Short path syntheses of α-diozonides by sequential ozonolyses of acetylenes and *O*-methyl oximes

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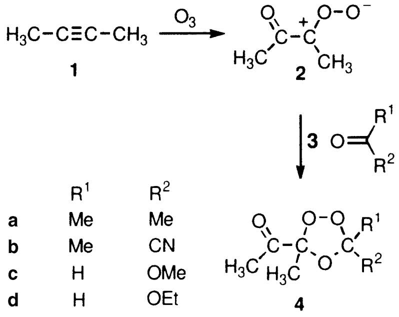
Ozonolyses of but-2-yne 1 in the presence of added carbonyl compounds 3 afford α-oxo ozonides 4. Subsequent cycloadditions between ozonides 4 and cyclohexanone oxide 6, generated *in situ* by ozonolysis of *O*-methylcyclohexanone oxime, yield in turn α-diozonides 7 into which have been incorporated the carbon skeletons of all three substrates involved. Ozonolyses of acyloxy-substituted but-2-ynes 9 yield the corresponding bicyclic α-oxo ozonides 11 which subsequently participate in analogous cycloadditions with 6 to produce the corresponding α-diozonides 12. X-Ray crystallographic analysis of the crystalline diozonide 12a shows that it has been formed exclusively by *exo*-addition of 6 to 11a.

Introduction

Reactions of ozone with acetylenes like but-2-yne **1** in the liquid phase have been reported to proceed *via* α-oxo carbonyl oxides of type **2**.[1] Recently, we have been able to trap the intermediates **2** using a variety of carbonyl compounds **3** to give the corresponding α-oxo ozonides of type **4** (Scheme 1).[2] Not surprisingly, most of these ozonides were found to be labile and tended to decompose during attempts to isolate them. This instability of ozonides **4** seems to be induced by the presence of the α-oxo groups because derivatization of these compounds with *O*-methylhydroxylamine afforded stable, readily isolable ozonides.[2]



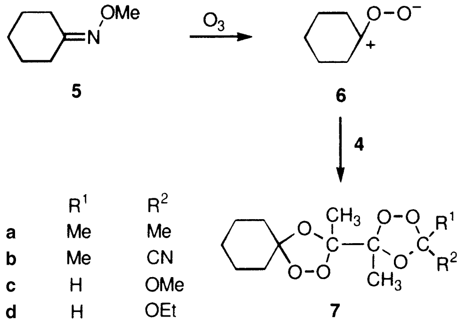
	R¹	R²
a	Me	Me
b	Me	CN
c	H	OMe
d	H	OEt

Scheme 1

We now report the results of our recent investigations into the [3 + 2] cycloadditions between the α-oxo groups in ozonides **4** and the carbonyl oxide, cyclohexanone oxide **6**, as a potential synthetic route to the structurally novel diozonides **7**.

Results and discussion

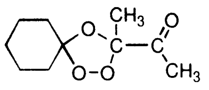
Treatment of but-2-yne **1** with ozone in the presence of one of the carbonyl compounds **3a**–**3d** gave a crude product mixture containing the corresponding ozonides **4**. *O*-Methylcyclohexanone oxime **5** was then added and the ozonolysis was resumed to generate the carbonyl oxide **6**[3] required to effect the proposed cycloaddition as outlined in Scheme 2. These sequential ozonolysis reactions resulted in the formation of the respective α-diozonides **7a** (14%), **7b** (20%), **7c** (8%) and **7d** (25%) which could be isolated by column chromatography on silica in the yields given in parentheses. In each case, they appeared to consist of mixtures of two diastereoisomers; those with the shorter HPLC retention times were designated as stereoisomers **I** and those with the longer elution times were designated as stereoisomers **II**.† Of these, diozonides **7a-I**, **7a-II**, **7b-I**, **7b-II**, **7c-II** and **7d-II** could be isolated as single stereoisomers by preparative HPLC, whereas **7c-I** and **7d-I** were only obtained in admixture with the corresponding isomers **II**. All ozonides were characterized by positive peroxide tests and satisfactory elemental analyses as well as their ^1H and ^{13}C NMR spectral data.



	R¹	R²
a	Me	Me
b	Me	CN
c	H	OMe
d	H	OEt

Scheme 2

Reductions of ozonides **7** with triphenylphosphine would be expected to produce three fragments: carbonyl compound **3**, butanedione and cyclohexanone in a molar ratio of *ca.* 1:1:1. While fragments **3** and cyclohexanone were indeed obtained in *ca.* 1:1 molar ratios, butanedione was only obtained in variable ratios of *ca.* 0.2–0.4 and the hitherto unexpected product, acetic anhydride, was identified additionally. On monitoring the reductions of **7c** and **7d** by ^1H NMR spectroscopy, the formation of the intermediate α-oxo ozonide **8** was observed, along with equimolar amounts of the respective carbonyl compounds **3**. In contrast, there was no evidence for the formation of the alternative possible products of stepwise reductions of **7c** and **7d**, *viz.* α-oxo ozonides **4c** and **4d**, respectively although these ozonides are known to be relatively stable and should,



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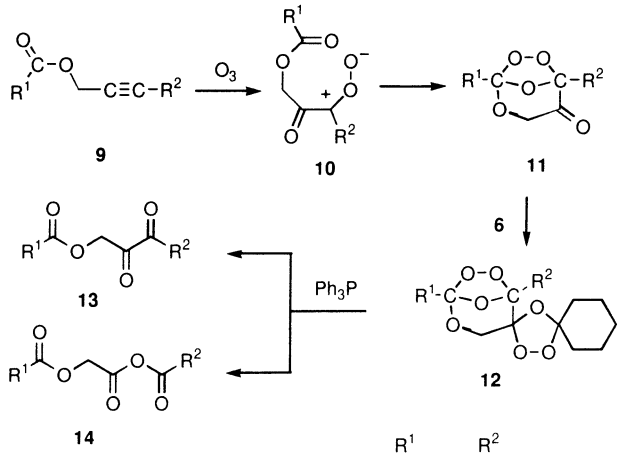
† The structures of these stereoisomers could not be determined unambiguously from the available analytical data. Diozonides **7b**–**d**, each having three chiral centres, should, in principle, give rise to diastereoisomers. However, ozonolyses of **1** in the presence of **2b**–**d** gave only one of the two possible diastereoisomers of **4c**–**d** (ref. 2). Subsequent reactions of **4c**–**d** could, therefore, produce only two diastereoisomers for each of **7b**–**d**.

therefore, have been readily detectable.[2] This suggests that diozonides **7c** and **7d** undergo stepwise reductions whereby the less substituted ozonide ring is reduced preferentially, probably due to lower steric hindrance towards the attacking triphenylphosphine. The subsequent reduction steps of **7c** and **7d**, *viz.* the conversion of intermediate ozonide **8** into cyclohexanone and butanedione, are obviously accompanied by the decomposition of the labile ozonide **8**[2] to give cyclohexanone and acetic anhydride according to an established fragmentation pattern for α-oxo ozonides.[4] Since acetic anhydride was also formed during the reductions of diozonides **7a** and **7b**, it is assumed that they had also been reduced in a similar stepwise fashion.

In previous work, it had been shown that, even in the presence of added carbonyl compounds **3**, ozonolyses of acetylenes **9a–9d** afforded the corresponding bicyclic ozonides **11** by intramolecular cycloadditions of the carbonyl oxide moieties in **10** with the carbonyl group attached to R^1 in **10**.[2] The sequential ozonolysis technique described above has also been investigated using acetylenes **9a–9d** as substrates and *O*-methylcyclohexanone oxime **5** as a method of producing, by analogy, the corresponding diozonides **12** (Scheme 3).



	R^1	R^2
a	Ph	CH_2OCOPh
b	Me	CH_2OCOMe
c	Ph	Me
d	Me	Me

Scheme 3

Thus, on following the above procedure, α-diozonides **12a** (26%), **12b** (26%), **12c** (17%) and **12d** (15%) were prepared and isolated by chromatography in the yields indicated in parentheses. Their respective analytical and spectral data were generally consistent with the structural formulae **12a–d**. Although diozonides **12a–c** were stable compounds, **12d** decomposed rapidly in $CDCl_3$ though only gradually in C_6D_6 at room temperature. From their ^{1}H and ^{13}C NMR spectral data, the isolated diozonides **12a–d** appeared to consist only of a single diastereoisomer in each case and there was no evidence for the presence of other diastereoisomers in the residual product mixtures.

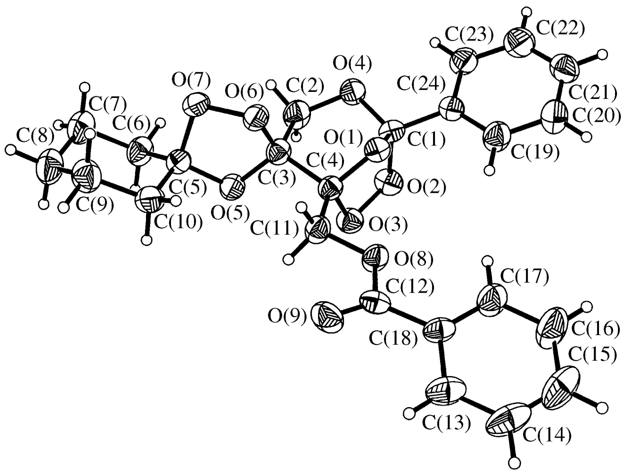
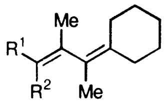


Fig. 1 The molecular structure of one molecule of compound **12a** (ORTEP,[11] the non-hydrogen atoms are represented by 30% probability ellipsoids and hydrogen atoms by spheres of arbitrary radius)

The molecular structure of **12a**, as determined by X-ray diffraction crystallographic analysis, is depicted in Fig. 1 along with the numbering system used in the structural study. Consistent with the spectral data obtained, diozonide **12a** is a single diastereoisomer with relative configuration *S**,*R** at C(3) and C(4) respectively, formed by the approach of the cyclohexanone oxide **6** to the carbonyl group of intermediate bicyclic ozonide **11a** exclusively from the nominally less hindered *exo*-face.‡ The trioxolane ring O(1)–C(1)–O(2)–O(3)–C(4), which is an integral part of the relatively rigid [3.2.1] bicyclic skeleton, has an envelope conformation, whereby the four atoms C(1), O(2), O(3) and C(4) essentially lie in a plane (rms deviation 0.011 Å) and the oxygen atom of the ether bridge is displaced out of the plane by 0.604(5) Å. The monocyclic ozonide moiety O(5)–C(3)–O(6)–O(7)–C(5), being conformationally less restricted, adopts a distorted half-chair arrangement with the peroxidic oxygen atoms O(6) and O(7) being displaced from the plane defined by C(3)–O(5)–C(5) by 0.457(9) and −0.259(10) Å respectively. Despite the marked differences in chemical environments of the ozonide rings, the O–O bond distances of 1.476(4) Å for O(2)–O(3) and 1.467(4) Å for O(6)–O(7) are not significantly different from each other and are in reasonable agreement with the expected value of 1.47 Å for monocyclic peroxides[5] and also some polycyclic peroxides.[6] It should, however, be noted that lengthened O–O bond distances have been reported for several related [3.2.1] bicyclic peroxide systems.[7]

Reduction of diozonides **12a–12d** using triphenylphosphine not only yielded cyclohexanone and the diketones **13**, but also the corresponding anhydrides **14**. Although this was probably indicative of a stepwise reduction of the two ozonide rings, it is not known which of the two ozonide rings is reduced initially because neither of the putative intermediate monoozonides was observed.

The sequential ozonolysis of acetylenes and of *O*-methyl oximes described above provides a short and convenient route to the synthesis of structurally novel α-diozonides *via* a one-pot procedure. This route not only obviates the synthesis of the parent dialkenes of types **15** or **16**, but it may, in many cases, offer the only access to such α-diozonides because direct ozonolysis of conjugated dienes with persubstituted double bonds sometimes does not provide the corresponding diozonides.[8] Thus, by a judicious selection of the acetylenic substrate, carbonyl compound and the *O*-methyl oxime, this method provides considerable scope for the synthesis of a large variety of α-diozonides.



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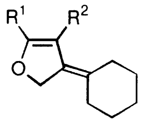

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Experimental

General

^{1}H and ^{13}C NMR spectra were measured on a Bruker AC 250 in $CDCl_3$ solution with tetramethylsilane (TMS) as internal reference unless otherwise stated. Coupling constants *J* are given in Hz.

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‡ Since the crystal structure of **12a** is centrosymmetric, both the *S*,*R* and the *R*,*S* enantiomers are present in the crystal.

Chromatographic separations: flash chromatography[9] was carried out on silica gel (Macherey and Nagel, type Si 60, 0.04–0.063 mm) and preparative HPLC using a Merck/Hitachi 655 A-11 Chromatograph (stainless steel column, 25 × 3.2 cm, stationary phase: Li Chrosorb Si 60].

But-2-yne **1** was supplied by Fluka AG and acetylenes **9a–d** were prepared from the corresponding alcohols and acyl chlorides.

Co-ozonolyses of but-2-yne 1 and carbonyl compounds 3, followed by ozonolyses of *O*-methylcyclohexanone oxime 5

Co-ozonolyses of but-2-yne **1** in the presence of carbonyl compounds **3** were carried out in CH_2Cl_2 at −75 °C. The solvent and residual carbonyl compounds **3** were distilled off under reduced pressure at 10 °C. A cold (−20 °C) solution of *O*-methylcyclohexanone oxime **5** in pentane (100 ml) was added to the resulting residue and the ozonolysis was continued until the solution turned blue. The crude product mixture was washed with saturated aqueous $NaHCO_3$, dried with $MgSO_4$ and the solvent was distilled off at room temp. Flash chromatography of the residue (eluent pentane–diethyl ether, 10:1) gave mixtures of diastereoisomeric diozonides, which were further separated by the HPLC methods.

Preparation of 3-methyl-3-(3,5,5-trimethyl-1,2,4-trioxolan-3-yl)-1,2,4-trioxaspiro[4.5]decane 7a. Ozonolysis of a solution of **1** (1.09 g, 20.2 mmol) in CH_2Cl_2 (40 ml) and in the presence of acetone (1.17 g, 20.2 mmol) was followed by the addition of a solution of **5** (1.79 g, 14.1 mmol) in pentane and further ozonolysis to give a residue (2.52 g) from which was isolated **7a** as a mixture of isomers (0.79 g, 14%; isomer ratio 1:2.5) (Found: C, 56.54; H, 8.07. $C_{13}H_{22}O_6$ requires C, 56.92; H, 8.08%). Subsequent separation by HPLC (pentane–diethyl ether, 96:4) gave **7a-I** as a colourless liquid (0.14 g, 3%) [t_R 20.6 min; δ_H 1.51 (s, 3 H), 1.54 (s, 9 H), 1.30–2.00 (m, 10 H); δ_C 20.16, 20.40, 23.20, 23.77, 23.84, 24.90, 24.97, 32.76, 34.53, 108.52, 108.96, 109.53, 110.40] and **7a-II** as a colourless liquid (0.43 g, 8%) [t_R 21.6 min; δ_H 1.51, 1.53, 1.54 (overlapping s, total of 12 H), 1.30–2.00 (m, 10 H); δ_C 20.21, 20.36, 23.56, 23.73, 23.86, 24.87, 24.92, 32.97, 34.65, 108.35, 109.02, 109.72, 110.53].

Reduction of diozonide 7a. A solution of one drop of **7a** (mixture of isomers **I** and **II**) in $CDCl_3$ (0.8 ml) was treated with excess triphenylphosphine. ^1H NMR analysis after 2 days showed the presence of acetone [δ_H 2.18 (s)], butanedione [δ_H 2.33 (s)], acetic anhydride [δ_H 2.23 (s)] and cyclohexanone [δ_H 2.35 (t)] in a relative molar ratio of 2.7:1:2.3:3.3.

Preparation of 3-(5-cyano-3,5-dimethyl-1,2,4-trioxolan-3-yl)-3-methyl-1,2,4-trioxaspiro[4.5]decane 7b. Ozonolysis of a solution of **1** (1.17 g, 21.7 mmol) in CH_2Cl_2 (60 ml) in the presence of acetyl cyanide (1.47 g, 21.3 mmol) was followed by the addition of a solution of **5** (2.06 g, 16.2 mmol) in pentane and further ozonolysis to give a residue (5.53 g) from which a mixture of **7b-I** and **7b-II** as a colourless oil (1.22 g, 20%; isomer ratio 3:1) was isolated by chromatography (pentane–diethyl ether, 96:4) (Found: C, 55.12; H, 6.74; N, 5.23. $C_{13}H_{19}NO_6$ requires C, 54.73; H, 6.71; N, 4.91%). Further separation by HPLC gave **7b-I** (0.55 g, 9%) [colourless liquid; t_R 26.9 min; δ_H 1.30–1.90 (m, 10 H), 1.49 (s, 3 H), 1.70 (s, 3 H), 1.90 (s, 3 H); δ_C 18.28, 19.88, 19.92, 23.66, 23.85, 24.86, 32.57, 34.47, 98.49, 108.52, 107.90, 110.74, 111.49, 116.66] and **7b-II** (0.20 g, 3%) [colourless liquid; t_R 30.1 min; δ_H 1.30–1.90 (m, 10 H), 1.50 (s, 3 H), 1.70 (s, 3 H), 1.89 (s, 3 H); δ_C 18.20, 19.92, 20.16, 23.62, 23.88, 24.82, 32.78, 34.58, 98.42, 107.78, 110.99, 111.42, 116.61].

Reduction of diozonide 7b. A solution of **7b** (20 mg, mixture of isomers **I** and **II**) in $CDCl_3$ (0.8 ml) was treated with excess triphenylphosphine. ^1H NMR analysis after 3 days showed the presence of acetyl cyanide [δ_H 2.56 (s)], butanedione, acetic anhydride and cyclohexanone in a relative molar ratio of 4.5:1:4.5:5.

Preparation of 3-(5-methoxy-3-methyl-1,2,4-trioxolan-3-yl)-3-methyl-1,2,4-trioxaspiro[4.5]decane 7c. Ozonolysis of a solution of **1** (1.60 g, 29.6 mmol) in CH_2Cl_2 (60 ml) in the presence of methyl formate (1.78 g, 29.7 mmol) was followed by the addition of a solution of **5** (2.63 g, 20.7 mmol) in pentane and further ozonolysis to give an oily residue (2.73 g) from which a mixture of **7c-I** and **7c-II** (0.65 g, 8%; isomer ratio 1:7) was isolated (pentane–diethyl ether, 98:2) (Found: C, 52.33; H, 7.49. $C_{12}H_{20}O_7$ requires C, 52.17; H, 7.30%). Further separation by HPLC gave an initial fraction containing **7c-I** (33% in admixture with 67% of **7c-II**) (0.13 g, 2%) [colourless oil; t_R 26.1 min; δ_H 1.50 (s, 3 H), 1.64 (s, 3 H), 1.30–2.00 (m, 10 H), 3.42 (s, 3 H), 6.06 (s, 1 H); δ_C 17.83, 20.03, 23.80, 23.84, 24.91, 33.03, 34.37, 51.47, 108.82, 109.51, 110.26, 113.94] and a second pure fraction of **7c-II** (0.26 g, 3%) [colourless oil; t_R 28.9 min; δ_H 1.51 (s, 3 H), 1.62 (s, 3 H), 1.30–2.00 (m, 10 H), 3.42 (s, 3 H), 6.04 (s, 1 H); δ_C 17.40, 19.87, 23.71, 23.88, 24.08, 32.80, 34.47, 51.42, 108.85, 109.41, 110.77, 113.91].

Reduction of diozonide 7c. A solution of one drop of the 1:7 mixture of **7c-I** and **7c-II** in $CDCl_3$ (0.8 ml) was treated with excess triphenylphosphine. Immediate ^1H NMR analysis showed the presence of ozonide **8** [δ_H 1.53 (s), 2.29 (s)] in 28% yield,[2] 28% of methyl formate [δ_H 3.77 (d), 8.06 (q)] and of unreacted ozonide **7c**. ^1H NMR analysis after 2 days showed the presence of methyl formate, butanedione, acetic anhydride and cyclohexanone in a relative molar ratio of 5:1:5.5:5.

Preparation of 3-(5-ethoxy-3-methyl-1,2,4-trioxolan-3-yl)-3-methyl-1,2,4-trioxaspiro[4.5]decane 7d. Ozonolysis of a solution of **1** (1.16 g, 21.5 mmol) in CH_2Cl_2 (70 ml) and in the presence of ethyl formate (1.59 g, 29.7 mmol) was followed by the addition of a solution of **5** (1.91 g, 15.0 mmol) in pentane and further ozonolysis to give an oily residue (4.09 g), from which a mixture of **7d-I** and **7d-II** (1.57 g, 25%; ratio 1:8) was isolated (pentane–diethyl ether, 97:3) (Found: C, 54.15; H, 7.67. $C_{13}H_{22}O_7$ requires C, 53.78; H, 7.64%). Further separation by HPLC gave an initial fraction enriched in **7d-I** (25% in admixture with 75% of **7d-II**) (0.53 g, 9%) [colourless oil; t_R 49.5 min; δ_H 1.26 (t, 3 H), 1.50 (s, 3 H), 1.64 (s, 3 H), 1.20–2.00 (m, 10 H), 3.70 (m, 2 H), 6.10 (s, 1 H); δ_C 14.90, 18.03, 20.03, 23.81, 23.84, 24.92, 33.05, 34.36, 60.61, 108.84, 109.39, 110.24, 113.53] and a second pure fraction of **7d-II** (0.45 g, 7%) [colourless oil; t_R 53.5 min; δ_H 1.26 (t, *J* 7.1, 3 H), 1.51 (s, 3 H), 1.62 (s, 3 H), 1.20–2.00 (m, 10 H), 3.70 (m, 2 H), 6.08 (s, 1 H); δ_C 14.90, 17.65, 19.90, 23.74, 23.90, 24.90, 32.83, 34.49, 60.53, 108.87, 109.32, 110.77, 113.51].

Reduction of diozonide 7d. A solution containing one drop of the 1:8 mixture of **7d-I** and **7d-II** in $CDCl_3$ (0.8 ml) was treated with excess triphenylphosphine. Immediate ^1H NMR analysis showed the presence of ozonide **8** (36%), ethyl formate (29%) [δ_H 1.31 (t), 8.05 (t)] and unreacted **7d**. After 2 days, **7d** had disappeared and ethyl formate, butanedione, acetic anhydride and cyclohexanone were present in a relative molar ratio of 2.3:1:1.5:2.5.

Sequential ozonolyses of acyloxy-substituted acetylenes 9 and *O*-methylcyclohexanone oxime 5

Solutions of the acetylene derivatives **9a–d** in CH_2Cl_2 were ozonized at −30 °C. Without work-up, a cold (−20 °C) solution of **5** in CH_2Cl_2 (10 ml) was added and the ozonolysis continued at −20 °C until the reaction solution turned blue. The solvent was removed by distillation and, unless mentioned otherwise, the diozonide was isolated by flash chromatography.

Preparation of 9-benzoyloxymethyl-9,12-epoxy-12-phenyl-7,10,11,13,15,16-hexaoxadispiro[5.1.6.2]hexadecane 12a. Following the initial ozonolysis of a solution of **9a** (2.25 g, 7.7 mmol) in CH_2Cl_2 (60 ml), a solution of **5** (1.07 g, 8.4 mmol) in CH_2Cl_2 (10 ml) was added and the reaction mixture ozonized to completion. From the crude residue (3.20 g), diozonide **12a** (0.91 g, 26%) was obtained by crystallization from diethyl ether at 0 °C as a colourless crystalline solid, mp 99.5 °C (sharp) (Found: C, 62.90; H, 5.37. $C_{24}H_{24}O_9$ requires C, 63.16; H, 5.30%); δ_H 1.30–1.90 (m, 10 H), 4.19 (d, *J* 11.9, 1 H), 4.63 (d, *J*

11.9, 1 H), 4.90 (d, *J* 13.1, 1 H), 4.98 (d, *J* 13.1, 1 H), 7.30–8.20 (m, 10 H); δ_C 23.58, 24.54, 33.02, 34.31, 56.19, 65.71, 100.36, 106.88, 111.64, 118.70, 127.10, 128.28, 128.47, 129.12, 129.41, 129.93, 130.92, 133.38, 165.80.

Reduction of diozonide 12a. A solution of **12a** (30 mg) in $CDCl_3$ (1 ml) was treated with excess triphenylphosphine at room temp. ^1H NMR analysis after 3 days showed the presence of **13a** [δ_H 5.40 (s)], **14a** [δ_H 4.99 (s)] and cyclohexanone [δ_H 2.35 (t)] in a molar ratio of 1:2.5:5. These assignments were confirmed with reference to authentic samples.

Preparation of 9-acetoxymethyl-9,12-epoxy-12-methyl-7,10,11,13,15,16-hexaoxadispiro[5.1.6.2]hexadecane 12b. Ozonolysis of a solution of **9b** (1.52 g, 8.9 mmol) in CH_2Cl_2 (50 ml) was followed by the addition of a solution of **5** (1.14 g, 9.0 mmol) in CH_2Cl_2 (10 ml) and further ozonolysis to completion. From the crude product mixture (2.20 g), **12b** (0.77 g, 26%) was isolated by chromatography (solvent pentane–diethyl ether, 9:1) as a colourless oil (Found: C, 50.36; H, 6.05. $C_{14}H_{20}O_9$ requires C, 50.60; H, 6.07%); δ_H 1.73 (s, 3 H), 1.30–1.80 (m, 10 H), 2.14 (s, 3 H), 3.90 (d, *J* 11.9, 1 H), 4.34 (d, *J* 11.9, 1 H), 4.52 (d, *J* 13.2, 1 H), 4.64 (d, *J* 13.2, 1 H); δ_C 18.04, 20.53, 23.28, 24.57, 33.04, 34.30, 55.57, 62.25, 100.10, 105.91, 111.48, 119.73, 170.12.

Reduction of diozonide 12b. A solution of one drop of **12b** in $CDCl_3$ (1 ml) was treated with excess triphenylphosphine at room temp. ^1H NMR analysis after 4 days showed the presence of **13b** [δ_H 2.19 (s), 5.12 (s)], **14b** [δ_H 2.19 (s), 4.75 (s)] and cyclohexanone [δ_H 2.35 (t)] in a relative molar ratio of 1:1.5:2.5. These assignments were confirmed with reference to authentic samples.

Preparation of 9,12-epoxy-9-methyl-12-phenyl-7,10,11,13,15,16-hexaoxadispiro[5.1.6.2]hexadecane 12c. Ozonolysis of a solution of **9c** (2.45 g, 14.1 mmol) in CH_2Cl_2 (70 ml) was followed by the addition of **5** (1.79 g, 14.1 mmol) and further ozonolysis to completion. From the crude product mixture (3.76 g), **12c** (0.82 g, 17%) was isolated by chromatography (solvent pentane–diethyl ether, 9:1) as a colourless solid (mp 87 °C from pentane) (Found: C, 60.37; H, 6.19. $C_{17}H_{20}O_7$ requires C, 60.71; H, 5.99%); δ_H 1.74 (s, 3 H), 1.20–2.00 (m, 10 H), 4.15 (d, *J* 11.8, 1 H), 4.49 (d, *J* 11.8, 1 H), 7.30–7.80 (m, 5 H); δ_C 14.05, 23.49, 23.77, 24.65, 33.71, 34.29, 65.67, 100.64, 108.47, 111.15, 118.72, 127.01, 128.28, 130.02, 130.74.

Reduction of diozonide 12c. A solution of **12c** (20 mg) in $CDCl_3$ (1 ml) was treated with excess triphenylphosphine at room temp. ^1H NMR analysis after 3 days showed the presence of **13c** [δ_H 2.41 (s), 5.35 (s)], **14c** [δ_H 2.28 (s), 4.95 (s)] and cyclohexanone [δ_H 2.35 (t)] in a relative molar ratio of 2.5:1:5. These assignments were confirmed with reference to *authentic samples.*

Preparation of 9,12-epoxy-9,12-dimethyl-7,10,11,13,14,16-hexaoxadispiro[5.1.6.2]hexadecane 12d. Ozonolysis of a solution of **9d** (1.89 g, 16.9 mmol) in CH_2Cl_2 (50 ml) was followed by the addition of a solution of **5** (2.14 g, 16.9 mmol) in CH_2Cl_2 (10 ml) and further ozonolysis to completion. From the crude product mixture (3.84 g), diozonide **12d** was isolated (0.69 g, 15%) by chromatography (solvent pentane–diethyl ether, 20:1) as a colourless oil [δ_H 1.63 (s, 3 H), 1.69 (s, 3 H), 1.20–2.00 (m, 10 H), 3.91 (d, *J* 11.8, 1 H), 4.25 (d, *J* 11.8, 1 H); δ_C 13.89, 18.36, 23.46, 23.74, 24.65, 33.68, 34.27, 62.20, 100.44, 107.61, 111.00, 119.64]. Owing to the inherent instability of diozonide **12d**, no elemental analysis was carried out.

Reduction of diozonide 12d. A solution of **12d** (20 mg) in $CDCl_3$ (1 ml) was treated with excess triphenylphosphine at room temp. ^1H NMR analysis after 6 h showed the presence of **13d** [δ_H 2.18 (s), 2.37 (s), 5.11 (s)], **14d** [δ_H 2.18 (s), 2.27 (s), 4.70 (s)] and cyclohexanone [δ_H 2.35 (t)] in a relative molar ratio of 1:1.7:3.3. These assignments were confirmed with reference to authentic samples.

Crystal structure determination of the α-diozonide 12a

The crystal of diozonide **12a** used for X-ray data collection (approx. dimensions 0.6 × 0.6 × 0.2 mm) was grown by slow evaporation from a diethyl ether solution and mounted in a sealed Lindemann capillary tube.

Crystal data. $C_{24}H_{24}O_9$, $M = 456.4$, colourless prisms, orthorhombic, space group *Pbca* (No. 61), $a = 14.382(3)$, $b = 11.050(2)$, $c = 27.797(6)$ Å, $V = 4418(2)$ Å^3, $Z = 8$, $D_c = 1.373$ g cm^{-3}, $F(000) = 1920$, μ(Mo-Kα) = 0.106 mm^{-1}.

Data collection. The intensity data were collected on a Siemens P4 four-circle diffractometer [temperature 293(2) K; θ range: 2.04 to 25.0°; $-1 \le h \le 17$, $-1 \le k \le 11$, $-33 \le l \le 1$] using graphite monochromated Mo-Kα X-radiation (λ 0.710 73 Å) and ω-scanning. Of the 3706 unique data [R(int) = 0.039] measured, 1913 had $F_o > 4\sigma(F_o)$. The data were corrected for Lorentz and polarisation effects, but not for absorption.

Structure solution and refinement. The approximate positions of the non-hydrogen atoms were determined by direct methods (SHELX-86[10]). The structure was refined by full-matrix least-squares methods on F^2 (SHELXTL/PC[11]) using all F_o^2 data and anisotropic temperature factors for all the non-hydrogen atoms. All the hydrogen atoms were located on difference Fourier maps and included in the refinement process at idealized positions with isotropic temperature factors (1.5 times U_{iso} of the bonded heavy atom). At convergence, the discrepancy factors R and wR^2 [$F_o > 4\sigma(F_o)$] were 0.063 and 0.13 respectively. The weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.0416P)^2 + 4.3414P]$ where $P = (F_o^2 + 2F_c^2)/3$, was found to give satisfactory analyses of variance. The final difference Fourier map was essentially featureless (general noise level less than ±0.10 e Å^{-3}) with a largest difference peak and hole of 0.18 and −0.20 e Å^{-3} respectively.

Atomic coordinates, thermal parameters, and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/11.

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