further 30 min. The reaction was quenched by the addition of water (10 ml). The solution was extracted with ether (3 × 20 ml), dried (over $MgSO_4$) and evaporated under vacuum. The residue was purified by flash chromatography on silica gel eluting with light petroleum (40–60°C):ether (9:1) to give 2-deuterio-2-methyl-tetralone-[D_1]-**3** (55 mg, 70%) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by* Et_3N **6**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (47 mg, 0.23 mmol), methyl lithium (0.29 ml, 0.47 mmol, 1.6 M in diethyl ether), triethylamine **6** (23 mg, 0.23 mmol) in THF (1 ml) and D_2O (5 mg, 0.23 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (9 mg, 24%) ([D]:[H] = 55:45) as an oil, which was spectroscopically identical to that previously obtained.

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Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by* Et_3N **6**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (49 mg, 0.24 mmol), methyl lithium (0.31 ml, 0.49 mmol, 1.6 M in diethyl ether), triethylamine **6** (24 mg, 0.24 mmol) in THF (1 ml) and D_2O (15 mg, 0.73 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (20 mg, 53%) ([D]:[H] = 66:34) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by* Et_3N **6**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (49 mg, 0.24 mmol), methyl lithium (0.31 ml, 0.49 mmol, 1.6 M in diethyl ether), triethylamine **6** (24 mg, 0.24 mmol) in THF (1 ml) and [D_4]-methanol (26 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (23 mg, 59%) ([D]:[H] = 62:38) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by* Et_3N **6**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (55 mg, 0.27 mmol), methyl lithium (0.34 ml, 0.54 mmol, 1.6 M in diethyl ether), triethylamine **6** (27 mg, 0.27 mmol) in THF (1 ml) and [D_4]-methanol (10 mg, 0.27 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (23 mg, 52%) ([D]:[H] = 45:55) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by* Et_3N **6**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), triethylamine **6** (24 mg, 0.24 mmol) in THF (1 ml) and [D_4]-acetic acid (15 mg, 0.24 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (11 mg, 29%) ([D]:[H] = 50:50) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by* Et_3N **6**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (46 mg, 0.23 mmol), methyl lithium (0.29 ml, 0.46 mmol, 1.6 M in diethyl ether), triethylamine **6** (23 mg, 0.23 mmol) in THF (1 ml) and [D_4]-acetic acid

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(44 mg, 0.69 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (25 mg, 68%) ([D]:[H] = 46:54) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by* Et_3N **6**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.25 mmol, 1.6 M in diethyl ether), triethylamine **6** (26 mg, 0.26 mmol) in THF (1 ml) and D_2O (5 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (25 mg, 61%) ([D]:[H] = 8:92) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by* Et_3N **6**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.25 mmol, 1.6 M in diethyl ether), triethylamine **6** (26 mg, 0.26 mmol) in THF (1 ml) and D_2O (15 mg, 0.77 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-3,4-dihydronaphthylene-1-one [D_1]-**3** (25 mg, 61%) ([D]:[H] = 55:45) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by* Et_3N **6**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.25 mmol, 1.6 M in diethyl ether), triethylamine **6** (26 mg, 0.26 mmol) in THF (1 ml) and [D_4]-methanol (9 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (30 mg, 71%) ([D]:[H] = 9:91) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by* Et_3N **6**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.25 mmol, 1.6 M in diethyl ether), triethylamine **6** (26 mg, 0.26 mmol) in THF (1 ml) and [D_4]-methanol (28 mg, 0.78 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (26 mg, 63%) ([D]:[H] = 35:65) as an oil, which was spectroscopically identical to that previously obtained.

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Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by* Et_3N **6**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.25 mmol, 1.6 M in diethyl ether), triethylamine **6** (26 mg, 0.26 mmol) in THF (1 ml) and [D_4]-acetic acid (17 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (32 mg, 77%) ([D]:[H] = 1:99) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by* Et_3N **6**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.25 mmol, 1.6 M in diethyl ether), triethylamine **6** (26 mg, 0.26 mmol) in THF (1 ml) and [D_4]-acetic acid (50 mg, 0.78 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (31 mg, 74%) ([D]:[H] = 22:78) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (32 mg, 0.24 mmol) in THF (1 ml) and D_2O (5 mg, 0.24 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (19 mg, 49%) ([D]:[H] = 66:34) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (46 mg, 0.23 mmol), methyl lithium (0.29 ml, 0.46 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (31 mg, 0.23 mmol) in THF (1 ml) and D_2O (4 mg, 0.69 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (20 mg, 54%) ([D]:[H] = 81:19) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (32 mg, 0.24 mmol) in THF (1 ml) and

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[D_4]-methanol (8 mg, 0.24 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (26 mg, 68%) ([D]:[H] = 57:43) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (49 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.49 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (32 mg, 0.24 mmol) in THF (1 ml) and [D_4]-methanol (26 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (22 mg, 56%) ([D]:[H] = 67:33) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (52 mg, 0.26 mmol), methyl lithium (0.33 ml, 0.52 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (35 mg, 0.26 mmol) in THF (1 ml) and [D_4]-acetic acid (16 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (33 mg, 80%) ([D]:[H] = 26:74) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (32 mg, 0.24 mmol) in THF (1 ml) and [D_4]-acetic acid (46 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (16 mg, 42%) ([D]:[H] = 56:44) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (35 mg, 0.26 mmol) in THF (1 ml) and D_2O (13 mg, 0.65 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (17 mg, 40%) ([D]:[H] = 12:88) as an oil, which was spectroscopically identical to that previously obtained.

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Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (35 mg, 0.26 mmol) in THF (1 ml) and D_2O (5.2 mg, 0.62 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (22 mg, 54%) ([D]:[H] = 13:87) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (35 mg, 0.26 mmol) in THF (1 ml) and [D_4]-methanol (9 mg, 0.24 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (34 mg, 83%) ([D]:[H] = 3:97) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (35 mg, 0.26 mmol) in THF (1 ml) and [D_4]-methanol (27 mg, 0.76 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (28 mg, 66%) ([D]:[H] = 7:93) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine 7 (29 mg, 0.22 mmol) in THF (1 ml) and [D_4]-acetic acid (50 mg, 0.78 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (19 mg, 46%) ([D]:[H] = 8:92) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by N,N-dimethyl benzylamine* **7**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), *N,N*-dimethyl benzylamine **7** (35 mg, 0.26 mmol) in THF (1 ml) and [D_4]-acetic acid

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(17 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (18 mg, 43%) ([D]:[H] = 3:97) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by DABCO* **8**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (60 mg, 0.26 mmol), methyl lithium (0.32 ml, 0.52 mmol, 1.6 M in diethyl ether), DABCO 8 (29 mg, 0.26 mmol) in THF (1 ml) and D_2O (5 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (28 mg, 67%) ([D]:[H] = 47:53) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by DABCO* **8**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (46 mg, 0.23 mmol), methyl lithium (0.29 ml, 0.46 mmol, 1.6 M in diethyl ether), DABCO **8** (26 mg 0.23 mmol) in THF (1 ml) and D_2O (14 mg, 0.69 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (25 mg, 68%) ([D]:[H] = 75:25) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by DABCO* **8**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (55 mg, 0.27 mmol), methyl lithium (0.34 ml, 0.54 mmol, 1.6 M in diethyl ether), DABCO **8** (30 mg, 0.27 mmol) in THF (1 ml) and [D_4]-methanol (10 mg, 0.27 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (17 mg, 39%) ([D]:[H] = 31:69) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by DABCO* **8**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (46 mg, 0.23 mmol), methyl lithium (0.29 ml, 0.46 mmol, 1.6 M in diethyl ether), DABCO **8** (26 mg, 0.23 mmol) in THF (1 ml) and [D_4]-methanol (25 mg, 0.69 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (12 mg, 32%) ([D]:[H] = 33:67) as an oil, which was spectroscopically identical to that previously obtained.

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Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by DABCO* **8**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (50 mg, 0.25 mmol), methyl lithium (0.31 ml, 0.50 mmol, 1.6 M in diethyl ether), DABCO **8** (28 mg, 0.25 mmol) in THF (1 ml) and [D_4]-acetic acid (16 mg, 0.25 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (15 mg, 37%) ([D]:[H] = 37:63) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by DABCO* **8**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), DABCO **8** (27 mg, 0.24 mmol) in THF (1 ml) and [D_4]-acetic acid (46 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (19 mg, 50%) ([D]:[H] = 34:67) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by DABCO* **8**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), DABCO **8** (29 mg, 0.26 mmol) in THF (1 ml) and D_2O (5.2 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (26 mg, 63%) ([D]:[H] = 6:94) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by DABCO* **8**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), DABCO **8** (29 mg, 0.26 mmol) in THF (1 ml) and D_2O (15 mg, 0.78 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (13 mg, 31%) ([D]:[H] = 5:95) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by DABCO* **8**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), DABCO **8** (29 mg, 0.26 mmol) in THF (1 ml) and [D_4]-methanol (9 mg,

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0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (32 mg, 77%) ([D]:[H] = 5:95) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by DABCO* **8**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (60 mg, 0.26 mmol), methyl lithium (0.16 ml, 0.26 mmol, 1.6 M in diethyl ether), DABCO **8** (29 mg, 0.26 mmol) in THF (1 ml) and [D_4]-methanol (28 mg, 0.78 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (26 mg, 63%) ([D]:[H] = 5:95) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by DABCO* **8**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), DABCO **8** (24 mg, 0.22 mmol) in THF (1 ml) and [D_4]-acetic acid (14 mg, 0.22 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (21 mg, 60%) ([D]:[H] = 1:99) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by DABCO* **8**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), DABCO **8** (24 mg, 0.22 mmol) in THF (1 ml) and [D_4]-acetic acid (42 mg, 0.66 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (25 mg, 71%) ([D]:[H] = 12:88) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by TMEDA* **9**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (50 mg, 0.25 mmol), methyl lithium (0.31 ml, 0.50 mmol, 1.6 M in diethyl ether), TMEDA **9** (29 mg, 0.25 mmol) in THF (1 ml) and D_2O (5 mg, 0.25 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (15 mg, 37%) ([D]:[H] = 61:39) as an oil, which was spectroscopically identical to that previously obtained.

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Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by TMEDA* **9**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), TMEDA **9** (28 mg, 0.24 mmol) in THF (1 ml) and D_2O (15 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (11 mg, 29%) ([D]:[H] = 72:28) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by TMEDA* **9**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (53 mg, 0.26 mmol), methyl lithium (0.32 ml, 0.52 mmol, 1.6 M in diethyl ether), TMEDA **9** (30 mg, 0.26 mmol) in THF (1 ml) and [D_4]-methanol (9 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (22 mg, 60%) ([D]:[H] = 55:45) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by TMEDA* **9**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (46 mg, 0.23 mmol), methyl lithium (0.29 ml, 0.46 mmol, 1.6 M in diethyl ether), TMEDA **9** (27 mg, 0.23 mmol) in THF (1 ml) and [D_4]-methanol (25 mg, 0.69 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (31 mg, 73%) ([D]:[H] = 67:33) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by TMEDA* **9**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (53 mg, 0.26 mmol), methyl lithium (0.32 ml, 0.52 mmol, 1.6 M in diethyl ether), TMEDA **9** (30 mg, 0.26 mmol) in THF (1 ml) and [D_4]-acetic acid (16 mg, 0.26 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (21 mg, 49%) ([D]:[H] = 31:69) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4f** *derived from enol acetate* **10** *mediated by TMEDA* **9**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), TMEDA **9** (28 mg, 0.24 mmol) in THF (1 ml) and [D_4]-acetic acid

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(46 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (13 mg, 34%) ([D]:[H] = 35:65) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by TMEDA* **9**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), TMEDA **9** (25 mg, 0.22 mmol) in THF (1 ml) and D_2O (4.4 mg, 0.22 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (29 mg, 83%) ([D]:[H] = 12:88) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by TMEDA* **9**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), TMEDA **9** (25 mg, 0.22 mmol) in THF (1 ml) and D_2O (13 mg, 0.65 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (23 mg, 66%) ([D]:[H] = 32:68) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by TMEDA* **9**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), TMEDA **9** (25 mg, 0.22 mmol) in THF (1 ml) and [D_4]-methanol (8 mg, 0.24 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (29 mg, 83%) ([D]:[H] = 1:99) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by TMEDA* **9**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), TMEDA **9** (25 mg, 0.22 mmol) in THF (1 ml) and [D_4]-methanol (24 mg, 0.71 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-3,4-tetralone [D_1]-**3** (33 mg, 94%) ([D]:[H] = 20:80) as an oil, which was spectroscopically identical to that previously obtained.

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Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by TMEDA* **9**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), TMEDA **9** (25 mg, 0.22 mmol) in THF (1 ml) and [D_4]-acetic acid (14 mg, 0.22 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (11 mg, 31%) ([D]:[H] = 1:99) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by TMEDA* **9**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), TMEDA **9** (25 mg, 0.22 mmol) in THF (1 ml) and [D_4]-acetic acid (42 mg, 0.65 mmol) in THF (0.5 ml) gave 2-deuterio-tetralone [D_1]-**3** (13 mg, 37%) ([D]:[H] = 5:95) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from enol acetate* **10** *mediated by tetrabenzyl-1,2-diamine (rac)*-**14**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), tetrabenzyl-1,2-diamine (*rac*)-**14** (0.11 g, 0.24 mmol) in THF (1 ml) and [D_4]-acetic acid (46 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (14 mg, 36%) ([D]:[H] = 88:12) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from enol acetate* **10** *mediated by tetrabenzyl-1,2-diamine (rac)*-**14**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (48 mg, 0.24 mmol), methyl lithium (0.30 ml, 0.48 mmol, 1.6 M in diethyl ether), tetrabenzyl-1,2-diamine (*rac*)-**14** (0.11 g, 0.24 mmol) in THF (1 ml) and D_2O (14 mg, 0.72 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (14 mg, 37%) ([D]:[H] = 84:16) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by tetrabenzyl-1,2-diamine (rac)*-**14**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), tetrabenzyl-1,2-diamine (*rac*)-**14** (0.1 g, 0.22 mmol) in THF (1 ml) and D_2O

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(13 mg, 0.65 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (29 mg, 83%) ([D]:[H] = 12:88) as an oil, which was spectroscopically identical to that previously obtained.

Deuteriation of lithium enolate **4b** *derived from silyl enol ether* **5** *mediated by tetrabenzyl-1,2-diamine (rac)*-**14**

In the same way as above, 1-trimethylsiloxy-2-methyl-tetral-1-ene **5** (51 mg, 0.22 mmol), methyl lithium (0.14 ml, 0.22 mmol, 1.6 M in diethyl ether), tetrabenzyl-1,2-diamine **14** (0.1 g, 0.22 mmol) in THF (1 ml) and [D_4]-acetic acid (42 mg, 0.65 mmol) in THF (0.5 ml) gave 2-deuterio-2-methyl-tetralone [D_1]-**3** (27 mg, 77%) ([D]:[H] = 6:94) as an oil, which was spectroscopically identical to that previously obtained.

Synthesis of 2-Methyl Tetralone (R)-3: representative experimental procedure for the enantioselective protonation of enolate 4b (derived from silyl enol ether 5) using 1,2-diamine (R,R)-**15**

A solution of MeLi (0.10 ml, 1.50 M in ether, 0.15 mmol) was added dropwise to the silyl enol ether **5** (35 mg, 0.15 mmol) at room temperature. The resulting solution was stirred for 30 min and then cooled to –78°C. A pre-cooled solution of 1,2-diamine (*R*,*R*)-**15** (80 mg, 0.15 mmol) in THF (1 ml) at –78°C was slowly added, and the resulting solution was stirred for 1 h. Acetic acid (29 mg, 0.45 mmol) was added and the resulting solution stirred for 15 min. A saturated solution of $NaHCO_3$ was added and the resulting solution was extracted with ether (3 × 10 ml). The organic phase was washed again with a saturated solution of $NaHCO_3$ and the solvent was removed under vacuum. The residue was purified by flash chromatography on silica gel eluting with light petroleum:ether (19:1) to give 2-methyl-1-tetralone (*R*)-**3**[18] (11 mg, 57%) as a colourless oil with 20% enantiomeric excess (determined by chiral HPLC using a Chiralcel OD column[18],[††] – solvent hexane:isopropyl alcohol (98:2): flow rate: 0.7 ml/min; retention time (*S*)-enantiomer 10.8 min, (*R*)-enantiomer 11.6 min); R_F [light petroleum (40–60°C):ether (9:1)] 0.5; ν_{max}(film)/cm^{-1} 1686 (CO); δ_H(250 MHz, $CDCl_3$) 8.00 (1 H, d, J = 7.7, CH; Ar), 7.47 (1 H, dd, J = 7.7 and 7.6, CH; Ar), 7.25 (1 H, t, J = 7.7, CH; Ar), 7.22 (1 H, d, J = 7.6, CH; Ar), 3.00 (2 H, m, $CH_2C{=}C$), 2.60 (1 H, m, CHMe), 2.20 (1 H, dt, J = 13.2 and 4.4, CH_AH_B), 1.87 (1 H, m, CH_AH_B) and 1.28 (3 H, d, J = 7.3, MeCH); δ_C(62.5 MHz, $CDCl_3$) 200.8 (C = O), 144.2 (*i*-C; Ar), 133.1 (*i*-C; Ar), 132.4, 128.7, 127.4 and 126.6 (4 × CH; Ar), 42.0 (*C*HMe), 31.3 (CH_2), 28.8 (CH_2) and 15.3 (CH_3) (Found M^+, 160.0882. $C_{11}H_{12}O$ requires M^+, 160.0882); m/z 160.1 (100%, M). The purity was > 99% determined by HPLC.

[††] For 2-methyl-tetralone **3**; solvent hexane:isopropyl alcohol (98:2): flow rate: 0.5 ml/min; retention time (*R*)-enantiomer 14.4 min, (*S*)-enantiomer 13.1 min.

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Enantioselective protonation of enolate 4f derived from enol acetate 10 mediated by 1,2-diamine (R,R)-**15**

In the same way as above, 3,4-dihydro-2-methylnapthal-1-enyl acetate **10** (30 mg, 0.15 mmol), methyl lithium (0.19 ml, 0.30 mmol, 1.6 M in diethyl ether), 1,2-diamine (*R*,*R*)-**15** (80 mg, 0.15 mmol) in THF (1 ml) and [D_4]-acetic acid (29 mg, 0.45 mmol) in THF (0.5 ml) gave 2-methyl-tetralone (*rac*)-**3** (10 mg, 40%) as an oil, which was spectroscopically identical to that previously obtained.

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