Hydrazinium Carbazate–H_2O_2: An Ideal Combination for Diimide Reduction of Base-Sensitive Unsaturated Peroxides[1]

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Abstract: The utility of a hydrazinium carbazate ($N_2H_3COON_2H_5$) and H_2O_2 combination for the double bond reduction of base-sensitive unsaturated 1,2,4-trioxanes, 1,2,4-trioxepanes, and their precursors β- and γ-hydroxyhydroperoxides is presented. The method is superior to the conventional diimide reduction using $N_2H_4{\cdot}H_2O$–H_2O_2 and catalytic hydrogenation.

Key words: diimide reduction, hydrazinium carbazate, hydrogen peroxide, β-/γ-hydroxyhydroperoxides, 1,2,4-trioxanes

Artemisinin, a naturally occurring 1,2,4-trioxane from *Artemisia annua* and its semi-synthetic derivatives such as artemether and arteether (Figure 1) are currently the drugs of choice for the treatment of malaria caused by *Plasmodium falciparum*.[2]

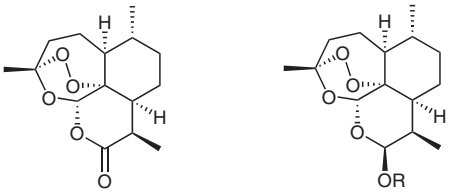
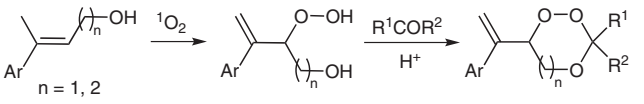


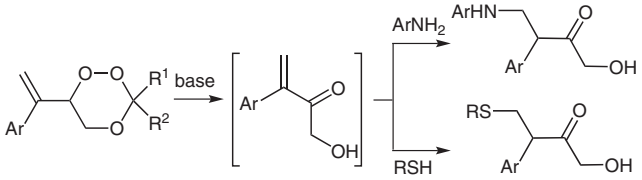
Figure 1 Artemisinin and its semi-synthetic derivatives

As a part of an endeavor to develop synthetic substitutes for artemisinin and its derivatives, we have earlier reported photooxygenation routes for the preparation of 1,2,4-trioxanes[3,4] and 1,2,4-trioxepanes[5,6] (Scheme 1).



Scheme 1 Synthesis of 1,2,4-trioxanes (n = 1) and 1,2,4-trioxepanes (n = 2) via photooxygenation of allylic and homoallylic alcohols

Several of the 6-arylvinyl-1,2,4-trioxanes prepared by this method have shown promising antimalarial activity.[7] We have also shown that these trioxanes undergo a facile fragmentation under basic conditions to furnish α,β-unsaturated keto alcohols, which react with various amines and thiols to give Michael adducts (Scheme 2). Based on these results we have earlier suggested that this facile formation of α,β-unsaturated keto systems under basic conditions and their equally facile reaction with amines and thiols might have relevance to the mechanism of action of these trioxanes as antimalarials.[8] This suggestion naturally makes the double bond the key group for the activity of this group of 1,2,4-trioxanes and calls for the preparation and antimalarial assessment of the corresponding saturated 1,2,4-trioxanes.



Scheme 2 Base mediated fragmentation of 1,2,4-trioxanes into α,β-unsaturated keto alcohols and their entrapment by amines and thiols

In our efforts to achieve this objective, we have discovered hydrazinium carbazate/hydrogen peroxide ($N_2H_3COON_2H_5$–H_2O_2) as a new combination for the diimide reduction of these base-sensitive 1,2,4-trioxanes and 1,2,4-trioxepanes and their precursors, β- and γ-hydroxyhydroperoxides. In the present study, we demonstrate the superiority of this new diimide reduction method over the conventional diimide reduction using $N_2H_4{\cdot}H_2O$–H_2O_2[9,10]and catalytic hydrogenation.[11] Towards this end, we first attempted catalytic hydrogenation of trioxane **1a** with hydrogen over platinum(IV) oxide at room temperature and atmospheric pressure, which furnished only diol **2** and ketone **3** in 64 and 89% yield, respectively, and no trace of the corresponding saturated trioxane was isolated[12] (Scheme 3).

Further we attempted diimide reduction using a $N_2H_4{\cdot}H_2O$–H_2O_2 combination (Method A). Thus, the reaction of trioxane **1a** with $N_2H_4{\cdot}H_2O$–30% H_2O_2 in a 1:1 mixture of THF–EtOH was complete within three days and furnished the corresponding saturated trioxanes **4a** (less polar) and **5a** (more polar) as a diastereomeric mixture in 44% yield and in a ratio of 2:3. Reduction of the trioxanes **1b–e** under similar conditions furnished a mixture of the corresponding saturated trioxanes **4b–e** (less polar) and **5b–e** (more polar) in 36–58% yields. Similar reduc-

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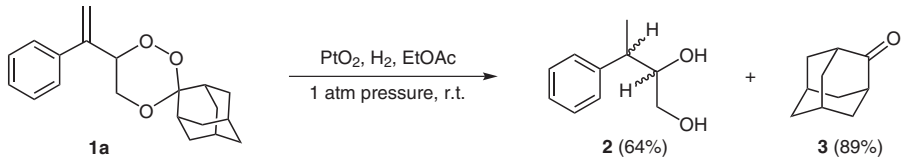
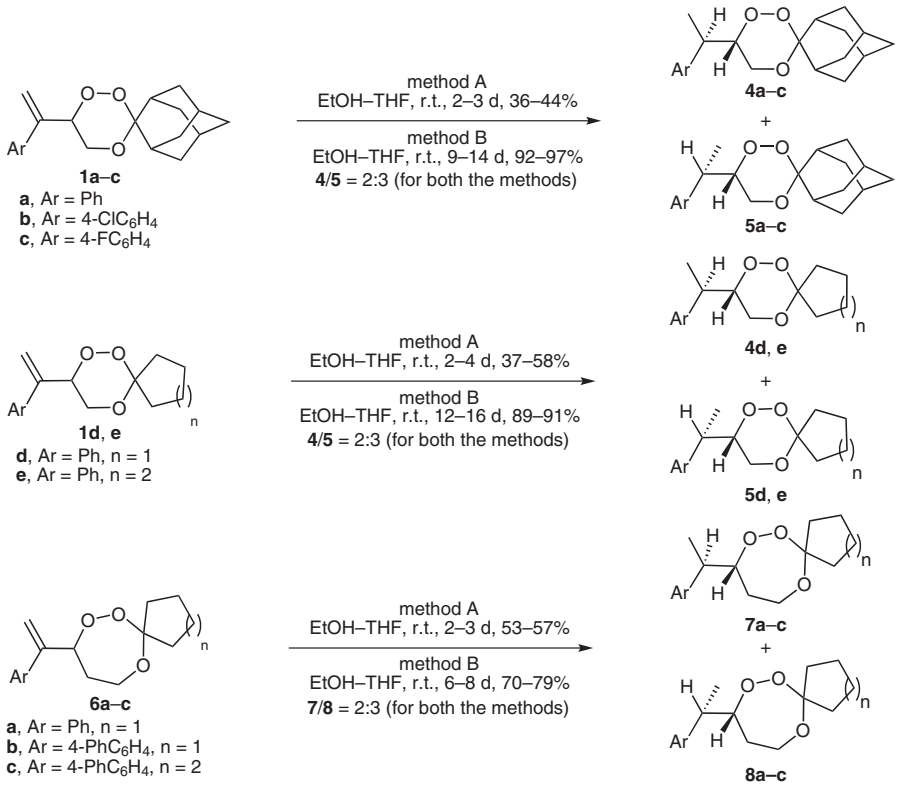


Scheme 3 Catalytic hydrogenation of unsaturated 1,2,4-trioxane **1a**



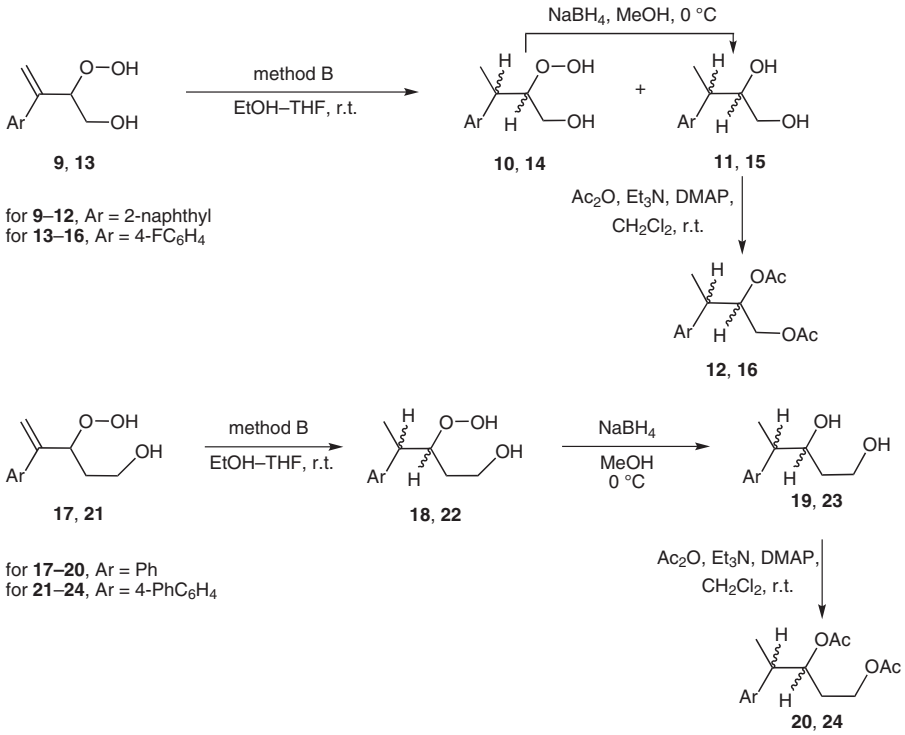
Scheme 4 Reduction of unsaturated 1,2,4-trioxanes **1a–e** and 1,2,4-trioxepanes **6a–c** by $N_2H_4{\cdot}H_2O$–30% H_2O_2 (method A) and $N_2H_3COON_2H_5$–30% H_2O_2 (method B)

tion of the trioxepanes **6a–c** furnished a mixture of the corresponding saturated trioxepanes **7a–c** (less polar) and **8a–c** (more polar) in 53-57% yields (Scheme 4, Table 1).

We believed that the poor yields in diimide reduction of trioxanes **1a–e**, were due to the high basicity of $N_2H_4{\cdot}H_2O$, which can lead to a fragmentation of the trioxane moiety by a mechanism similar to that shown in Scheme 2. On the other hand, hydrazine hydrate is known to react with CO_2 to form hydrazinium carbazate ($N_2H_3COON_2H_5$), a 2:1 adduct of hydrazine and CO_2.[13,14] A comparison of the pH values of aqueous solutions of $N_2H_4{\cdot}H_2O$ and $N_2H_3COON_2H_5$, prepared in our laboratory, showed that the latter was much less basic and therefore more suitable for our work.[15] In fact, the reaction of trioxane **1a** with $N_2H_3COON_2H_5$–30% H_2O_2 (method B) took more time to complete, but gave a mixture of the corresponding saturated trioxanes **4a** and **5a** in a 2:3 ratio in 97% yield. Similarly, reduction of the trioxanes **1b–e** under these conditions furnished the corresponding saturated trioxanes **4b–e** and **5b–e** in 89–95% yields. A similar reduction of the trioxepanes **6a–c** furnished the corresponding saturated trioxepanes **7a–c** and **8a–c** in 70–79% yields (Scheme 4, Table 1). The diastereomers were separated by column chromatography and characterized individually.[16]

The lower basicity of $N_2H_3COON_2H_5$ as compared with N_2H_4 could be the main reason for the sluggishness of this reaction. The oxidation of N_2H_4 to N_2H_2, the actual reducing species, is known to be influenced by the pH of the reaction; at pH <8 it is very slow.[17]

The difference in diimide reduction using $N_2H_4{\cdot}H_2O$–H_2O_2 and $N_2H_3COON_2H_5$–H_2O_2 was found to be even more dramatic in the reduction of unsaturated β- and γ-hydroxyhydroperoxides. The diimide reduction of β-hydroxyhydroperoxide **9** with $N_2H_3COON_2H_5$–H_2O_2 furnished the saturated β-hydroxyhydroperoxide **10** as an inseparable mixture of diastereomers in 50% yield together with saturated diol **11** in 17% yield, also as an inseparable mixture of diastereomers. Similarly, the reduction of β-hydroxyhydroperoxide **13** under these conditions furnished saturated β-hydroxyhydroperoxide **14** and diol **15** in 51 and 28% yield, respectively. Analogous reduction of unsaturated γ-hydroxyhydroperoxides **17** and **21** with $N_2H_3COON_2H_5$–H_2O_2 furnished the corresponding satu-



Scheme 5 Reduction of β-hydroxyhydroperoxides **9** and **13** and γ-hydroxyhydroperoxides **17** and **21** by $N_2H_3COON_2H_5$–30% H_2O_2

rated hydroperoxides **18** and **22** in 62 and 63% yield, respectively; no corresponding diols were obtained in this case (Scheme 5, Table 2).

Table 1 Comparative Yields of Diimide Reduction of 1,2,4-Trioxanes **1a–e** and 1,2,4-Trioxepanes **6a–c**[a]

Unsaturated peroxide	Method	Time (d)	Products	Yield (%)[b]
1a	A	3	**4a** + **5a**	44
	B	9	**4a** + **5a**	97
1b	A	2	**4b** + **5b**	36
	B	14	**4b** + **5b**	95
1c	A	2	**4c** + **5c**	36
	B	10	**4c** + **5c**	92
1d	A	2	**4d** + **5d**	37
	B	12	**4d** + **5d**	89
1e	A	4	**4e** + **5e**	58
	B	16	**4e** + **5e**	91
6a	A	2	**7a** + **8a**	57
	B	6	**7a** + **8a**	79
6b	A	2	**7b** + **8b**	55
	B	6	**7b** + **8b**	70
6c	A	3	**7c** + **8c**	53
	B	8	**7c** + **8c**	76

[a] Method A: $N_2H_4{\cdot}H_2O$–30% H_2O_2; Method B: $N_2H_3COON_2H_5$–30% H_2O_2.
[b] The ratio of the two diastereomers **4**:**5** and **7**:**8** is around 2:3 as seen by ^1H NMR spectra of the crude mixtures of the diastereomers.

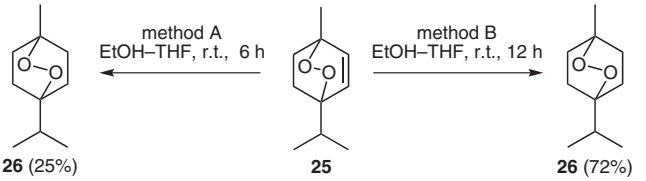
Table 2 Yield of Diimide Reduction of Unsaturated Hydroperoxides with $N_2H_3COON_2H_5$–30% H_2O_2

Unsaturated hydroperoxide	Time (d)	Product	Yield (%)
9	4	**10**	50
13	4	**14**	51
17	3.5	**18**	62
21	3.5	**22**	63

Reduction of β-hydroxyhydroperoxides **9** and **13** and γ-hydroxyhydroperoxides **17** and **21** by the conventional method using $N_2H_4{\cdot}H_2O$–H_2O_2 provided only the corresponding saturated diols. Also, the catalytic reduction of hydroperoxide **9** furnished only diol **11** in 97% yield and no trace of the corresponding saturated hydroperoxide was isolated. To the best of our knowledge, this is the first report on the reduction of the unsaturated hydroxyhydroperoxides to the saturated hydroxyhydroperoxides.

The saturated hydroxyhydroperoxides **10**, **14**, **18**, and **22** were reduced with $NaBH_4$ to furnish saturated diols **11**, **15**, **19**, and **23**, which on acetylation furnished the corresponding diacetates **12**, **16**, **20**, and **24**, respectively, as inseparable mixtures of diastereomers.[18]

The comparative superiority of $N_2H_3COON_2H_5$–H_2O_2 over $N_2H_4{\cdot}H_2O$–H_2O_2 was also evident in the double bond reduction of ascaridole (**25**). While the reaction of ascaridole (**25**) with $N_2H_4{\cdot}H_2O$–H_2O_2 furnished dihydroascaridole (**26**) in only 25% yield,[19] the reaction with



Scheme 6 Reduction of ascaridole (**25**) to dihydroascaridole (**26**) by N_2H_4·H_2O–30% H_2O_2 (method A) and $N_2H_3COON_2H_5$–30% H_2O_2 (method B)

$N_2H_3COON_2H_5$–H_2O_2 furnished the same compound in 72% yield (Scheme 6).

Since the objective of these studies was to figure out the role of the double bond in the biological activity of the trioxanes, we evaluated some of these saturated trioxanes for antimalarial activity. Several of the saturated trioxanes, particularly the less polar isomers, were found to be several fold more active than the parent unsaturated trioxanes. The details of the biological activity of the saturated trioxanes will be disclosed elsewhere.

In conclusion, we have discovered $N_2H_3COON_2H_5$–H_2O_2 as a new combination for the double bond reduction of base-sensitive arylvinyl-1,2,4-trioxanes/trioxepanes and their precursors β-/γ-hydroxyhydroperoxides.[20] This new method is superior to the conventional diimide reduction with N_2H_4·H_2O–H_2O_2 and catalytic hydrogenation. While there are several precedents in the literature on the double bond reduction of unsaturated peroxides, to the best of our knowledge, this is the first report on the preparation of saturated hydroxyhydroperoxides from unsaturated hydroxyhydroperoxides.

All glass apparatus were oven dried prior to use. Melting points were recorded in open capillaries and are uncorrected. Compounds were characterized by IR, ^{1}H, ^{13}C, ^{1}H–^{1}H COSY (correlation spectroscopy), HSQC (heteronuclear single quantum coherence spectra), HMBC (heteronuclear multiple bond correlation spectra), ESI-MS (electron spray ionization mass spectra), FAB-MS (fast atom bombardment mass spectra), EI-HRMS (electron impact high-resolution mass spectra), and elemental analysis (C, H). ^{1}H and ^{13}C NMR spectra were obtained using $CDCl_3$ as a solvent. TMS (δ 0.00 ppm) served as an internal standard in ^{1}H NMR and $CDCl_3$ (δ 77.0 ppm) in ^{13}C NMR. Chemical shifts are reported in parts per million. Column chromatography was performed over silica gel (particle size: 60–120 mesh), or flash silica gel (particle size: 230–400 mesh).

Catalytic Hydrogenation of Trioxane 1a

A solution of 6-arylvinyl-1,2,4-trioxane **1a** (0.200 g, 0.64 mmol) in EtOAc (15 mL) was hydrogenated in the presence of Adam's catalyst (PtO_2, 0.003 g) using a Parr shaker assembly at r.t. and atmospheric pressure for 1.5 h. The reaction mixture was filtered over Celite, concentrated under vacuum, and the crude product was purified by column chromatography over silica gel to furnish the saturated diol **2** (0.060 g, 64%) as a colorless oil together with 2-adamantanone (**3**; 0.080 g, 89%) as a white solid.

3-Phenylbutane-1,2-diol (2)

Oil.

FT-IR (neat): 1057, 1593, 2923, 3403 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.17 (m, 5 H), 3.79–3.75 (br m, 1 H), 3.58–3.35 (br m, 1 H), 2.88 and 2.81 (2 quint, J = 7.2 Hz,1 H), 2.13–2.03 (br m, 4 H), 1.35 and 1.27 (2 d, J = 7.0, 7.1 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.4 (C), 141.8 (C), 127.5 (CH), 127.3 (CH), 126.7 (CH), 126.3 (CH), 125.6 (CH), 125.4 (CH), 76.2 (CH), 75.0 (CH), 63.30 (CH_2), 63.27 (CH_2), 41.7 (CH), 41.5 (CH), 16.5 (CH_3), 16.1 (CH_3).

ESI-MS: m/z = 167 [M + H$^+$].

EI-HRMS: m/z calcd for $C_{10}H_{14}O_2$ [M$^+$]: 166.0994; found: 166.0990.

2-Adamantanone (3)

White solid; mp 256–259 °C.

FT-IR (KBr): 1717, 2920 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.53 (br s, 2 H), 2.12–1.95 (m, 12 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 217.7 (C), 46.7 (3 × CH_2), 38.9 (3 × CH), 36.0 (CH), 27.2 (2 × CH_2).

FAB-MS: m/z = 151 [M + H$^+$].

Hydrazinium Carbazate Solution

A slow stream of CO_2 gas was bubbled through ice cooled hydrazine hydrate (N_2H_4·H_2O, 103 g, 2.06 mol) till the weight of reaction mixture became constant (150 g, which corresponded to a 2:1 adduct of N_2H_4·H_2O and CO_2). A small amount (1 g) of this highly viscous material (density = 1.45 g/mL) was dissolved in H_2O (100 mL) for the measurement of pH, which was found to be 7.51, while the pH value of 1% aq N_2H_4·H_2O was found to be 9.79.

Diimide Reduction of 1,2,4-Trioxanes/Trioxepanes, β-/γ-Hydroxyhydroperoxides and Ascaridole Using Hydrazine Hydrate and 30% H_2O_2; Typical Procedure for the Reduction of 1,2,4-Trioxane 1a (Method A)

To a stirred and ice cooled solution of trioxane **1a** (1.00 g, 3.205 mmol) and N_2H_4·H_2O (3.2 mL, 20 equiv) in a 1:1 mixture of EtOH–THF (50 mL) was added 30% H_2O_2 (10.89 mL, 30 equiv) dropwise over 30 min and the reaction mixture was allowed to stir at r.t. for 3 d. The mixture was concentrated under vacuum, diluted with H_2O (20 mL) and extracted with Et_2O (2 × 50 mL). The combined organic extracts were washed successively with aq 10% HCl (10 mL), H_2O (10 mL), and with sat. aq $NaHCO_3$ (10 mL), dried (Na_2SO_4), and concentrated under vacuum. The crude product was purified by column chromatography over silica gel to furnish saturated trioxanes **4a** and **5a** (0.440 g, 44%) as a mixture of diastereomers in approximately 2:3 ratio, which on flash chromatography furnished the pure isomers **4a** (less polar, oil) and **5a** (more polar, white solid, mp 84–85 °C).

Diimide Reduction of 1,2,4-Trioxanes/Trioxepanes, β-/γ-Hydroxyhydroperoxides and Ascaridole Using Hydrazinium Carbazate and 30% H_2O_2; Typical Procedure for the Reduction of 1,2,4-Trioxane 1a (Method B)

To a stirred and ice cooled solution of trioxane **1a** (3.00 g, 9.62 mmol) and hydrazinium carbazate (9.55 mL, 10 equiv) in a mixture of EtOH–THF (1:1; 150 mL) was added 30% H_2O_2 (32.69 mL, 30 equiv) dropwise over 30 min and the reaction mixture was allowed to stir at r.t. for 9 d. The mixture was worked up and the crude product was chromatographed as above to furnish a mixture of **4a** and **5a** (2.92 g, 97%). No significant difference in yield and reaction time was observed when **1a** was reacted with a large excess of $N_2H_3COON_2H_5$–H_2O_2.

Trioxane 4a

Oil.

FT-IR (neat): 763, 1025, 1117, 1223, 1602, 2914 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.35–7.18 (m, 5 H), 4.35 (dt, *J* = 9.6, 2.6 Hz, 1 H), 3.62 (dd, *J* = 11.8, 9.6 Hz, 1 H), 3.34 (dd, *J* = 11.8, 2.6 Hz, 1 H), 2.81 (s, 1 H), 2.76 (quint, *J* = 6.9 Hz, 1 H), 2.06–1.59 (m, 13 H), 1.39 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.0 (C), 128.9 (2 × CH), 127.8 (2 × CH), 127.3 (CH), 104.5 (C), 83.3 (CH), 61.2 (CH_2), 41.0 (CH), 37.4 (CH_2), 35.7 (CH), 33.7 (2 × CH_2), 33.5 (CH_2), 33.2 (CH_2), 30.1 (CH), 27.4 (2 × CH), 18.6 (CH_3).

FAB-MS: *m*/*z* = 315 [M + H^+].

Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.10; H, 8.40.

Trioxane 5a
White solid; mp 84–85 °C.

FT-IR (KBr): 759, 1029, 1086, 1113, 1219, 1604, 2914 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.23 (m, 5 H), 4.35 (ddd, *J* = 9.6, 7.6, 3.4 Hz, 1 H), 3.83 (dd, *J* = 11.6, 9.6 Hz,1 H), 3.77 (dd, *J* = 11.6, 3.4 Hz, 1 H), 2.87 (quint, *J* = 7.2 Hz, 1 H), 2.77 (s, 1 H), 2.08–1.55 (m, 13 H), 1.29 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.5 (C), 128.7 (2 × CH), 127.8 (2 × CH), 126.9 (CH), 104.60 (C), 82.6 (CH), 60.9 (CH_2), 40.7 (CH), 37.4 (CH_2), 36.1 (CH), 33.7 (CH_2), 33.6 (CH_2), 33.3 (CH_2), 33.2 (CH_2), 29.7 (CH), 27.33 (CH), 27.29 (CH), 17.5 (CH_3).

FAB-MS: *m*/*z* = 315 [M + H^+].

Anal. Calcd for $C_{20}H_{26}O_3$: C, 76.40; H, 8.33. Found: C, 76.37; H, 7.96.

Trioxane 4b
White solid; mp 92–94 °C.

FT-IR (KBr): 768, 1091, 1112, 1217, 1655, 29117 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.4 Hz, 2 H), 7.13 (d, *J* = 8.4 Hz, 2 H), 4.28 (dt, *J* = 9.1, 2.3 Hz, 1 H), 3.59 (dd, *J* = 11.7, 9.4 Hz, 1 H), 3.36 (dd, *J* = 11.8, 2.5 Hz, 1 H), 2.83–2.77 (m, 2 H), 2.03–1.60 (m, 13 H), 1.36 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.6 (C), 133.0 (C), 129.14 (2 × CH), 129.08 (2 × CH), 104.6 (C), 83.0 (CH), 60.9 (CH_2), 40.3 (CH), 37.4 (CH_2), 35.5 (CH), 33.6 (2 × CH_2), 33.4 (CH_2), 33.2 (CH_2), 30.2 (CH), 27.3 (2 × CH), 18.5 (CH_3).

FAB-MS: *m*/*z* = 349 [M + H^+].

Anal. Calcd for $C_{20}H_{25}ClO_3$: C, 68.86; H, 7.22. Found: C, 68.69; H, 6.99.

Trioxane 5b
White solid; mp 114–115 °C.

FT-IR (KBr): 772, 1089, 1113, 1220, 1636, 2918 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.29 (d, *J* = 8.3 Hz, 2 H), 7.16 (d, *J* = 8.3 Hz, 2 H), 4.41 (br ddd, 1 H), 3.80–3.78 (m, 2 H), 2.84 (quint, *J* = 7.2 Hz, 1 H), 2.71 (s, 1 H), 2.06–1.55 (m, 13 H), 1.26 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.1 (C), 132.7 (C), 129.2 (2 × CH), 128.8 (2 × CH), 104.7 (C), 82.5 (CH), 60.9 (CH_2), 40.2 (CH), 37.4 (CH_2), 35.9 (CH), 33.7 (CH), 33.6 (CH_2), 33.4 (CH_2), 33.2 (CH_2), 29.9 (CH), 27.4 (CH), 27.3 (CH), 17.7 (CH_3).

FAB-MS: *m*/*z* = 349 [M + H^+].

Anal. Calcd for $C_{20}H_{25}ClO_3$: C, 68.86; H, 7.22. Found: C, 68.78; H, 6.88.

Trioxane 4c
Oil.

FT-IR (neat): 772, 1111, 1653, 2925 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.16–6.96 (m, 4 H), 4.26 (dt, *J* = 9.3, 2.6 Hz, 1 H), 3.58 (dd, *J* = 11.8, 9.3 Hz, 1 H), 3.32 (dd, *J* = 11.8, 2.6 Hz, 1 H), 2.78 (br quint, 1 H), 2.75 (s, 1 H), 2.02–1.57 (m, 13 H), 1.35 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0 (C, d, $J_{C,F}$ = 244 Hz), 137.8 (C), 129.2 (2 × CH, d, $J_{C,F}$ = 7.5 Hz), 115.8 (2 × CH, d, $J_{C,F}$ = 21 Hz), 104.6 (C), 83.2 (CH), 61.0 (CH_2), 40.2 (CH), 37.4 (CH_2), 35.6 (CH), 33.7 (2 × CH_2), 33.5 (CH_2), 33.2 (CH_2), 30.2 (CH), 27.4 (2 × CH), 18.6 (CH_3).

FAB-MS: *m*/*z* = 333 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{20}H_{25}FO_3$ [M^+]: 332.1788; found: 332.1786.

Trioxane 5c
White solid; mp 80–81 °C.

FT-IR (KBr): 767, 1113, 1637, 2923 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.22–6.98 (m, 4 H), 4.41 (br ddd, 1 H), 3.85–3.75 (m, 2 H), 2.86 (quint, *J* = 7.2 Hz, 1 H), 2.73 (s, 1 H), 2.07–1.55 (m, 13 H), 1.26 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.8 (C, d, $J_{C,F}$ = 242 Hz), 138.2 (C, d, $J_{C,F}$ = 3 Hz), 129.2 (2 × CH, d, $J_{C,F}$ = 7.5 Hz), 115.4 (2 × CH, d, $J_{C,F}$ = 21 Hz), 104.64 (C), 82.5 (CH), 60.9 (CH_2), 40.0 (CH), 37.4 (CH_2), 36.0 (CH), 33.6 (CH_2), 33.5 (CH_2), 33.3 (CH_2), 33.2 (CH_2), 29.8 (CH), 27.30 (CH), 27.26 (CH), 17.7 (CH_3).

FAB-MS: *m*/*z* = 333 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{20}H_{25}FO_3$ [M^+]: 332.1788; found: 332.1781.

8-(1-Phenylethyl)-6,7,10-trioxaspiro[4.5]decane (4d)
Oil.

FT-IR (neat): 760, 1063, 1118, 1604, 2970 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.16 (m, 5 H), 4.34 (dt, *J* = 9.0, 2.9 Hz, 1 H), 3.52 (dd, *J* = 11.8, 9.0 Hz, 1 H), 3.41 (dd, *J* = 11.8, 2.9 Hz, 1 H), 2.80 (quint, *J* = 6.9 Hz, 1 H), 2.37–2.32 (m, 1 H), 1.85–1.63 (m, 7 H), 1.36 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.0 (C), 128.9 (2 × CH), 127.8 (2 × CH), 127.2 (CH), 114.4 (C), 83.2 (CH), 63.9 (CH_2), 40.7 (CH), 36.6 (CH_2), 33.4 (CH_2), 24.7 (CH_2), 23.6 (CH_2), 18.4 (CH_3).

FAB-MS: *m*/*z* = 249 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{15}H_{20}O_3$ [M^+]: 248.14125; found: 248.13959.

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C 72.32; H, 7.95.

8-(1-Phenylethyl)-6,7,10-trioxaspiro[4.5]decane (5d)
Oil.

FT-IR (neat): 701, 1031, 1110, 1603, 2966 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.20 (m, 5 H), 4.48 (ddd, *J* = 9.8, 7.6, 2.8 Hz, 1 H), 3.82 (dd, *J* = 11.5, 2.8 Hz, 1 H), 3.69 (dd, *J* = 11.5, 9.8 Hz, 1 H), 2.86 (quint, *J* = 7.2 Hz, 1 H), 2.34–2.29 (m, 1 H), 1.78–1.60 (m, 7 H), 1.27 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.2 (C), 128.5 (2 × CH), 127.8 (2 × CH), 126.8 (CH), 114.4 (C), 82.5 (CH), 63.6 (CH_2), 40.5 (CH), 36.9 (CH_2), 33.0 (CH_2), 24.7 (CH_2), 23.5 (CH_2), 17.4 (CH_3).

FAB-MS: *m*/*z* = 249 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{15}H_{20}O_3$ [M^+]: 248.1413; found: 248.1413.

Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.90; H, 8.50.

3-(1-Phenylethyl)-1,2,5-trioxaspiro[5.5]undecane (4e)
Oil.

FT-IR (neat): 764, 1023, 1097, 1602, 2935 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.16 (m, 5 H), 4.30 (dt, *J* = 9.2, 2.1 Hz, 1 H), 3.62 (dd, *J* = 11.8, 9.2 Hz, 1 H), 3.33 (dd, *J* = 11.8, 2.1 Hz, 1 H), 2.80 (br quint, 1 H), 2.13–2.07 (m, 1 H), 1.91–1.84 (m, 1 H), 1.64–1.44 (m, 8 H), 1.37 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.0 (C), 128.9 (2 × CH), 127.8 (2 × CH), 127.3 (CH), 102.5 (C), 83.3 (CH), 61.6 (CH_2), 40.9 (CH), 34.2 (CH_2), 29.7 (CH_2), 25.7 (CH_2), 22.5 (CH_2), 22.47 (CH_2), 18.5 (CH_3).

FAB-MS: *m*/*z* = 263 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{16}H_{22}O_3$ [M^+]: 262.1569; found: 262.1569.

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.35; H, 8.50.

3-(1-Phenylethyl)-1,2,5-trioxaspiro[5.5]undecane (5e)
Oil.

FT-IR (neat): 765, 1030, 1091, 1602, 2940 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.32–7.20 (m, 5 H), 4.44 (ddd, *J* = 9.9, 7.8, 3.2 Hz, 1 H), 3.82 (dd, *J* = 11.7, 9.9 Hz, 1 H), 3.73 (dd, *J* = 11.7, 3.2 Hz, 1 H), 2.86 (quint, *J* = 7.3 Hz, 1 H), 2.11–2.03 (m, 1 H), 1.87–1.79 (m, 1 H), 1.61–1.38 (m, 8 H), 1.27 (d, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 142.3 (C), 128.7 (2 × CH), 127.9 (2 × CH), 126.9 (CH), 102.6 (C), 82.7 (CH), 61.4 (CH_2), 40.7 (CH), 34.6 (CH_2), 29.4 (CH_2), 25.7 (CH_2), 22.5 (CH_2), 22.4 (CH_2), 17.5 (CH_3).

FAB-MS: *m*/*z* = 263 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{16}H_{22}O_3$ [M^+]: 262.1569; found: 262.1534.

Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.10; H, 8.70.

8-(1-Phenylethyl)-6,7,11-trioxaspiro[4.6]undecane (7a)
Oil.

FT-IR (neat): 1023, 1100, 1607, 2920 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.33–7.16 (m, 5 H), 4.22 (dt, *J* = 9.7, 3.8 Hz, 1 H), 3.80 (dt, *J* = 12.0, 1.2 Hz, 1 H), 3.67 (td, *J* = 12.2, 3.7 Hz, 1 H), 2.75 (quint, *J* = 6.9 Hz, 1 H), 2.15–1.47 (m, 10 H), 1.37 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 144.5 (C), 128.9 (2 × CH), 128.1 (2 × CH), 126.9 (CH), 118.3 (C), 88.8 (CH), 62.5 (CH_2), 43.9 (CH), 36.8 (CH_2), 36.5 (CH_2), 34.9 (CH_2), 24.4 (2 × CH_2), 19.3 (CH_3).

ESI-MS: *m*/*z* = 263 [M + H^+], 285 [M + Na^+].

EI-HRMS: *m*/*z* calcd for $C_{16}H_{22}O_3$ [M^+]: 262.1569; found: 262.1583.

8-(1-Phenylethyl)-6,7,11-trioxaspiro[4.6]undecane (8a)
Oil.

FT-IR (neat): 1020, 1150, 1615, 2925 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.33–7.20 (m, 5 H), 4.40–4.29 (m, 1 H), 3.87–3.72 (m, 2 H), 2.93 (quint, *J* = 7.2 Hz, 1 H), 2.14–1.57 (m, 10 H), 1.29 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 143.7 (C), 128.7 (2 × CH), 128.4 (2 × CH), 126.9 (CH), 118.2 (C), 88.0 (CH), 62.3 (CH_2), 43.4 (CH), 36.5 (CH_2), 35.2 (CH_2), 35.0 (CH_2), 24.4 (2 × CH_2), 18.1 (CH_3).

ESI-MS: *m*/*z* = 269 [M + Li^+], 285 [M + Na^+], 301 [M + K^+].

EI-HRMS: *m*/*z* calcd for $C_{16}H_{22}O_3$ [M^+]: 262.1569; found: 262.1593.

8-(1-Biphenyl-4-ylethyl)-6,7,11-trioxaspiro[4.6]undecane (7b)
White solid; mp 76–79 °C.

FT-IR (KBr): 1041, 1158, 1605, 2945 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.59–7.23 (m, 9 H), 4.26 (dt, *J* = 9.6, 3.8 Hz, 1 H), 3.82 (dt, *J* = 12.2, 1.8 Hz, 1 H), 3.69 (td, *J* = 12.2, 3.7 Hz, 1 H), 2.81 (quint, *J* = 6.9 Hz, 1 H), 2.16–1.47 (m, 10 H), 1.41 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 143.5 (C), 141.2 (C), 139.9 (C), 129.2 (2 × CH), 128.5 (2 × CH), 127.7 (CH), 127.6 (2 × CH), 127.4 (2 × CH), 118.3 (C), 88.7 (CH), 62.4 (CH_2), 43.5 (CH), 36.8 (CH_2), 36.5 (CH_2), 34.9 (CH_2), 24.4 (2 × CH_2), 19.2 (CH_3).

ESI-MS: *m*/*z* = 339 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{22}H_{26}O_3$ [M^+]: 338.1882; found: 338.1834.

8-(1-Biphenyl-4-ylethyl)-6,7,11-trioxaspiro[4.6]undecane (8b)
White solid; mp 100–104 °C.

FT-IR (KBr): 1036, 1163, 1609, 2950 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.60–7.26 (m, 9 H), 4.37 (ddd, *J* = 10.5, 6.8, 4.1 Hz, 1 H), 3.89 (dt, *J* = 11.9, 1.9 Hz, 1 H), 3.77 (td, *J* = 12.1, 3.8 Hz, 1 H), 2.92 (quint, *J* = 7.2 Hz, 1 H), 2.15–1.65 (m, 10 H), 1.32 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 142.9 (C), 141.5 (C), 139.7 (C), 129.1 (2 × CH), 128.7 (2 × CH), 127.5 (5 × CH), 118.2 (C), 88.0 (CH), 62.3 (CH_2), 43.0 (CH), 36.4 (CH_2), 35.3 (CH_2), 34.9 (CH_2), 24.4 (2 × CH_2), 18.2 (CH_3).

ESI-MS: *m*/*z* = 339 [M + H^+], 377 [M + $K]^+$.

EI-HRMS: *m*/*z* calcd for $C_{22}H_{26}O_3$ [M^+]: 338.1882; found: 338.1886.

9-(1-Biphenyl-4-ylethyl)-7,8,12-trioxaspiro[5.6]dodecane (7c)
White solid; mp 70–73 °C.

FT-IR (KBr): 1010, 1153, 1611, 2930 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.60–7.22 (m, 9 H), 4.22 (dt, *J* = 12.3, 3.5 Hz, 1 H), 3.87 (t, *J* = 11.4 Hz, 1 H), 3.68–3.62 (m, 1 H), 2.80 (br m, 1 H), 1.81–1.56 (m, 12 H), 1.40 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 143.5 (C), 141.3 (C), 139.9 (C), 129.2 (2 × CH), 128.5 (2 × CH), 127.7 (CH), 127.6 (2 × CH), 127.4 (2 × CH), 106.8 (C), 88.5 (CH), 60.5 (CH_2), 43.4 (CH), 36.9 (CH_2), 34.4 (CH_2), 32.0 (CH_2), 25.9 (CH_2), 23.4 (CH_2), 23.2 (CH_2), 19.1 (CH_3).

ESI-MS: *m*/*z* = 353 [M + H^+], 371 [M + NH_4^+].

EI-HRMS: *m*/*z* calcd for $C_{23}H_{28}O_3$ [M^+]: 352.2039; found: 352.2036.

9-(1-Biphenyl-4-ylethyl)-7,8,12-trioxaspiro[5.6]dodecane (8c)
White solid; mp 76–80 °C.

FT-IR (KBr): 1008, 1150, 1615, 2935 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.60–7.24 (m, 9 H), 4.32 (ddd, *J* = 10.9, 10.2, 3.5 Hz, 1 H), 3.93 (dt, *J* = 12.0, 0.9 Hz, 1 H), 3.70 (td, *J* = 12.3, 3.3 Hz, 1 H), 2.99 (quint, *J* = 7.2 Hz, 1 H), 1.86–1.39 (m, 12 H), 1.33 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 142.7 (C), 141.4 (C), 139.7 (C), 129.1 (2 × CH), 128.8 (2 × CH), 128.5 (CH), 127.4 (4 × CH), 106.8 (C), 87.9 (CH), 60.6 (CH_2), 42.9 (CH), 35.1 (CH_2), 34.6 (CH_2), 31.8 (CH_2), 25.9 (CH_2), 23.5 (CH_2), 23.1 (CH_2), 17.8 (CH_3).

ESI-MS: *m*/*z* = 353 [M + H$^+$].

EI-HRMS: *m*/*z* calcd for $C_{23}H_{28}O_3$ [M$^+$]: 352.2039; found: 352.2052.

2-Hydroperoxy-3-naphthalen-2-ylbutan-1-ol (10)
Oil.

FT-IR (neat): 750, 820, 1063, 1599, 2928, 3405 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.72 (br m, 1 H, OOH), 7.77–7.21 (m, 7 H), 4.15–4.02 (m, 1 H), 3.74 (dd, *J* = 12.3, 2.3 Hz) and 3.50 (dd, *J* = 12.2, 2.9 Hz, 1 H total), 3.66 (dd, *J* = 12.3, 6.2 Hz) and 3.42 (dd, *J* = 12.2, 6.4 Hz, 1 H total), 3.09 (br quint, *J* = 7.2 Hz) and 2.20 (quint, *J* = 7.2 Hz, 1 H total), 1.40 (d, *J* = 7.0 Hz) and 1.28 (d, *J* = 7.2 Hz, 3 H total).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.0 (C), 139.4 (C), 133.7 (C), 132.8 (C), 132.7 (C), 128.7 (CH), 128.4 (CH), 127.9 (CH), 127.83 (CH), 127.78 (CH), 126.6 (CH), 126.5 (CH), 126.4 (CH), 126.14 (CH), 126.11 (CH), 125.9 (CH), 125.7 (CH), 83.2 (CH), 82.6 (CH), 61.2 (CH_2), 61.0 (CH_2), 41.04 (CH), 40.98 (CH), 18.8 (CH_3), 17.8 (CH_3).

ESI-MS: *m*/z = 255 [M + Na$^+$].

3-(4-Fluorophenyl)-2-hydroperoxybutan-1-ol (14)
Oil.

FT-IR (neat): 841, 1045, 1603, 2932, 3405 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.73 (br m, 1 H, OOH), 7.22–6.98 (m, 4 H), 4.05 and 3.96 (2 m, 1 H), 3.89 (dd, *J* = 12.3, 2.6 Hz) and 3.56 (dd, *J* = 12.2, 2.8 Hz, 1 H total), 3.70 (dd, *J* = 12.3, 6.6 Hz) and 3.44 (dd, *J* = 12.2, 6.6 Hz, 1 H total), 3.09 (quint, *J* = 7.2 Hz) and 3.03 (quint, *J* = 7.0 Hz, 1 H total), 1.34 (d, *J* = 7.0 Hz) and 1.25 (d, *J* = 7.2 Hz, 3 H total).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 162.0 (d, C, $J_{C,F}$ = 244 Hz), 161.9 (d, C, $J_{C,F}$ = 243 Hz), 138.0 (d, C, $J_{C,F}$ = 3.0 Hz), 137.7 (d, C, $J_{C,F}$ = 3.0 Hz), 129.3 (d, CH, $J_{C,F}$ = 7.5 Hz), 129.2 (d, CH, $J_{C,F}$ = 7.5 Hz), 115.8 (d, CH, $J_{C,F}$ = 22 Hz), 115.4 (d, CH, $J_{C,F}$ = 21 Hz), 83.2 (CH), 82.7 (CH), 61.44 (CH_2), 61.37 (CH_2), 40.05 (CH), 39.99 (CH), 18.5 (CH_3), 17.7 (CH_3).

ESI-MS: *m*/*z* = 223 [M + Na$^+$].

3-Hydroperoxy-4-phenylpentan-1-ol (18)
Oil.

FT-IR (neat): 836, 1038, 1601, 2926, 3396 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.49 (br m, 1 H, OOH), 7.39–7.15 (m, 5 H), 4.16–3.54 (m, 3 H), 3.27 (quint, *J* = 6.7 Hz) and 3.08 (quint, *J* = 7.4 Hz, 1 H total), 1.79–1.49 (m, 2 H), 1.35 (d, *J* = 6.9 Hz) and 1.27 (d, *J* = 6.9 Hz, 3 H total).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 144.2 (C), 143.6 (C), 128.9 (CH), 128.8 (CH), 128.4 (CH), 128.3 (CH), 126.9 (CH), 126.8 (CH), 88.8 (CH), 88.7 (CH), 60.6 (CH_2), 42.9 (CH), 41.9 (CH), 33.2 (CH_2), 31.9 (CH_2), 18.7 (CH_3), 15.8 (CH_3).

ESI-MS: *m*/*z* = 197 [M + H$^+$].

4-Biphenyl-4-yl-3-hydroperoxypentan-1-ol (22)
Oil.

FT-IR (neat): 821, 1042, 1600, 2949, 3401 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.59–7.23 (m, 9 H), 4.27–4.01 (m, 1 H), 3.88–3.64 (m, 2 H), 3.34–3.05 (m, 2 H), 1.82–1.62 (m, 2 H), 1.41 (d, *J* = 7.0 Hz) and 1.33 (d, *J* = 7.2 Hz, 3 H total).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 143.3 (C), 142.7 (C), 141.3 (C), 139.7 (C), 129.2 (CH), 128.8 (CH), 128.7 (CH), 127.5 (CH), 127.4 (CH), 89.3 (CH), 89.1 (CH), 61.0 (CH_2), 42.7 (CH), 42.0 (CH), 33.2 (CH_2), 32.4 (CH_2), 30.1 (CH_2), 29.8 (CH_2), 18.7 (CH_3), 16.5 (CH_3).

ESI-MS: *m*/*z* = 273 [M + H$^+$].

1-Isopropyl-4-methyl-2,3-dioxabicyclo[2,2,2]octane (Dihydroascaridole, 26)
Oil.

FT-IR (neat): 1039, 1116, 2965 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.97–1.81 (br m, 4 H), 1.75–1.63 (br m, 5 H), 1.11 (s, 3 H), 0.87 (d, *J* = 7.1 Hz, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 79.1 (C), 74.4 (C), 34.4 (CH), 30.8 (2 × CH_2), 26.1 (2 × CH_2), 24.1 (CH_3), 16.9 (2 × CH_3).

ESI-MS: *m*/*z* = 171 [M + H$^+$].

EI-HRMS: *m*/*z* calcd for $C_{10}H_{18}O_2$ [M$^+$]: 170.1307; found: 170.1284.

Borohydride Reduction of Saturated β-Hydroxyhydroperoxides and γ-Hydroxyhydroperoxides; Typical Procedure for the Reduction of Saturated β-Hydroxyhydroperoxide 10
To a stirred and ice cooled solution of β-hydroxyhydroperoxide **10** (0.100 g, 0.431 mmol) in MeOH (5 mL), was added $NaBH_4$ (0.033 g, 2 equiv) and the reaction mixture was allowed to stir for 5 min. The mixture was quenched with glacial AcOH (0.5 mL), concentrated under vacuum, diluted with H_2O (5 mL), and extracted with EtOAc (3 × 10 mL). The combined organic extracts were washed with brine (5 mL), concentrated, and the crude product was purified by column chromatography over silica gel to furnish the saturated diol **11** (0.090 g, 97%) as a colorless oil.

Hydroperoxides **14**, **18**, and **22** were also reduced by the same procedure to furnish diols **15**, **19**, and **23** as inseparable diastereomeric mixtures in 87, 81, and 85% yields, respectively.

Catalytic Hydrogenation of β-Hydroxyhydroperoxide 9
A solution of β-hydroxyhydroperoxide **9** (0.200 g, 0.869 mmol) in EtOAc (15 mL) was hydrogenated in the presence of Adam's catalyst (PtO_2, 0.003 g) using a Parr shaker assembly at r.t. and pressure for 1 h. The reaction mixture was filtered over Celite, concentrated, and the crude product was purified by column chromatography over silica gel to furnish the saturated diol **11** (96%) as a colorless oil.

3-Naphthalen-2-ylbutane-1,2-diol (11)
Oil.

FT-IR (neat): 751, 1068, 1109, 1623, 2929, 3282 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.67–7.28 (m, 7 H), 3.81 (dt, *J* = 7.4, 2.6, 1 H), 3.73 (dd, *J* = 11.4, 2.8 Hz) and 3.39 (dd, *J* = 11.3, 2.9 Hz, 1 H total), 3.49 (dd, *J* = 11.4, 7.2 Hz) and 3.29 (dd, *J* = 11.3, 7.5 Hz, 1 H total), 2.98 (quint, *J* = 7.0 Hz) and 2.89 (quint, *J* = 7.0 Hz, 1 H total), 3.02–2.84 (br m, 2 H, 2 OH), 1.41 (d, *J* = 7.0 Hz) and 1.32 (d, *J* = 7.0 Hz, 3 H total).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.9 (C), 133.7 (C), 133.6 (C), 132.6 (C), 132.5 (C), 128.4 (CH), 128.3 (CH), 127.79 (H), 127.76 (CH), 126.8 (CH), 126.30 (CH), 126.27 (CH), 126.21 (CH), 126.17 (CH), 125.7 (CH), 125.6 (CH), 76.7 (CH), 76.3 (CH), 65.2 (CH_2), 64.8 (CH_2), 43.1 (CH), 43.0 (CH), 18.0 (CH_3), 17.7 (CH_3).

ESI-MS: *m*/*z* = 239 [M + Na$^+$].

EI-HRMS: *m*/*z* calcd for $C_{14}H_{16}O_2$ [M$^+$]: 216.1150; found: 216.1148.

3-(4-Fluorophenyl)butane-1,2-diol (15)
Oil.

FT-IR (neat): 1035, 1066, 1605, 2929, 3322 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.21–6.95 (m, 4 H), 3.72–3.64 (m, 2 H), 3.45 (dd, *J* = 11.8, 7.7) and 3.27 (dd, *J* = 11.1, 7.6 Hz, 1 H total), 2.82 (quint, *J* = 7.0 Hz) and 2.75 (quint, *J* = 7.1 Hz, 1 H total), 2.86–2.70 (br m, 2 H, 2 OH), 1.30 (d, *J* = 7.0 Hz) and 1.24 (d, *J* = 7.1 Hz, 3 H total).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.9 (C, d, $J_{C,F}$ = 243 Hz) 161.8 (C, d, $J_{C,F}$ = 244 Hz), 139.6 (C, d, $J_{C,F}$ = 3.0 Hz), 139.0 (C, d, $J_{C,F}$ = 3.0 Hz), 129.6 (CH, d, $J_{C,F}$ = 8.0 Hz), 129.1 (d, CH, $J_{C,F}$ = 7.5 Hz), 115.5 (d, CH, $J_{C,F}$ = 21 Hz), 76.8 (CH), 76.4 (CH), 65.1 (CH_2), 64.8 (CH_2), 42.3 (CH), 42.2 (CH), 18.2 (CH_3), 17.7 (CH_3).

ESI-MS: *m*/*z* = 185 [M + H^+].

4-Phenylpentane-1,3-diol (19)
Oil.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.35–7.17 (m, 5 H), 3.94–3.70 (m, 3 H), 2.84–2.70 (m, 3 H), 1.70–1.51 (m, 2 H), 1.32 (d, *J* = 7.1 Hz) and 1.26 (d, *J* = 7.0 Hz, 3 H total).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 146.4 (C), 129.0 (CH), 128.9 (CH), 128.7 (CH), 128.5 (CH), 128.2 (CH), 127.2 (CH), 126.9 (CH), 125.3 (CH), 124.9 (CH), 76.8 (CH), 65.4 (CH_2), 46.9 (CH), 46.7 (CH), 36.4 (CH_2), 35.9 (CH_2), 17.9 (CH_3), 16.8 (CH_3).

ESI-MS: *m*/*z* = 198.4 [M + NH_4^+].

4-Biphenyl-4-ylpentane-1,3-diol (23)
Oil.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.65–7.30 (m, 9 H), 4.02–3.78 (m, 3 H), 2.91–2.85 (m, 1 H), 1.89–1.64 (m, 3 H), 1.39 (d, *J* = 7.0 Hz) and 1.36 (d, *J* = 7.0 Hz, 3 H total).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 143.7 (C), 142.7 (C), 141.2 (C), 140.1 (C), 139.8 (C), 129.2 (CH), 128.9 (CH), 128.7 (CH), 127.6 (CH), 127.4 (CH), 77.0 (CH), 76.8 (CH), 62.3 (CH_2), 62.0 (CH_2), 46.6 (CH), 46.4 (CH), 36.4 (CH_2), 35.9 (CH_2), 17.9 (CH_3), 16.9 (CH_3).

ESI-MS: *m*/*z* = 257.2 [M + H^+].

Acetylation of Saturated Diols; Typical Procedure
To a stirred solution of diol **11** (0.100 g, 0.463 mmol) in CH_2Cl_2 (5 mL) were added Ac_2O (0.23 mL, 5 equiv), Et_3N (0.23 mL, 5 equiv), and a catalytic amount of DMAP (2 mg) in succession and the reaction mixture was allowed to stir for 2 h. The mixture was concentrated under vacuum and the crude product was purified by column chromatography over silica gel to furnish the diacetate **12** (0.125 g, 91%) as an oil.

Saturated diols **15, 19** and **23** were also acetylated by the same procedure to furnish corresponding diacetates **16, 20** and **24** as inseparable diastereomeric mixtures in 93, 91, and 89% yields, respectively.

Acetic Acid 1-Acetoxymethyl-2-naphthalen-2-ylpropyl Ester (12)
Oil.

FT-IR (neat): 1047, 1650, 1744, 2971 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.85–7.38 (m, 7 H), 5.44–5.37 (m, 1 H), 4.32 (dd, *J* = 12.0, 3.0 Hz) and 4.17 (dd, *J* = 12.0, 2.8 Hz, 1 H total), 4.08 (dd, *J* = 12.0, 7.1 Hz) and 3.85 (dd, *J* = 12.0, 6.6 Hz, 1 H total), 2.15 (s) and 2.06 (s, 3 H total), 3.30 (br quint, *J* = 7.1 Hz) and 3.22 (quint, *J* = 7.1 Hz, 1 H total), 1.42 (merged d) and 1.40 (d, *J* = 7.1 Hz, 3 H total), 2.03 (s) and 1.95 (s, 3 H total).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9 (C), 170.82 (C), 170.78 (C), 170.5 (C), 139.8 (C), 139.6 (C), 133.8 (C), 133.6 (C), 132.8 (C), 132.6 (C), 132.7 (C), 128.7 (CH), 128.2 (CH), 127.9 (CH), 127.8 (CH), 127.8 (CH), 126.7 (CH), 126.5 (CH), 126.4 (CH), 126.2 (CH), 125.9 (CH), 125.8 (CH), 75.4 (CH), 74.9 (CH), 64.3 (CH_2), 64.1 (CH_2), 41.4 (CH), 41.1 (CH), 21.2 (CH_3), 21.0 (CH_3), 20.9 (CH_3), 20.9 (CH_3), 18.2 (CH_3), 17.5 (CH_3).

FAB-MS: *m*/*z* = 301 [M + H^+].

EI-HRMS: *m*/*z* calcd for $C_{18}H_{20}O_4$ [M^+]: 300.1362; found: 300.1360.

Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 72.25; H, 6.50.

Acetic Acid 1-Acetoxymethyl-2-(4-fluorophenyl)propyl Ester (16)
Oil.

FT-IR (neat): 1049, 1604, 1743, 2973 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.22–6.95 (m, 4 H), 5.27–5.20 (m, 1 H), 4.23 (dd, *J* = 12.0, 3.3 Hz) and 4.13 (dd, *J* = 12.0, 2.9 Hz, 1 H total), 4.00 (dd, *J* = 12.0, 6.8 Hz) and 3.78 (dd, *J* = 12.0, 6.5 Hz, 1 H total), 3.08 (quint, *J* = 7.1 Hz) and 3.04 (quint, *J* = 6.8 Hz, 1 H total), 2.01 (s) and 1.94 (s, 3 H total), 2.09 (s) and 2.04 (s, 3 H total), 1.30 (d, *J* = 7.1 Hz) and 1.28 (d, *J* = 6.8 Hz, 3 H total).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8 (C), 170.7 (C), 170.65 (C), 170.4 (C), 162.0 (d, C, $J_{C,F}$ = 244 Hz), 161.9 (d, C, $J_{C,F}$ = 243 Hz), 138.0 (d, C, $J_{C,F}$ = 3.0 Hz), 137.8 (d, C, $J_{C,F}$ = 3.0 Hz), 129.5 (d, CH, $J_{C,F}$ = 8.0 Hz), 129.2 (d, CH, $J_{C,F}$ = 8.0 Hz), 115.7 (d, CH, $J_{C,F}$ = 22 Hz), 115.3 (d, CH, $J_{C,F}$ = 21 Hz), 75.3 (CH), 74.8 (CH), 63.9 (CH_2), 63.9 (CH_2), 40.4 (CH), 40.2 (CH), 21.1 (CH_3), 20.9 (CH_3), 17.9 (CH_3), 17.6 (CH_3).

ESI-MS: *m*/*z* = 286 [M + NH_4^+].

Acetic Acid 1-(2-Acetoxyethyl)-2-phenylpropyl Ester (20)
Oil.

FT-IR (neat): 1741 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.64–7.21 (m, 5 H), 4.10–3.95 (m, 3 H), 3.00–2.97 (m, 1 H), 2.31–2.16 (m, 2 H), 2.07 (s) and 1.95 (s, 3 H total), 2.00 (s) and 1.88 (s, 3 H total), 1.30–1.25 (m, 3 H).

ESI-MS: *m*/*z* = 282.4 [M + NH_4^+].

Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.82; H, 7.29.

Acetic Acid 1-(2-Acetoxyethyl)-2-biphenyl-4-ylpropyl Ester (24)
Oil.

FT-IR (neat): 1741 cm^{-1}.

^1H NMR (200 MHz, $CDCl_3$): δ = 7.62–7.23 (m, 9 H), 5.29–5.23 (m, 1 H), 4.10–4.02 (m, 2 H), 3.08 (quint, *J* = 7.1 Hz) and 3.00 (quint, *J* = 7.1 Hz, 1 H total), 2.12 (s) and 2.03 (s, 3 H total), 2.04 (s) and 2.01 (s, 3 H total), 1.67–1.52 (m, 2 H), 1.36–1.31 (m, 3 H).

ESI-MS: *m*/*z* = 358.4 [M + NH_4^+].

EI-HRMS: *m*/*z* calcd for $C_{21}H_{24}O_4$: 340.1675; found: 340.1678.

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(18) Due to intramolecular hydrogen bonding in diols **11**, **15**, **19**, and **23**, ^{1}H NMR spectra of these compounds show complex multiplicity pattern. Conversion of these diols into the corresponding diacetates, on the other hand, provides clear multiplicity pattern in ^{1}H NMR spectra.

(19) Diimide reduction of ascaridole using dipotassium azodicarboxylate is known to furnish dihydroascaridole in ~40% yield: see reference 10a.

(20) In our hands all these peroxides have behaved well, but the usual precautions for handling of peroxides are recommended.