Photocyclization of 3-styrylcyclohex-2-enones to 2,3-dihydro-1*H*-phenanthren-4-ones

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Abstract

3-Styrylcyclohex-2-enones (**3a–d**) are cyclized photochemically to 2,3-dihydro-1*H*-phenanthren-4-ones (**4a–d**). The corresponding phenanthren-4-ones with a methoxy group at C-5 (opposing the carbonyl at C-4) are not formed.

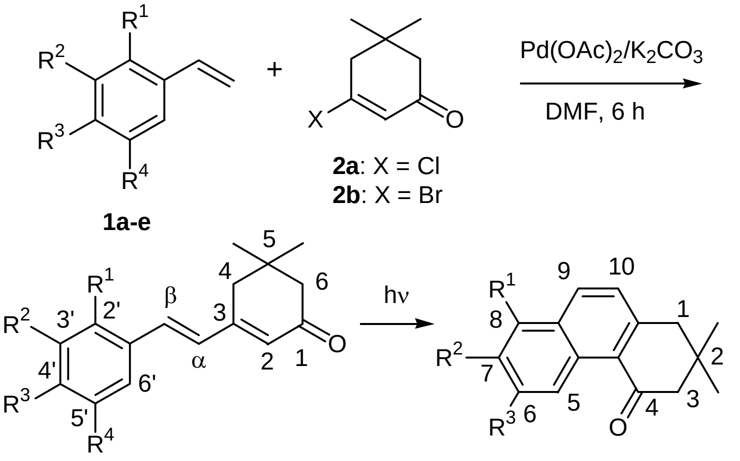
Keywords: Heck reaction, photocyclization, phenanthrenones

Introduction

In connection with our interest in the total synthesis of the angularly condensed angucyclinones,[1,2] we were interested in convenient ways for the synthesis of dihydrophenanthrenones, which have essential structural elements in common with the angucyclinones. As model compounds we selected substituted 5,5-dimethyl-3-styrylcyclohex-2-enones (**3**) and investigated their photochemical cyclization to 2,2-dimethyl-2,3-dihydro-1*H*-phenanthren-4-ones (**4**). Whereas the photoisomerisation and oxidative cyclization of stilbenes to phenanthrenes is a well known process (reviews:[3,4]), the photochemical behavior of the phenyl-substituted dienones such as **3a–e** has not yet been investigated in detail. As required for the photocyclization of stilbenes, a *trans/cis*-photoisomerisation has to precede the photocyclization reaction.

Results and Discussion

The starting material **3a** was prepared employing a Heck reaction of the styrenes **1a** with 5,5-dimethyl-3-chlorocyclohex-2-enone (**2a**) and 5,5-dimethyl-3-bromocyclohex-2-enone (**2b**) (Scheme 1). Since both of the halides afforded the dienone **3a** in good yield, the more easily available chloro compound **2a** was used in the subsequent preparation of **3b–e** starting from the styrenes **1b–e**. The crystalline dienones had the *E* configuration as deduced from the coupling constants of the vinylic protons of ca. 14-16 Hz seen in . The dienones **3a–e** were then irradiated in dichloromethane solution with ultraviolet light using Pyrex glass vessels (Scheme 1).



	R^1	R^2	R^3	R^4
3a	H	H	H	H
3b	OCH_3	H	H	H
3c	H	OCH_3	H	H
3d	H	H	OCH_3	H
3e	OCH_3	H	H	OCH_3

	R^1	R^2	R^3	R^4
4a	H	H	H	H
4b	OCH_3	H	H	H
4c	H	OCH_3	H	H
4d	H	H	OCH_3	H

Scheme 1

The photocyclization products **4a–d** were isolated in 36–53 % yield after chromatographic purification and crystallization. The fate of the two hydrogens lost in the dehydrogenation products **4** has not yet been investigated. Possibly, the yield of dehydrogenated cyclization products **4** might increase by addition of an external hydrogen acceptor such as chalcones.[4a] Interestingly, the 2',5'-dimethoxy-5,5-dimethyl-3-styrylcyclohex-2-enone (**3e**) could not be cyclized to the corresponding dihydrophenanthrenone **4e**, probably due to steric hindrance in the transition state leading to a dihydrophenanthrenone with a methoxy group at C-5 and a carbonyl group at C-4. Similarly, a possible regioisomeric dihydrophenanthrenone with a methoxy group at C-5 was not formed during the irradiation of **3c**, probably for the same steric reasons. Also, the unprotected phenols, corresponding to the methyl ethers **3a–e**, did not undergo the cyclization reaction.

Experimental Part

General Procedures. For instrumentation and general methods see ref.[5] NMR spectra are recorded on an AMX-300 Bruker spectrometer (compounds **3**) and with a AMX-200 MHz Bruker spectrometer for compounds **4**.

General procedure for the Heck reaction of the styrenes 1a–e and the vinyl halides 2a or 2b
A solution of the styrenes **1a–e** (1 equiv.) and the β-halovinyl ketones **2a** or **2b** (1 equiv.) in DMF (50 mL) was treated with lithium chloride (1 equiv.), tetrabutylammonium bromide (1 equiv.), potassium carbonate (5 equiv.) and palladium acetate (0.01 equiv.). The mixture was refluxed for the times indicated in Table 1. The suspension was then neutralized with cold 1 N HCl (50 ml) and extracted three times with dichloromethane (each 30 mL). The combined organic extracts were washed twice with brine (each 10 mL), dried ($MgSO_4$), and filtered. The solvent was removed at reduced pressure and the residue purified by flash chromatography on silica gel (dichloromethane) and crystallized from diethyl ether. Conditions and yields are listed in Table 1.

Table 1. Heck reaction of the styrenes **1a–e** and the vinyl halides **2a** or **2b** to dienones **3a–3e**

Styrene*	Halide	K_2CO_3	LiCl	NR_4Br	$Pd(OAc)_2$	Time $^{\#}$	Dienone	M.p. °C	Yield
1a, 0.66	**2a**, 1.00	4.35	0.27	2.03	0.028	6	**3a**, 1.26	72–73	88
1a, 0.33	**2b**, 0.50	1.73	0.11	0.81	0.028	5	**3a**, 0.56	72–73	84
1b, 1.34	**2a**, 1.58	6.90	0.43	3.22	0.030	5	**3b**, 1.62	97–98	63
1c, 1.81	**2a**, 1.60	6.90	0.43	3.22	0.030	12	**3c**, 1.82	63–64	71
1d, 1.81	**2a**, 1.62	6.90	0.43	3.22	0.030	15	**3d**, 2.38	65–66	77
1e, 0.50	**2a**, 0.49	2.10	0.15	1.20	0.030	17	**3e**, 0.63	91–92	71

*amounts in g. $^{\#}$ reaction time in h.

5,5-Dimethyl-3-styrylcyclohex-2-enone (3a). M.p. 72–73 °C. IR (KBr): ν = 2955 cm^{-1}, 2925, 1652 (C=O), 1616 (C=C, Ar), 1583 (C=C, Ar), 1378, 1302, 1271, 957; **UV** (CH_2Cl_2): λ_{max} (lg ε) = 218 nm (3.73), 319 nm (4.23); ^1H NMR ($CDCl_3$): δ = 1.12 (s, 6 H, 2 x CH_3), 2.33 (s, 2 H, 4-H), 2.49 (s, 2 H, 6-H), 6.09 (s, 1 H, 2-H), 6.96 (d, *J* = 14.2 Hz, 1 H, vinyl-H), 7.30 (d, *J* = 14.2 Hz, 1 H, vinyl-H), 7.32–7.42 (m, 3 H, 3', 4', 5'-H), 7.32–7.42 (m, 2 H, 2', 6'-H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (q, 2 CH_3), 33.2 (s, C-5), 38.8 (t, C-4), 51.2 (t, C-6), 127.0 (2 d), 127.1 (d), 128.7 (2 d), 128.9 (d), 129.4 (d), 134.9 (d), 135.8 (s, C-1'), 154.6 (s, C-3), 200.2 (s, C-1); MS (70 eV) *m/z* (%): 227 (19) [M^+ + 1], 226 (100) [M^+], 211 (6), 208 (8), 193 (32), 170 (69) [$M^+ - CH_2C(CH_3)_2$], 169 (40), 155 (15), 143 (15), 142 (85) [$M^+ - CH_2C(CH_3)_2 - CO$], 141 (84), 128 (15), 115 (20), 91 (18); HRMS calcd for ($C_{16}H_{18}O$): 226.136. Found: 226.135.

5,5-Dimethyl-3-[2-(2-methoxystyryl)]-cyclohex-2-enone (3b). M.p. 97–98 °C. IR (KBr): ν = 2948 cm^{-1}, 1643 (C=O), 1607 (C=C, Ar), 1576 (C=C, Ar), 1492, 1246, 1021, 967, 754; UV (CH_2Cl_2): λ_{max} (lg ε) = 208 nm (3.94), 344 nm (4.15); ^1H NMR ($CDCl_3$): δ = 1.12 (s, 6 H, 2 CH_3), 2.3 (s, 2 H, 4-H), 2.51 (s, 2 H, 6-H), 3.90 (s, 3 H, OCH_3), 6.07 (s, 1 H, 2-H), 6.91 (br d, 1 H, 3'-H), 6,93 (d, 1 H, *J* = 16 Hz, α-vinyl-H), 6.97 (br t, 1H, 5'-H), 7.30 (br dt, 1 H, 4'-H), 7.39 (, 1 H, *J* = 16 Hz, β-vinyl-H), 7.57 (dd, H = 1.5, J = 7.6 Hz, 6'-H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (q, 2 CH_3), 33.2 (s, C-5), 38.8 (t, C-4), 51.3 (t, C-6), 55.3 (q, OCH_3), 110.8 (d, C-3'), 120.7 (d), 124.7 (s, C-1'), 126.6 (d), 126.7 (d), 129.6 (2 d), 130.1 (d), 155.5 (s, C-2' (C-3)), 157.2 (s, C-3 (C-2')), 200.3 (s, C-1); MS (70 eV) *m/z* (%): 257 (18) [M^+ + 1], 256 (80) [M^+], 241 (10) [$M^+ - CH_3$], 225 (12), 223 (14), 213 (8), 200 (17) [$M^+ - CH_2C(CH_3)_2$], 199 (14), 172 (100) [$M^+ - CH_2C(CH_3)_2 - CO$], 171 (24), 169 (29), 159 (16), 157 (26), 141 (40), 135 (21), 128 (23), 121 (38), 115 (20), 91 (26), 77 (12), 55 (10); HRMS calcd for $C_{17}H_{20}O_2$: 256.146. Found: 256.146.

5,5-Dimethyl-3-[2-(3-methoxystyryl)]-cyclohex-2-enone (3c). M.p. 63–64 °C. IR (KBr): ν = 2954 cm^{-1}, 1659 (C=O), 1621 (C=C, Ar), 1584 (C=C, Ar), 1287, 1249, 1157; UV (CH_2Cl_2): λ_{max} (lg ε) = 230 nm (3.93), 319 nm (4.41); ^1H NMR ($CDCl_3$): δ = 1.12 (s, 6 H, 2 CH_3), 2.32 (s, 2 H, 4-H), 2.48 (s, 2 H, 6-H), 3.85 (s, 3 H, OCH_3), 6.08 (s, 1 H, 2-H), 6.87 (dd, 1 H, 4'-H) (6'-H)), 6.89 (d, 1 H, vinyl-H); 6.98, (d, 1 H, vinyl-H), 7.03 (t, 1H, 2'-H), 7.06 (d, 1 H, 6'-H (4'-H)), 7.29 (t, *J* = 7.5 Hz, 1 H, 5-H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (q, 2 CH_3), 33.2 (s, C-5), 38.8 (t, C-4), 51.2 (t, C-6), 55.1 (q, OCH_3), 112.1 (d), 114.6 (d), 119.8 (d), 127.1 (d), 129.7 (2 d), 134.7 (d), 137.2 (s, C-1'), 154.5 (s, C-3'), 159.7 (s, C-3), 200.1 (s, C-1); MS (70 eV) *m/z* (%): 257 (26) [M^+ + 1], 256 (100) [M^+], 255 (33), 241 (15) [M^+ - CH_3], 238 (24), 223 (74), 213 (19), 200 (71) [$M^+ - CH_2C(CH_3)_2$], 199 (43), 185 (33), 173 (19), 172 (64) [$M^+ - CH_2C(CH_3)_2 - CO$], 171 (65), 169 (24), 157 (42), 141 (33), 129 (54), 128 (53), 115 (24), 102 (5), 91 (8), 83 (2), 77 (7), 65 (5), 55 (3); HRMS calcd for $C_{17}H_{20}O_2$: 256.146. Found: 256.146.

5,5-Dimethyl-3-[2-(4-methoxystyryl)]-cyclohex-2-enone (3d). M.p. 65–66 °C. IR (KBr): ν = 2956 cm^{-1}, 1654 (C=O), 1601 (C=C, Ar), 1509, 1276, 1247, 1175, 1032, 956, 841; UV (CH_2Cl_2): λ_{max} (lg ε) = 246 nm (3.98), 345 m (4.45); ^1H NMR ($CDCl_3$): δ = 1.11 (s, 6 H, 2 x CH_3), 2.31 (s, 2 H, 4-H), 2.47 (s, 2 H, 6-H), 3.84 (s, 3 H, OCH_3), 6.05 (s, 1 H, 2-H), 6.79 (d, *J* = 15.5 Hz, 1 H, vinyl-H), 6.90 (d, 2 H, *J* = 7.5 Hz, 3'-H, 5'-H) 6.97 (d, *J* = 15.5 Hz, 1 H, vinyl-H), 7.45 (d, *J* = 7.5 Hz, 2 H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (q, 2 CH_3), 33.2 (s, C-5), 38.8 (t, C-4), 51.2 (t, C-6), 55.2 (q, 4'-OCH_3), 114.1 (d, C-3', C-5'), 126.1 (d, C-2), 127.2 (d), 128.5 (2 d, C-2', C-6; s, C-1'), 134.5 (2 d), 155.0 (s), 160.2 (s), 200.1 (s, C-1); MS (70 eV) *m/z* (%): 257 (11) [M^+ + 1], 256 (63) [M^+], 255 (11) [M^+ - H], 241 (4) [M^+ - CH_3], 239 (5), 225 (7), 223 (9), 213 (4), 200 (16) [$M^+ - CH_2C(CH_3)_2$], 199 (9), 185 (8), 173 (15), 172 (100) [$M^+ - CH_2C(CH_3)_2 - CO$], 171 (24), 169 (18), 159 (9), 157 (12), 141 (13), 129 (15), 128 (15), 121 (43), 115 (10); HRMS calcd for $C_{17}H_{20}O_2$: 256.146. Found: 256.146.

5,5-Dimethyl-3-[2-(2,5-dimethoxystyryl)]-cyclohex-2-enone (3e). M.p. 91–92 °C. IR (KBr): ν = 2958 cm^{-1}, 1652 (C=O), 1610 (C=C, Ar), 1496, 1400, 1245, 1218, 1046; UV (CH_2Cl_2): λ_{max} (lg ε) = 232 nm (3.97), 306 nm (4.18), 369 nm (4.00); ^1H NMR ($CDCl_3$): δ = 1.08 (s, 6 H, 2 CH_3), 2.31 (s, 2 H, 4-H), 2.51 (s, 2 H, 6-H), 3.81 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 6.07 (s, 1 H, 2-H), 6.85 (s, 2 H, 2 vinyl-H), 6.9 (br d, *J* = 7.3 Hz, 1 H, 4'-H), 7.14 (br s, 1 H, 6'-H), 7.35 (d, *J* = 7.3 Hz, 1 H, 3'-H); ^{13}C NMR ($CDCl_3$): δ = 28.3 (q, 2 CH_3), 33.2 (s, C-5), 38.8 (t, C-4), 51.3 (t, C-6), 55.6 and 55.9 (2 q, 2 OCH_3), 111.5 (d), 112.0 (d), 115.4 (d), 125.4 (s, C-1'), 126.7 (d), 129.4 (d), 129.8 (d), 151.7 (s, C-2'), 153.5 (s, C-5'), 155.2 (s, C-3), 200.2 (s, C-1); MS (70 eV) *m/z* (%): 287 (22) [M^+ + 1], 286 (100) [M^+], 271 (32) [$M^+ - CH_3$], 255 (26), 253 (24), 227 (12), 215 (13), 213 (16), 202 (29) [$M^+ - CH_2C(CH_3)_2$ - CO], 201 (15), 199 (20), 187 (21), 172 (10), 171 (51), 151 (23), 128 (10), 115 (12); HRMS calcd for $C_{18}H_{22}O_3$: 286.157. Found: 286.156.

General procedure for the photocyclizations of 3a-3e

For standard techniques see ref.[6] A solution of the dienones **3a-3d** in dichloromethane (300 ml) was irradiated with UV light (medium pressure mercury lamp, Hanau, Pyrex glass vessels) at the times indicated for the individual compounds (TLC monitoring). The solvent was removed at reduced pressure and the products purified by flash chromatography on silica gel (dichloromethane) and crystallized from diethyl ether.

2,2-Dimethyl-2,3-dihydro-1*H*-phenanthren-4-one (4a). Starting material: (**3a**) (268 mg, 11.86 mmol). Irradiation time: 5 h. Yield: 140 mg (53 %), m.p.: 41 °C; IR (KBr): ν = 2954 cm^{-1}, 1663 (C=O), 1595, 1508, 1429, 1368, 1220; **UV** (CH_2Cl_2): λ_{max} (lg ε) = 248 nm (4.21), 313 nm (3.80); ^1H NMR ($CDCl_3$): δ = 1.12 (s, 6 H, 2 CH_3), 2.62 (s, 2 H, 1-H), 2.98 (s, 2 H, 3-H), 7.25 (d, *J* = 8.4 Hz, 1 H, 10-H), 7.49 (br t, 1 H, 7(6)-H), 7.63 (br t, 1 H, 6(7)-H), 7.79 (br d, *J* = 8.1 Hz, 1 H, 8-H), 7.91 (d, *J* = 8.4 Hz, 1 H, 9-H), 9.50 (br d, *J* = 8.6 Hz, 1 H, 5-H); ^{13}C NMR ($CDCl_3$): δ = 27.9 (q, 2 CH_3), 33.5 (s, C-2), 45.3 (t, C-1), 54.5 (t, C-3), 125.6 (d), 126.0 (s), 126.4 (d), 127.3 (d), 128.1 (d), 128.6 (d), 131.0 (s), 132.5 (s), 134.2 (d), 144.7 (s), 220.6 (s, C-4); MS (70 eV) *m/z* (%): 225 (11) [M^+ + 1], 224 (58) [M^+], 168 (100) [$M^+ - CH_2C(CH_3)_2$], 152 (7), 140 (62) [$M^+ - CH_2C(CH_3)_2 - CO$], 115 (5); HRMS calcd for $C_{16}H_{16}O$: 224.120. Found: 224.120.

8-Methoxy-2,2-dimethyl-2,3-dihydro-1*H*-phenanthren-4-one (4b). Starting material: (**3b**) (150 mg, 0.59 mmol), Irradiation time: 2 h. Yield: 52 mg (35 %), m.p.: 47 °C. IR (KBr): ν = 2957 cm^{-1}, 2928, 1734 (C=O), 1457, 1437, 1217, 1039; UV (CH_2Cl_2): λ_{max} (lg ε) = 241 nm (3.67); ^1H NMR ($CDCl_3$): δ = 1.13 (s, 6 H, 2 CH_3), 2.64 (s, 2 H, 1-H), 3.03 (s, 2 H, 3-H), 4.00 (s, 3 H, OCH_3), 6.86 (br d, 1 H, 7-H), 7.28 (d, *J* = 8.4 Hz, 1 H, 10-H), 7.53 (t, 1 H, 6-H), 8.46 (d, *J* = 8.4 Hz, 1 H, 9-H), 9.03 (d, *J* = 8.7 Hz, 1 H, 10-H); ^{13}C NMR ($CDCl_3$): δ = 28.6 (q, 2 CH_3), 34.1 (s, C-2), 46.1 (t, C-1), 55.1 (t, C-3), 55.6 (q, OCH_3), 106.2 (d), 119.0 (d), 126.7 (d), 127.5 (s), 129.7 (d), 131.4 (s), 131.7 (s), 133.4 (d), 145.1 (s), 161.1 (s, C-8), 201.5 (s, C-4); MS (70 eV) *m/z* (%): 255 (9) [M^+ + 1], 254 (40) [M^+], 224 (38), 198 (32) [$M^+ - CH_2C(CH_3)_2$], 168 (91), 152 (51), 140 (42), 135 (92), 121 (58), 105 (80), 77 (100); HRMS calcd for $C_{17}H_{18}O_2$: 254.131. Found: 254.130.

7-Methoxy-2,2-dimethyl-2,3-dihydro-1H-phenanthren-4-one (4c). Starting material: (**3c**) (150 mg, 0.59 mmol). Irradiation time: 2 h. Yield: 56 mg (38 %), m.p.: 55 °C. IR (KBr): ν = 2957 cm^{-1}, 1685 (C-4), 1618, 1243, 1036; **UV** (CH_2Cl_2): λ_{max} (lg ε) = 246 nm (4.09); ^1H NMR ($CDCl_3$): δ = 1.16 (s, 6 H, 2 CH_3), 2.66 (s, 2 H, 1-H), 3.09 (s, 2 H, 3-H), 3.96 (s, 3 H, OCH_3), 7.10 (d, 1 H, 10-H), 7.2-7.4 (m, 2 H, 6-H, 8-H), 7.88 (d, *J* = 8.4 Hz, 1 H, 9-H), 9.41 (d, *J* = 8.8 Hz, 1 H, 5-H); ^{13}C NMR ($CDCl_3$): δ = 28.5 (q, 2 x CH_3), 34.2 (s, C-2), 45.7 (t, C-1), 55.1 (t, C-3), 55.7 (q, OCH_3), 107.1 (d), 121.1 (d), 123.5 (s), 127.0 (s), 128.5 (d), 128.6 (d), 132.1 (s), 133.8 (d), 143.0 (s), 157.6 (s, C-7), 201.5 (s, C-4); MS (70 eV) *m/z* (%): 255 (17) [M^+ + 1], 254 (85), 225 (7), 198 (55) [$M^+ - CH_2C(CH_3)_2$], 184 (11), 170 (100) [$M^+ - CH_2C(CH_3)_2 - CO$], 152 (47), 135 (19), 127 (30), 107 (15), 91 (9), 77 (22); HRMS calcd for $C_{17}H_{18}O_2$: 254.131. Found: 254.130.

6-Methoxy-2,2-dimethyl-2,3-dihydro-1H-phenanthren-4-one (4d). Starting material: (**3d**) (200 mg, 0.78 mmol). Irradiation time: 2,5 h. Yield: 62 mg (31 %), m.p.: 60 °C; **IR** (KBr): ν = 2960 cm^{-1}, 1728 (C=O), 1649, 1603, 1512, 1465, 1254, 1174; UV (CH_2Cl_2): λ_{max} (lg ε) = 248 nm

(3.80); ^{1}H NMR ($CDCl_3$): δ = 1.16 (s, 6 H, 2 CH_3), 2.66 (s, 2 H, 1-H), 3.05 (s, 2 H, 3-H), 3.92 (s, 3 H, OCH_3), 7.04 (d, 1 H, 7(10)-H), 7.18 (d, 1 H, 10(7)-H), 7.73 (d, J = 8.8 Hz, 1 H, 8(9)-H), 7.88 (d, Hz, 1 H, 9(8)-H), 7.95 (s, 1 H, 5-H); ^{13}C NMR ($CDCl_3$): δ = 28.5 (q, 2 x CH_3), 34.0 (s, C-2), 46.1 (t, C-1), 55.1 (t, C-3), 55.8 (q, OCH_3), 105.5 (d, C-5), 114.7 (d), 118.8 (d), 125.5 (s), 127.0 (s), 130.1 (s), 132.4 (s), 134.8 (d), 146.5 (s), 161.1 (s, C-6), 191.3 (s, C-4); MS (70 eV) *m/z* (%): 255 (17) [$M^+ + 1$], 254 (85), 225 (7), 198 (55) [$M^+ - CH_2C(CH_3)_2$], 184 (11), 170 (100) [$M^+ - CH_2C(CH_3)_2 - CO$], 152 (47), 135 (19), 127 (30), 107 (15), 91 (9), 77 (22); HRMS calcd for $C_{17}H_{18}O_2$: 254.131. Found: 254.130.

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