SYNTHESIS OF $[11-{}^{2}H_{2}]$, $[8-{}^{2}H_{2}]$, $[7-{}^{2}H_{2}]$, $[6-{}^{2}H_{2}]$, $[5-{}^{2}H_{2}]$, $[4-{}^{2}H_{2}]$ and $[3-{}^{2}H_{2}]$ cis-9-OCTADECENOATES***

A.P. TULLOCH

National Research Council of Canada, Prairie Regional Laboratory, Saskatoon, Saskatchewan S7N OW9 (Canada)

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Deuterated oleates have been synthesized by semihydrogenation of acetylenic intermediates. $[11^{-2}H_{2}]$ Oleate was prepared by two-carbon chain extension of the C₁₆ alcohol obtained from $[1^{-2}H_{2}]$ octyl bromide and 7-octyn-1-ol. $[8^{-2}H_{2}]$ and $[7^{-2}H_{2}]$ oleates were both prepared from dimethyl suberate, tetradeutero intermediate C₁₆ alcohols were synthesized from $[1,8^{-2}H_{4}]$ and $[2,7^{-2}H_{4}]$ octane diols by monobromination, conversion to deuterated 9-decyn-1-ols and reaction with octyl bromide. Oxidation gave $[8^{-2}H_{2}]^{-9}$ -octadecynoate and $[2,7^{-2}H_{4}]^{-9}$ -octadecynoate, after semihydrogenation of the latter, deuterons at C-2 were removed by exchange with aqueous alkali. $[6^{-2}H_{2}]$ and $[5^{-2}H_{2}]^{-2}$ and two malonate extensions gave $[6^{-2}H_{2}]^{-2}$ oleate; reduction with lithium aluminum deuteride, two malonate extensions and semihydrogenation gave the $[5^{-2}H_{2}]$ ester. $[4^{-2}H_{2}]$ and $[3^{-2}H_{2}]^{-2}$ loeates were both obtained from methyl 7-cis-hexadecenoate, exchange of the α protons and chain extension gave the $[3^{-2}H_{2}]^{-2}$ ester.

Introduction

Specifically dideuterated fatty acids have been used in investigations of membrane structure [1,2], of ¹³C NMR spectra [3-6] and in medical studies where non-radioactive isotope labelling is necessary [7]. Previously syntheses of $[18-{}^{2}H_{3}]$, $[17-{}^{2}H_{2}]$, $[16-{}^{2}H_{2}]$, $[14-{}^{2}H_{2}]$ and $[12-{}^{2}H_{2}]$ oleates were described [8] and $[2-{}^{2}H_{2}]$ oleate [9] and $[11-{}^{2}H_{2}]$ oleate [10] have also been synthesized. A new more convenient, synthesis of $[11-{}^{2}H_{2}]$ oleate and synthesis of the remaining gem dideutero oleates, in which deuterium is attached to carbons on the ester side of the double bond, are now discussed.

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Results and discussion

 $[11-{}^{2}H_{2}]$ Oleate was prepared by the acetylenic route employed previously [8], methyl octanoate was reduced with lithium aluminum deuteride, the $[1-{}^{2}H_{2}]$ -octanol brominated with triphenylphosphine dibromide and the $[1-{}^{2}H_{2}]$ octyl bromide allowed to react with the tetrahydropyranyl ether of 7-octyn-1-ol to give $[9-{}^{2}H_{2}]$ -7-hexadecyn-1-ol. The chain was lengthened by malonate synthesis and the oleate obtained by semihydrogenation.

Syntheses of $[8^{-2}H_2]$ and $[7^{-2}H_2]$ oleates both began with dimethyl suberate (see Fig. 1); since it was difficult to prepare a suitable intermediate deuterated at only one end, a C₈ intermediate deuterated at both ends was used and the extra deuterons were removed in one of the last steps in the synthesis. Reduction of the C₈ diester with lithium aluminum deuteride gave $[1,8^{-2}H_4]$ octane-1,8-diol which was monobrominated with hydrogen bromide to the tetradeutero 8-bromooctanol. Reaction as the tetrahydropyranyl ether with lithium acetylide gave $[1,8^{-2}H_4]$ -9-decyn-1-ol and further reaction with octyl bromide gave $[1,8^{-2}H_4]$ -

CH₃O₂C (CH₂)₆CO₂CH₃

$$\downarrow$$
 LiAID₄
HOD₂C (CH₂)₆CD₂OH
 \downarrow HBr
BrD₂C (CH₂)₆CD₂OH
 \downarrow LiC = CH . H₂N CH₂CH₂NH₂
HC = CCD₂(CH₂)₆CD₂OH
 \downarrow LiNH₂ , CH₃(CH₂)₆CH₂Br
CH₃(CH₂)₇C = CCD₂(CH₂)₆CD₂OH
 \downarrow CrO₃
CH₃(CH₂)₇C = CCD₂(CH₂)₆CO₂H
 \downarrow H₂
CH₃(CH₂)₇CH = CHCD₂(CH₂)₆CO₂H
Fig. 1. Synthesis of [8-³H₃]-cis-9-octadecenoic acid.

9-octadecyn-1-ol. Oxidation removed the deuterons at C-1 and at the same time gave $[8^{-2}H_2]$ stearolic acid, semihydrogenation then yielded $[8^{-2}H_2]$ oleate.

 $[7-{}^{2}H_{2}]$ Oleate was prepared by a similar series of reactions except that, initially, both pairs of α protons of suberic acid were replaced by deuterons by exchange with alkaline deuterium oxide at 200°C and the tetradeutero C₈ diacid was reduced to $[2,7-{}^{2}H_{4}]$ octane-1,8-diol with lithium aluminum hyride. The intermediate $[2,7-{}^{2}H_{4}]$ -9-octadecynoic acid was semihydrogenated to $[2,7-{}^{2}H_{4}]$ oleic acid and the α deuterons were then exchanged by reaction with 1% aqueous sodium hydroxide at 200°C.

To obtain $[5^{-2}H_2]$ and $[6^{-2}H_2]$ oleic acids, 5-hexyn-1-ol tetrahydropyranyl ether was prepared in the usual way from 4-chlorobutanol, converted by alkylation with octyl bromide to 5-tetradecyn-1-ol and oxidized to 5-tetradecynoic acid. For conversion to $[5^{-2}H_2]$ oleate the acid was reduced with lithium aluminum deuteride to the $[1^{-2}H_2]$ alcohol (Fig. 2). Malonate chain extensions using intermediate mesylates [8,11] then yielded $[5^{-2}H_2]$ stearolic acid and semihydrogenation gave $[5^{-2}H_2]$ oleic acid. It is desirable, where possible in these series of reactions, to retain the triple bond until the last stage because the acetylenic intermediates with 14–18 carbons can all be purified by crystallization whereas most olefinic intermediates cannot. Also if the *cis* double bond is introduced earlier some isomerization to *trans* isomer may occur.

5-Tetradecynoic acid was also the starting point for synthesis of $[6^{-2}H_2]$ oleic acid but the α protons could not be exchanged due to extensive triple bond migration and polymerization. *cis*-5-Tetradecenoic acid was prepared by semihydrogenation and the $[2^{-2}H_2]$ acid prepared by exchange. Two malonate chain extensions

$$CH_{3}(CH_{2})_{7} C \equiv C(CH_{2})_{3}CH_{2}OH$$

$$\downarrow CrO_{3}$$

$$CH_{3}(CH_{2})_{7}C \equiv C(CH_{2})_{3}CO_{2}H$$

$$\downarrow LiAID_{4}$$

$$CH_{3}(CH_{2})_{7}C \equiv C(CH_{2})_{3}CD_{2}OH$$

$$\downarrow MALONATE EXTENSION TWICE$$

$$CH_{3}(CH_{2})_{7}C \equiv C(CH_{2})_{3}CD_{2}(CH_{2})_{3}CO_{2}H$$

$$\downarrow H_{2}$$

$$CH_{3}(CH_{2})_{7}CH = CH(CH_{2})_{3}CD_{2}(CH_{2})_{3}CO_{2}H$$
Fig. 2. Synthesis of [5-³H_{3}]-cis-9-octadecenoic acid.

then yielded $[6^{-2}H_2]$ oleic acid, precautions were taken to prevent *cis* to *trans* isomerization and the product contained only 4.5% $[6^{-2}H_2]$ elaidic acid. The intermediate olefinic mesulates could not by crystallized from methanol but were stored in this solvent to remove acidic sulphur containing impurities. It was possible, however, to crystallize the olefinic malonic acid intermediates.

The $[4-{}^{2}H_{2}]$ and $[3-{}^{2}H_{2}]$ oleic acids were prepared by similar routes from *cis*-7-hexadecenoic acid. To prepare $[4-{}^{2}H_{2}]$ oleic acid the C₁₆ acid was exchanged to give $[2-{}^{2}H_{2}]$ -*cis*-9-hexadecenoic acid and the chain lengthened by two carbons. $[3-{}^{2}H_{2}]$ Oleic acid was obtained by lithium aluminum deuteride reduction of the C₁₆ acid and chain lengthening. Perhaps because sulphur containing impurities were not completely removed in the chain lengthening steps, the products contained 12% and 9% of the deuterated elaidic acids respectively and had to be purified by silver nitrate-silicic acid chromatography.

Specifically dideuterated oleic acids were thus prepared in overall yields from undeuterated starting materials of 20–40%. There was no evidence for loss of deuterium in any of the syntheses even during semihydrogenation of $[8-{}^{2}H_{2}]$ and $[11-{}^{2}H_{2}]$ stearolates where the deuterated carbon is adjacent to an unsaturated carbon. This result agrees with earlier work which showed that $[9,10-{}^{2}H_{2}]$ oleate could be obtained by partial reduction of stearolate with deuterium and Lindlar catalyst [12].

¹³C NMR spectra were recorded for all the deuterated stearolates and oleates, those of the stearolates are listed in Table I along with isotope effects. Chemical shifts of all carbons can be assigned unambiguously from isotope effects and agree with assignments reported by Gunstone et al. [13] from spectra of a large number of acetylenic acids with different chain lengths and triple bond positions. Effects of the triple bond on carbons on both sides of the bond were averaged and were $\alpha - 10.96$, $\beta - 0.54$, $\gamma - 0.84$, $\delta - 0.52$, $\epsilon - 0.13$, $\zeta - 0.07$ and $\eta - 0.04$, values which agree with the earlier results [13].

The effect of deuterium on signals of the triple bond carbons was of interest. In spectra of $[8-{}^{2}H_{2}]$ and $[11-{}^{2}H_{2}]$ stearolates the signal of the adjacent carbon, which in alkanes would have a second atom upfield displacement of about 0.2 ppm, showed a displacement of only -0.06 to -0.09 ppm; the line width was however, still increased 3-fold as is usually observed [3-6]. In these two spectra no displacement of the second triple bond carbon (third atom isotope effect) was observed and there was no line broadening (usually displacement of -0.05 ppm and appreciable line broadening is seen [3-6]). In the spectrum of $[2,7-{}^{2}H_{4}]$ stearolate the C-9 signal was not displaced but line width increased twofold.

Chemical shifts of the dideuterated oleates are listed in Table II, the spectra confirm the structures and also the assignments of signals for C-4, C-5 and C-6 made previously [4]. Effects on the unsaturated carbon signals in spectra of $[8-{}^{2}H_{2}]$ and $[11-{}^{2}H_{2}]$ oleates were unexpected, like those of corresponding stearolates. The second atom effect was -0.1 ppm but the third atom effect was a downfield displacement of 0.05 ppm and linewidth of both signals increased approximately

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CHEMICAL SHIFTS OF METHYL 9-OCTADECYNOATE AND OF METHYL [5-³H₄], [2,7-³H₄], [8-²H₄] and [11-²H₄]-9-OCTADECYNOATES In ppm from TMS isotope effects in parentheses.

Carbon	Stearolate ^a	Positions of deuterons			
		S	2,7	8	11
1	174.19	174.15	i	174.17	174.18
2	34.10	34.09	1	34.08	34.11
3	24.95	24.89 (-0.06)	24.82 (-0.13)	24.94	24.96
4	29.11	28.90 (-0.21)	29.05 (-0.06)	29.09	29.12
5	28.82		28.77 (-0.05)	28.82	28.82
6	28.67	28.45 (-0.22)	28.46 (-0.21)	28.60 (-0.07)	28.67
7	29.11	29.06 (-0.05)		28.91 (-0.20)	29.12
œ	18.77	18.75	18.56 (-0.21)		18.77
6	80.07	80.08	^b 80.07 (-0.00)	°79.98 (-0.09)	80.08 (+0.01)
10	80.33	80.33	80.32	80.32 (-0.01)	^c 80.27 (-0.06)
11	18.79	18.78	18.80	18.78	
12	29.22	29.21	29.25	29.21	29.04 (-0.18)
13	28.91	28.90	28.92	28.91	28.84 (-0.04)
14	29.17	29.16	29.17	29.16	29.18
15	29.25	29.25	29.25	29.25	29.26
16	31.89	31.88	31.89	31.88	31.90
17	22.69	22.68	22.69	22.68	22.67
18	14.09	14.07	14.09	14.09	14.09
^a Average values cal ^b Line broadened 2. ^c Line broadened 3.	culated from carbons no fold. fold.	ot affected by deuterium.			

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In ppm 1	rom TMS,	isotope effects in	parenthesis.			;		
Carbon	Oleate ^a	Positions of deu	terons					
		3	4	5	6	7	8	11
5	34.14	33.94 (-0.20)	34.08 (-0.06)	34.14	34.14	34.13	34.13	34.14
ŝ	25.00		24.80 (-0.20)	24.95 (-0.05)	25.02	25.00	25.01	25.00
4	29.19	28.97 (-0.22)	, , 1	28.96 (-0.23)	29.14 (-0.05)	29.19	29.19	29.18
S	29.19	29.14 (-0.05)	29.00 (-0.19)	, , ,	29.03 (-0.16)	29.15 (-0.04)	29.19	29.18
9	29.14	29.14	29.08 (-0.06)	28.96 (-0.18)		28.93 (-0.21)	29.08 (-0.06)	29.13
7	29.73	29.72	29.74	29.67 (-0.06)	29.57 (-0.16)	1	29.57 (-0.16)	29.73
œ	27.20	27.19	27.20	27.22	27.17 (-0.03)	27.02 (-0.18)	1	27.21
6	129.77	I	ı	129.76	129.78	129.74 ^b (-0.03)	129.66 ^c (-0.11)	129.82 (+0.05)
10	130.00	ł	l	130.00	130.01	129.99	130.04 ^c (+ 0.04)	129.91 (-0.09)
8 A verso	a valnee fer	un cerhone not ef	facted by dantari					

CHEMICAL SHIFTS OF CARBONS 2 TO 10 OF METHYL DIDEUTERATED OLEATES

TABLE II

umuanad 2 ⁻ Average values from carbons: ^b Signal broadened 1.5 times ^c Signal broadened 2 times

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2-fold. ¹³C NMR spectra of deuterated olefinic and acetylenic compounds with deuterium substitution close to unsaturated carbons, do not seem to have been investigated before but the present results show that the isotope effects differ from those observed for compounds with CD_2 groups separated from the unsaturated carbons by several methylene groups.

Materials and methods

Mass spectrometry, gas liquid chromatography (including determination of *cis* and *trans* isomers) and column chromatography were carried out as previously described [8] and ¹³C NMR spectra in deuterochloroform were obtained with a Varian XL-100-15 spectrometer in the Fourier transform mode at 25.16 MHz with proton noise decoupling. Reduction with lithium aluminum deuteride was performed as before [9].

Methyl $[11-{}^{2}H_{2}]$ -cis-9-octadecenoate

Methyl octanoate was reduced with lithium aluminum deuteride and bromination of the resulting alcohol with triphenylphosphine dibromide [14] gave $[1-{}^{2}H_{2}]$ octyl bromide. Reaction with the lithium derivative of the tetrahydropyranyl ether of 7-octyn-1-ol [15] as previously reported [8] and cleavage of the ether gave $[9-{}^{2}H_{2}]$ -7-hexadecyn-1-ol. Malonate extension [8,11] then yielded $[11-{}^{2}H_{2}]$ -9-octadecynoic acid and esterification and semihydrogenation in ethanol over Lindlar catalyst gave methyl $[11-{}^{2}H_{2}]$ -cis-9-octadecenoate. The product contained 98.2% cis isomer and was 97% dideuterated; the overall yield from methyl octanoate was 38%.

Methyl $[8^{-2}H_2]$ -cis-9-octadecenoate

Dimethyl suberate (50.5 g) was reduced with lithium aluminum deuteride (13.4 g) and gave an apparently quantitative yield of $[1,8-^{2}H_{4}]$ octane-1,8-diol which was used without purification. A mixture of the diol (38.2) and hydrogen bromide (48%, 130 ml) was heated at 75°C for 24 h while being continuously extracted with heptane [16]. The heptane layer was extracted twice with 80% aqueous methanol (300 ml portions) and three times with 65% aqueous methanol (W.F. Steck, pers. comm.) and methanol removed from combined extracts. Crude bromoalcohol was separated from water by methylene chloride extraction and distilled at 0.1 mm, the b.p. was 100–108°C and yield was 33 g. The tetrahydropyranyl ether (45.9 g, b.p./0.1 mm 121–124°C) was prepared in the usual way and converted to the ether of $[1,8-^{2}H_{4}]$ -9-decyn-1-ol by reaction with the lithium acetylide/ethylene diamine complex as previously described [15]. The undistilled ether (34.7 g) was treated with lithium amide (4.2 g) in ethylene glycol dimethyl ether (225 ml) and the mixture refluxed with octyl bromide (35.7 g) [8]. The

ether group was removed with *p*-toluenesulphonic acid and methanol and $[1,8-{}^{2}H_{4}]$ -9-octadecyn-1-ol (25.2 g, b.p./0.1 mm 145–150°C) was obtained. The alcohol (25.2 g) was oxidized to $[8-{}^{2}H_{2}]$ -9-octacecynoic acid by the procedure described below for the preparation of 5-tetradecynoic acid and the acid converted to the methyl ester (18.0 g, b.p./0.1 mm 148°C). Methyl $[8-{}^{2}H_{2}]$ oleate was obtained by semihydrogenation and contained 98.7% oleate and was 97% dideuterated ester. The overall yield from dimethyl suberate was 24%.

Methyl $[7-^{2}H_{2}]$ -cis-9-octadecenoate

A mixture of dimethyl suberate (50.5 g) and sodium deuteroxide in deuterium oxide (from sodium (12.1 g) and deuterium oxide (125 ml)) was heated at 200°C for 3 days in a steel autoclave. The exchange reaction was repeated two further times, deuterium oxide being removed by freeze drying and replaced by fresh reagent each time. The solution was acidified with concentrated hydrochloric acid (100 ml) and cooled to 0°C and the precipitated [2,7-2H4] octanedioic acid (41.5 g) filtered and dried to constant weight. The acid was converted to dimethyl [2,7-²H₄]octanedioate (43.5 g) by refluxing with methanol (250 ml) containing concentrated sulphuric acid (2%), the ¹H NMR spectrum showed that no loss of deuterium occurred. Reduction of the diester with lithium aluminum hyride gave $[2.7-^{2}H_{4}]$ octanediol (32.2 g) and reaction with hydrogen bromide as described above gave [2,7-2H4]-8-bromooctan-1-ol (34.8 g). The series of reactions described above then yielded methyl $[2,7-^{2}H_{4}]$ -9-octadecynoate (26 g). The ester was semihydrogenated to the oleate derivative and hydrolyzed to the sodium salt and twice heated in 1% aqueous sodium hydroxide at 200°C for three days to yield $[7-{}^{2}H_{2}]$ -cis-9-octadecenoic acid. The methyl ester was prepared and contained 97.8% cis isomer and 98% dideuterated ester. The overall yield from dimethyl suberate was 32%.

Methyl $[6^{-2}H_2]$ -cis-9-octadecenoate

Methyl 5-tetradecynoate was first prepared as follows. Dihydropyran (100 g) was added to 4-chlorobutan-1-ol containing hydrogen chloride (109 g, Fluka AG) with stirring and cooling below 30°C. After 18 h the solution was stirred with sodium bicarbonate (10 g), filtered and distilled giving the tetrahydropyranyl ether of 4-chlorobutan-1-ol (170 g, b.p./0.1 mm 65-67°C). The ether (170 g) was added to a mixture of lithium acetylide ethylene diamine complex (100 g) in dimethyl sulphoxide (500 ml) with stirring and cooling below 25°C. After 18 h the reaction mixture was poured into ice water and product extracted with hexane, the yield of ether of 5-hexyn-1-ol after distillation (b.p./0.1 mm 66-68°C) was 132.6 g. A suspension of lithium amide (20 g) and the ether (132 g) in ethylene glycol dimethyl ether (700 ml) was refluxed for 3 h, octyl bromide (140.8 g) was added and reflux continued for 18 h. The reaction was decomposed with ice water

and product extracted with hexane, after removal of solvent the crude product was stirred in methanol (750 ml) containing p-toluenesulphonic acid (12 g) for 18 h at 24°C. The solution was neutralized (sodium bicarbonate), filtered, methanol distilled off, product taken up in methylene chloride, washed with water and dried over sodium sulphate. 5-Tetradecyn-1-ol (93.6 g, b.p./0.1 mm 115-125°C) was obtained by distillation.

The above alcohol (23.4 g) was dissolved in acetone (1 l), cooled to 15° C and a solution of chromium trioxide (16 g) in water (10 ml) and 25% sulphuric acid (62 ml) [17] added during 15 min with stirring and cooling below 25° C. After a further 30 min the mixture was poured into water (3.5 l), sulphur dioxide passed in and product extracted 4 times with ether. The oxidation was repeated three further times and the combined ether extracts were reduced in volume to 2 l. The ether solution was extracted twice with 5% aqueous potassium hydroxide (500 ml), combined alkali extracts washed twice with ether and ether solutions combined. The ether extract was washed with water which was added to the aqueous extracts, combined alkali extracts were acidified with concentrated hydrochloric acid (100 ml), acid was extracted with ether and dried. After isolation crude acid (87.8) was refluxed with 2.5% methanolic hydrogen chloride for 3 h and methyl 5-tetradecynoate isolated and distilled, yield was 84.9 g (80%) and b.p./0.1 mm was 108–110°C. 5-Tetradecynoic acid has been prepared previously by another route [18].

Ester (23.8 g) was heated with sodium deuteroxide (5 g) in deuterium oxide (125 ml) at 200°C for 3 days [9] and yielded a gummy acid which did not give a volatile methyl ester. The ¹³C NMR spectrum indicated that extensive deuteration, probably at C-2 to C-7, had occurred. Another portion of the ester (23.8 g) was semihydrogenated giving 99.2% methyl *cis*-5-tetradecenoate which was converted to $[2-^{2}H_{2}]$ -*cis*-5-tetradecenoic acid using the exchange conditions above. The acid was reduced with lithium aluminum hydride to $[2-^{2}H_{2}]$ -*cis*-5-tetradecenoic acid (the intermediate tetradecenylmalonic acid was crystallized from hexane and had m.p. 42-43°C) which contained 96.1% *cis* isomer. A second malonate extension then yielded $[6-^{2}H_{2}]$ -*cis*-octadecenoic acid (the intermediate hexadecenylmalonic acid was crystallized from benzene/hexane 1 : 2 and had m.p. 61-63°C). After conversion to the methyl ester the product contained 95.5% *cis* isomer and 98% dideuterated ester, the overall yield from methyl tetradecynoate was 34%.

Methyl $[5-^{2}H_{2}]$ cis-9-octadecenoate

Methyl 5-tetradecynoate (23.8 g) was reduced with lithium aluminum deuteride to $[1-{}^{2}H_{2}]$ -5-tetradecyn-1-ol. The mesylate was prepared as before [9] and crystallized from methanol at -15° C, the m.p. was $10-11^{\circ}$ C. $[1-{}^{2}H_{2}]$ -5-Tetradecynylmalonic acid was prepared in the usual way [11,9] and crystallized from benzene, the m.p. was $73-75^{\circ}$ C. The malonic acid was decarboxylated to $[3-{}^{2}H_{2}]$ -7-hexadecynoic acid and methyl $[5-{}^{2}H_{2}]$ -9-octadecynoate obtained by a second malonate extension and semihydrogenated giving methyl $[5-{}^{2}H_{2}]$ -cis-9-octadecenoate. The ester contained 98% cis isomer and 97% dideuterated ester, the overall yield from methyl 5-tetradecynoate was 40%.

Methyl [4-2H2]-cis-9-octadecenoate

7-Hexadecyn-1-ol was prepared as previously described for the dideuterated derivatives [8], semihydrogenated to the olefinic alcohol and oxidised as above to *cis*-7-hexadecenoic acid. Exchange with sodium deuteroxide in deuterium oxide gave the $[2-{}^{2}H_{2}]$ acid and malonate extension gave methyl $[4-{}^{2}H_{2}]$ -9-octadecenoate containing 12% *trans* isomer. The *cis* isomer, contaminated with only 2% *trans* isomer, was isolated by column chromatography on 30% silver nitrate/silicic acid, the yield of purified product from methyl 7-hexadecenoate was 21%.

Methyl $(3-^{2}H_{2})$ -cis-9-octadecenoate

Methyl 7-hexadecenoate was reduced with lithium aluminum deuteride and $[1-{}^{2}H_{2}]$ -7-hexadecenol converted to methyl $[3-{}^{2}H_{2}]$ -cis-9-octadecenoate by malonate extension. The product contained 9% trans isomer and almost pure ester (2% trans isomer) was obtained as described above. The yield of purified ester from methyl hexadecenoate was 39%.

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