Tetrahedron Vol. 42, No. 5, pp. 1285 to 1290, 1986
Printed in Great Britain.

0040-4020/86 $3.00 + .00
Pergamon Press Ltd.

SELECTIVE MIXED COUPLING OF CARBOXYLIC ACIDS - III. SYNTHESIS OF CYCLOPENTADECANONE FROM CYCLIC TETRAACYL DIPEROXIDES[1)]

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(*Received in Germany* 2 *September* 1985)

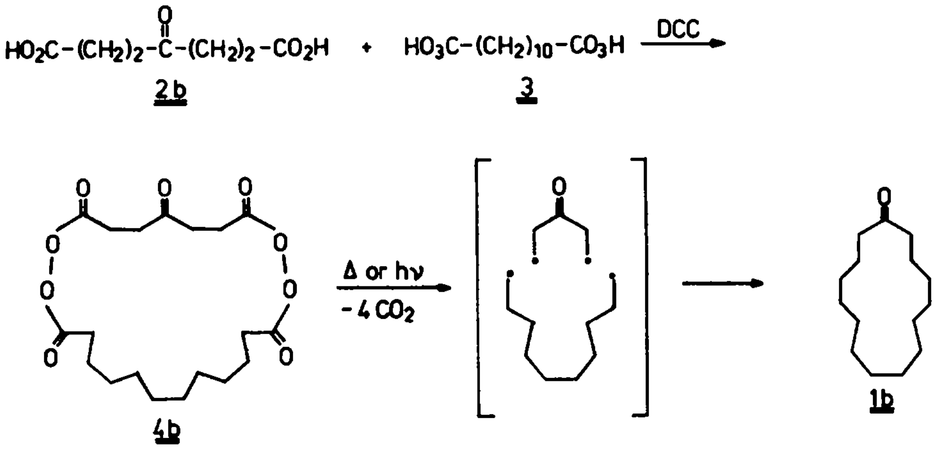
Abstract - Cyclopentadecanone (1b) and cyclotetradecane (1a) were prepared in 53 and 83% yield by thermolysis or photolysis of the cyclic tetraacyl diperoxides 4b and 4a. The compounds 4a, b were obtained from diperoxydodecanedioic acid (3) and the acyl chloride 5a or the dicarboxylic acid 2b.

INTRODUCTION

Cyclopentadecanone (1b) and muscone are 15-membered cyclic ketones, which are of interest for the perfume production[2)], because of their intense musk odor. Many syntheses for these ketones have been reported. A frequent route is the three-carbon ring expansion starting from the readily available cyclododecanone[3)], other approaches use acyclic precursors[4)]. These syntheses mostly need a fair number of steps and often expensive reagents. Applying the method to form C-C bonds by photolysis of diacyl peroxides[1)], we hoped to devise a short-step preparation of cyclopentadecanone (1b), that uses inexpensive chemicals. Our plan was to synthesize 1b by a twofold intramolecular radical coupling, where the two radical pairs are generated by photolysis or thermolysis of the cyclic tetraacyl diperoxide 4b (eq. 1). This approach was also stimulated by results from the decomposition of cycloalkanone diperoxides, whose reaction to cycloalkanes is thought to involve cyclic diacyl peroxides as intermediates[5)]. 4b should be prepared from the readily available 4-oxoheptanedioic acid (2b)[6)] and diperoxydodecanedioic acid (3).

RESULTS

Preparation of cyclic tetraacyl diperoxides (4a-c): In order to become familiar with the preparation and the reaction behaviour of tetraacyl diperoxides at first the unsubstituted 4a was prepared from 3 and adipic acid. To exclude Norrish type cleavages in the photodecomposition of the peroxides, 4c, bearing a ketalized keto group, was additionally synthesized. 4a-c were prepared from diperoxydodecanedioic acid (3) and adipoyl dichloride (5a) or from 3 and 2b,c with dicyclohexylcarbodiimide as condensation reagent (eq. 2).



$$HO_2C-(CH_2)_2-\overset{\overset{O}{\|}}{C}-(CH_2)_2-CO_2H + HO_3C-(CH_2)_{10}-CO_3H \xrightarrow{DCC}$$

(1)

3 was obtained in 49% yield by reaction of dodecanedioic acid and aqueous hydrogen peroxide in conc. sulfuric acid. Instead of the more hazardous 65% H_2O_2[7] commercially available 30% H_2O_2 was used, unreacted dodecanedioic acid was nearly quantitatively recovered. Dry 3 can be stored at 0° C for months without decomposition.

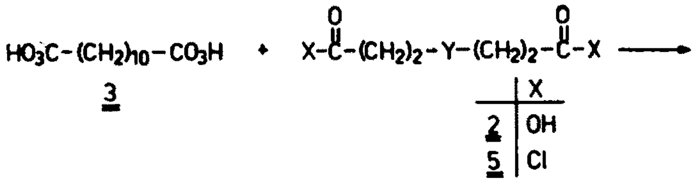
For the cyclization to 4 the dilution principle[8] has to be applied, otherwise polymeric diacyl peroxides are exclusively formed. For that equimolar solutions of 3 and 5a in tetrahydrofuran were slowly added from mechanically driven syringes to a solution of pyridine in ether. This way 22% 4a besides 50 to 60% oligomeric diacyl peroxide are obtained. The yield of 4a corresponds to this obtained in the preparation of cyclic diesters with similar ring size[9]. When dicyclohexylcarbodiimide (DCC) was used as condensation reagent, tetrahydrofuran solutions of 2a-c and 3 were syringed to an etheral solution of DCC. Thereby 16% 4a, 19% 4b or 18% 4c and additionally 50-60% oligomeric diacyl peroxides were obtained.

4a-c are white crystalline compounds, which have a relatively high melting point and are stable at room temperature for a longer period of time. Their IR-spectra exhibit the characteristic carbonyl absorption for diacyl peroxides[10] at 1805-1810/cm and 1775-1780/cm.

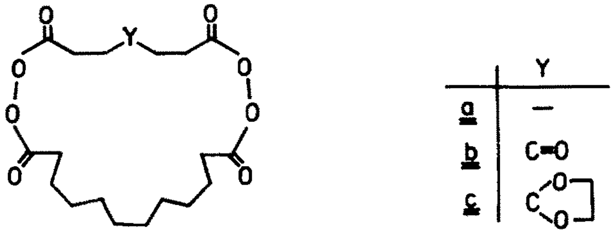
The oligomeric diacyl peroxides (n about 3 to 4) are white solids of low stability. They have to be handled with care, because dry they may detonate by slight friction. By stirring them for several days with aqueous KOH, the dodecanedioic acid can be nearly totally recovered.

Thermal and photochemical decomposition of 4a-c: The thermal decomposition of diacyl peroxides in solution affords only low yields of coupling product[11]. Much better results are achieved by an explosion like decomposition of the neat peroxides[12]. For the thermal decomposition of 4 to 1 50 mg portions of the peroxide were heated in a test-tube for a short time above their decomposition point. In the photolysis crystalline 4a-c were irradiated at -78° C with a low pressure mercury arc. The results are summarized in the Table and eq. 3.

This way 1b was by synthesized in only two steps from 3 and the inexpensive diacid 2b in 8% overall yield. As furthermore the diacids can be recovered from the oligomeric diacyl peroxides, this new preparation of cyclopentadecanone appears to be an interesting alternative to existing syntheses[3,4].



(2)



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(3)

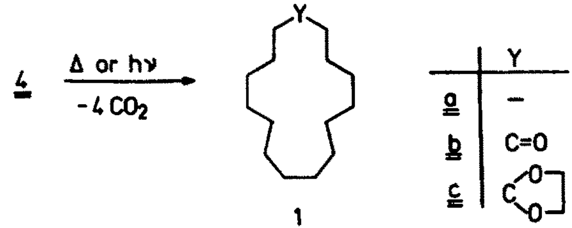

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Table 1: Decomposition of cyclic tetracyl diperoxides 4

Peroxide	Mode of decomposition	Product	Yield (%)
4a	Δ	1a[a)]	41 (48)[b)]
4a	hv	1a[a)]	73 (83)
4b	Δ	1b	40 (53)
4c	hv	1c[c)]	65 (72)

[a)] Additionally 5% (thermal) or 1% (photochemical) 1-tetradecene and 8% (thermal) or 2% (photochemical) 1,15 cyclopentadecanolide were found; [b)] Numbers in parenthesis correspond to gaschromatographic yields; [c)] 1c can be quantitatively converted into 1b by treatment with HCl.

EXPERIMENTAL

GENERAL. - The structures of products already described in the literature were confirmed by comparing their IR, NMR and mass spectra with the data reported. ^1H NMR spectra were obtained with the Bruker WM 300 spectrometer, ^{13}C NMR spectra with a Bruker WH 90 or WM 300 spectrometer. IR spectra were recorded on the Perkin-Elmer instruments 177, 257, 421; UV spectra were taken with the Leitz SP 800a spectrometer; mass spectra were obtained with the GC-MS combinations Varian MAT 111 (packed columns) and Varian CH 7A (capillary columns). Melting points were determined with a Kofler hot stage apparatus and are uncorrected; refraction indices were taken with a Zeiss refractometer. The purity of starting compounds was checked by GLC with the Varian instruments 1400 and 3700 on glass columns: column 1 (4.3 m x 2 mm) 4% SE 30 on chromosorb W AWDMCS 100/120; column 3 (capillary, 25 m x 0.3 mm) 0.3% SE 30. Photolyses were carried out with Gräntzel low-pressure mercury arcs 1 and 5a.

Diperoxydodecanedioic acid (**3**): 23.0 g (0.1 mol) finely divided dodecanedioic acid are dissolved in 90 ml conc. H_2SO_4 in a 250 ml beaker. With intensive stirring and ice-cooling 60 g (0.6 mol) 30% H_2O_2 are added in such a way, that a temperature between 15 to 25° C is maintained. After the addition of further 50 ml conc. H_2SO_4 and 4 h at 20° C the slurry is poured in 1 l ice water. The white solid is filtrated, washed with 200 ml ice-cold water and recrystallized at 50° C from ethanol : water (2 : 1, v,v) to afford 12.8 g (48.8 mmol, 49%) white crystalline **3**.
From the mother liquors unreacted dodecanedioic acid can be extensively recovered; the yield of **3** calculated on reacted dodecanedioic acid is 75-80%.
Mp slow decomposition above 80° C. - IR (nujol) 3150 (OH), 1745 (C=O), 1100 (C-O-O), 880 (O-O) cm^{-1}. - Calcd. for active oxygen: 12.20%. Found: 11.78%.

Preparation of cyclic tetraacyl diperoxides **4a**-**c**:
1,2,9,10-Tetraoxacyclodocosane-3,8,11,22-tetraone (**4a**): A 1 l three-necked flask is charged with 0.79 g (10 mmol) pyridine in 800 ml absolute ether. To the stirred solution are added at 5° C with two mechanical driven syringes continously within 24 h 1.31 g (5 mmol) **3** and 0.92 g (5 mmol) adipoyl dichloride (**5a**) each in 40 ml absolute THF. - Correspondingly to 2.06 g (10 mmol) dicyclohexylcarbodiimide (DCC) in 800 ml absolute ether 1.31 g **3** and 0.73 g (5 mmol) adipic acid are added.
After addition of another portion of 10 mmol pyridine or DCC to the reaction mixture further 5 mmol of **3** and acid chloride or acid are added within 24 h.
For workup the solvent is removed at the rotary evaporator at room temperature. The residue is dissolved in 100 ml CH_2Cl_2, insoluble pyridinium chloride or dicyclohexyl urea are removed by filtration through a glass frit. After rotaevaporation of CH_2Cl_2 **4a** is separated from oligomeric peroxide by extraction with petrol ether : ether (1 : 1, 3 x 50 ml). After column chromatography (silica gel, petrol ether : ether, 1 : 1, v,v) colourless crystals of **4a** are obtained (0.41 g, 22% from the acid chloride; 0.30 g, 16% by the DCC-method). Mp 77-78° C. - IR (KBr): 1805, 1775 (C=O), 1060 (C-O-O-C), 900 (O-O) cm^{-1}. - ^{13}C NMR ($CDCl_3$): δ = 169.1 (s, C-1'dodecanedioyl part), 168.4 (s, C-1), 30.0 (C-2'), 29.5 (C-2), 28.5 (C-6'), 28.0 (C-5'), 27.7 (C-4'), 24.7 (C-3'), 23.8 (C-3) ppm. - UV (cyclohexane, λ,(ε)): 215 nm (800). - Calcd. for active oxygen: 8.59%. Found: 8.64%. - Anal. calcd. for $C_{18}H_{28}O_8$ (372.4): C, 58.05; H, 7.58. Found: C, 58.23; H, 7.69. - Oligomeric diacyl peroxide: 1.02 g (from acid chloride) or 1.06 g (by DCC-method). - Mol. wt. about 1000. - Active oxygen found: 7.11%. - IR (nujol): 3150 (OH), 1805, 1775, 1740, 1700 (C=O), 1050 (C-O-O-C), 890 (O-O) cm^{-1}. - 1.02 g of oligomeric diacyl peroxide are stirred 2 d with 2n KOH, after acidification with conc. HCl 47% dodecanedioic acid (calculated on diperoxydodecanedioic acid used for preparation of **4a**) are obtained after recrystallization from water/ethanol (2 : 1).

1,2,10,11-Tetraoxacyclotricosane-3,6,9,12,23-pentaone (**4b**): 2.61 g (10 mmol) **3**, 1.74 g (20 mmol) **2b** and 4.12 g (20 mmol) DCC are reacted as above. **4b** is separated from oligomeric diacyl peroxide by extraction with hot ether (3 x 50 ml). At 0° C from the etheral solution 0.75 g (1.87 mmol) of white crystalline **4b** precipitate. - Mp 104-105° C. - IR (KBr): 1805, 1775, 1705 (C=O), 1055 (C-O-O-C), 905 (O-O) cm^{-1}. - ^{13}C NMR ($CDCl_3$): δ = 205.0 (s, C-4), 169.2 (s, C-1'), 168.0 (s, C-1), 36.5 (t, C-3), 30.2 (C-2'), 28.8 (C-6'), 28.5 (C-5'), 27.9 (C-4'), 24.8 (C-3'), 24.1 (C-2) ppm. - Calcd. for active oxygen: 7.99%. Found:

8.00%. - Anal. calcd. for $C_{19}H_{28}O_9$ (400.4): C, 56.99; H, 7.05. Found: C, 56.76; H, 7.05. - 2.36 g oligomeric diacyl peroxide were additionally obtained. Active oxygen found: 6.73%. - IR (nujol): 3150 (OH), 1805, 1775, 1745, 1700 (C=O), 1050 (C-O-O-C), 890 (O-O) cm^{-1}. By alkaline hydrolysis 54% dodecanedioic acid are recovered.

1,4,9,10,23,24-Hexaoxaspiro[4.22]heptacosane-8,11,22,25-tetraone (**4c**): **2c** was prepared in two steps and 67% yield from diethyl 4-oxoheptanedioate by ketalization[13] (ethylene glycol, p-toluenesulfonic acid) and subsequent hydrolysis of the ester with KOH in ethanol/water (2:1). - 2.62 g (10 mmol) **3**, 2.18 g (10 mmol) **2c** and 4.12 g (20 mmol) DCC afford after extraction of the crude product with hot ether (3 x 50 ml) 0.79 g (17.8 mmol, 18%) **4c** in long colorless needles. - Mp 74-75° C (from ether : petrol ether, 2 : 1). - IR (KBr): 1810, 1780 (C=O), 1055 (C-O-O-C), 880 (O-O) cm^{-1}. - ^{13}C NMR ($CDCl_3$): δ = 169.1 (s, C-1'), 168.9 (s, C-1), 109.4 (s, C-4), 65.0 (t, C-5), 3.10 (C-3), 30.1 (C-2'), 28.3 (C-6'), 27.8 (C-5'), 27.7 (C-4'), 24.5 (C-2,3') ppm. - UV (cyclohexane, λ,(ε)): 215 nm(800). - Calcd. for active oxygen: 7.20%. Found: 7.23%. - Anal. calcd. for $C_{21}H_{32}O_{10}$ (444.5): C, 56.75; H, 7.26. Found: C, 56.59; H, 7.29. - Furthermore 2.40 g oligomeric diacyl peroxide were obtained. Active oxygen found: 5.89%. - IR (nujol): 3150 (OH), 1805, 1775, 1745, 1700 (C=O), 1050 (C-O-O-C), 890 (O-O) cm^{-1}.

Thermal and photochemical decomposition of **4**:

Thermal decomposition. - Analytical scale: 20-30 mg **4** (exactly weighed) are exploded unter nitrogen in a test-tube by short time heating with a Bunsen burner. After cooling the test-tube in an ice bath dodecane (exactly weighed) is added for GLC-calibration. The contents are dissolved in ether and analyzed by GLC. - Preparative scale: 2 mmol **4** are distributed over 15 test-tubes (max. 50 mg per test-tube). After purging with nitrogen the outlets of the vertically holded test-tubes are inserted into the joint of a 2 l round-bottomed flask, then **4** is decomposed under explosion by short time heating with a Bunsen burner. The contents of the cooled test-tubes and the flask are dissolved in ether and the crude product purified by column chromatography and bulb-to-bulb distillation.

Photochemical decomposition. Procedures for analytical and preparative scale, see part I[1].

Decomposition of **4a**: *Thermal*, analytical (column 1, 50-280° C): 48% **1a**, 5% tetradecene, 8% 15-cyclopentadecanolide. - Preparative: 0.74 g (2 mmol) **4a** afford 0.16 g (0.82 mmol, 41%) cyclotetradecane (**1a**). - Mp 53-54° C (lit.[14] 54.2° C). - ^1H NMR ($CDCl_3$): δ = 1.32 (s) ppm. - MS: m/e = 196 (34%, M^+), 168 (9), 154 (3), 153 (4), 140 (7), 126 (12), 125 (18), 111 (36), 55 (100).
1-Tetradecene: MS: m/e = 196 (5%, M^+), 268 (2), 140 (2), 139 (3), 126 (5), 125 (7), 111 (10), corresponds to lit. [15].
15-Cyclopentadecanolide: MS: m/e = 240 (8%, M^+), 222 (11), 180 (10), 138 (10), 137 (8), 124 (11), 123 (12), 111 (16), 110 (18), corresponds to lit.[14].
Photochemical, analytical (column 1, 50-280° C): 83% **1a**, 1% 1-tetradecene, 2% 15-cyclopentadecanolide. - Preparative: 1.12 g (3 mmol) afford after 50 h irradiation at -78° C and column chromatography (petrol ether : ether, 10 : 1) 0.43 g (73%) **1a**.
Decomposition of **4b**: *Thermal*, analytical (column 1, 50-280° C): 53% **1b**. - Preparative: 0.8 g **4b** afford after decomposition and column chromatography

(petrol ether : ether, 3 : 1) 0.18 g (40%) cyclopentadecanone (**1b**). - Mp 65-66°C (lit.[16] = 65.6° C). - IR (film): 1705 (C=O) cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 2.42 (t, 4H), 1.65 (m, 4H), 1.31 (m, 20H) ppm. - MS: m/e = 224 (41%, M^+), 206 (6), 166 (13), 149 (8), 135 (12), 125 (25), 111 (26), 110 (19).

Decomposition of **4c**: *Photochemical*, analytical (column 1, 50-280° C): 72% **1c**. Preparative: 0.89 g (2 mmol) **4c** afford after 30 h irradiation and column chromatography (petrol ether : ether, 5 : 1) 0.35 g (65%) cyclopentadecanone ethylene acetal (**1c**). - Mp 27-28 ° C. - IR (film): 1070 (C-O) cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 3.91 (s, 4H), 1.59 (m, 4H), 1.34 (m, 22H) ppm. - MS: m/e = 268 (9%, M^+), 239 (4), 225 (19), 211 (6), 197 (6), 183 (5), 169 (5), 155 (20), 141 (8), 127 (2), 113 (7), 99 (100). - Anal. calcd. for $C_{17}H_{32}O_2$ (268.4): C, 76.06; H, 12.02. Found: C, 76.14; H, 12.05. - **1c** is converted with methanol/HCl to 98% **1b**.

Support of this work by a Ph.D. scholarship to M. Feldhues from the Fonds der Chemischen Industrie is gratefully acknowledged.

REFERENCES

1) Part. I: M. Feldhues and H.J. Schäfer, Tetrahedron **41**, 4195 (1985);
Part. II: M. Feldhues and H.J. Schäfer, Tetrahedron **41**, 4213 (1985).
2) G. Ohloff, G. Holzmer, H. Rode-Gowal in H. Aebi, E. Baumgartner, H.P. Fiedler and G. Ohloff, Kosmetika, Riechstoffe und Lebensmittelzusatzstoffe, p. 36., G. Thieme Verlag, Stuttgart 1978.
3) C. Fehr, G. Ohloff and G. Büchi, Helv. Chim. Acta **62**, 2655 (1979) and earlier papers; A. Fischli, Q. Branca and J. Daly, Helv. Chim. Acta **59**, 2443 (1979); M. Karpf and A.S. Dreiding, Helv. Chim. Acta **60**, 3045 (1977); J. Tsuji, T. Yamada and I. Shimizu, J. Org. Chem. **45**, 5209 (1980); B.M. Trost and J.E. Vincent, J. Am. Chem. Soc. **102**, 5680 (1980).
4) K. Utimoto, M. Tanaka, M. Kitai and H. Nozaki, Tetrahedron Lett. **1978**, 2301; K.H. Schulte-Elte, A. Hauser and G. Ohloff, Helv. Chim. Acta **62**, 2673 (1979).
5) P.R. Story, D.D. Denson, C.E. Bishop, B.C. Clark, Jr. and J.C. Farine, J. Am. Chem. Soc. **90**, 817 (1968).
6) W. Reppe, Liebigs Ann. Chem. **596**, 158 (1955); W.S. Emerson, R.I. Longley, Jr., W.S. Johnson and I.A. David, Org. Syntheses **33**, 25 (1953).
7) W.E. Parker, L.P. Witnauer and D. Swern, J. Am. Chem. Soc. **79**, 1929 (1957).
8) F. Vögtle, Chem. Ztg. **96**, 396 (1972).
9) M.D. Thompson, J.S. Bradshaw, S.F. Nielsen, C.T. Bishop, F.T. Cox, P.E. Fore, G.E. Maas, R.M. Izatt and J.J. Christensen, Tetrahedron **33**, 3317 (1977); J.S. Bradshaw, G.E. Maas, R.M. Izatt and J.J. Christensen, Chem. Rev. **79**, 37 (1979).
10) W.H.T. Davison, J. Chem. Soc. **1951**, 2456.
11) R. Hiatt, Organic Peroxides (Ed. D. Swern), Vol. II, p. 850, J. Wiley, New York 1970.
12) Part I, II[1]; F. Fichter and R. Zumbrunn, Helv. Chim. Acta **10**, 869 (1927).
13) R.M. Lukes, G.I. Poos and L.H. Sarett, J. Am. Chem. Soc. **74**, 1401 (1952).
14) Beilstein Vol. V, 3. Suppl., p. 152 (1963).
15) Eight Peak Index of Mass Spectra, 2. Ed., Lamport Gilbert Printers, Reading 1974.
16) Beilstein Vol. VII, 3. Suppl., p. 203 (1968).