Synthesis of unsaturated dibasic acid esters from five-, six-, and seven-membered cycloalkanones*

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A new route to diesters of symmetrical octene-, decene-, and dodecenedioic acids was proposed. The ratio of the *cis*/*trans*-isomers was 1 : 4. The synthesis involved oxidative splitting of five-, six-, and seven-membered cycloalkanones with hydrogen peroxide into the corresponding ω-alkenoic acids followed by esterification and metathesis over $Re_2O_7/B_2O_3—Al_2O_3—SnMe_4$.

Key words: cycloalkanones, ω-alkenoic acids and esters, diesters of alkenedioic acids, metathesis reaction, catalyst for the metathesis, rhenium.

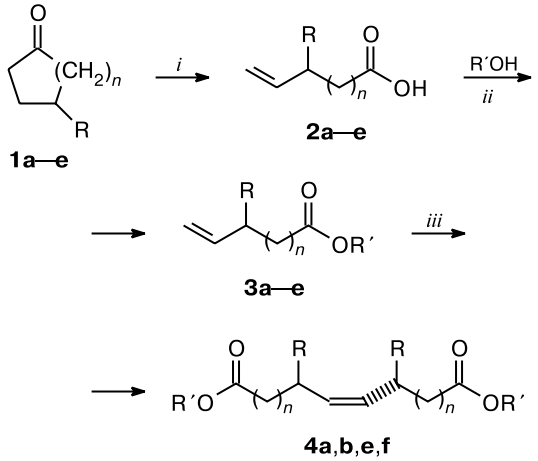
Organic peroxides are widely used to initiate free radical processes for production of polymeric materials but much more rarely employed as reagents in organic synthesis. Among peroxides that function as building blocks in organic chemistry, cycloalkanone peroxides are of primary importance; they are easily derived from cyclic ketones and H_2O_2 (see Refs 1 and 2).

Straightforward schemes for the synthesis of oxo carboxylic,[3] ω-alkenoic,[3] and ω-haloalkanoic acids[4] involve reactions of cycloalkanone peroxides with methyl vinyl ketone and Fe^{II} sulfate, with the $FeSO_4—CuSO_4$ or $FeSO_4—CuX_2—MX_2$ system (M = Na and K; X = Cl, Br, and I).

At the same time, ω-alkenoic acids are employed as starting materials for the synthesis of ω- and (ω – 1)-alkynoic acids[5] used to obtain natural compounds.

Previous investigations of oxidative decyclization of cycloalkanones in the presence of H_2O_2 have been aimed at obtaining functionalized aliphatic compounds.[3—5] Here we report on the results of stepwise transformation of cyclic ketones into symmetrical alkenedioic acid esters. The proposed method involves three successive steps, *viz.*, oxidation of cycloalkanones (**1a—e**) into ω-alkenoic acids (**2a—e**), their transformation into esters (**3a—f**), and metathesis leading to alkenedioic acid esters (**4a,b,e,f**).

ω-Alkenoic acids **2a—e** were synthesized according to a known procedure.[2,4] Reactions of cycloalkanones **1a—c** with 30% H_2O_2 gave 1-hydroperoxy-1-hydroxycycloalkanes, which decomposed under the action of



i. 1) 30% H_2O_2, 2) $FeSO_4—CuSO_4$. *ii*. H_2SO_4.
iii. $Re_2O_7—B_2O_3/Al_2O_3—SnMe_4$ or $Re_2O_7/Al_2O_3—SnMe_4$.

Compound	*n*	R	R′
1a—4a	1	H	Me
1b—4b	2	H	Me
1c—4c	2	Me	Me
1d—4d	2	Bu^t	Me
1e—4e	3	H	Me
3f, **4f**	2	H	Et

$FeSO_4—CuSO_4$ to acids **2a—e**. The yields of acids **2b—d** were 60—65% and the yields of acids **2a** and **2e** were 20 and 40%, respectively (calculated to the starting cycloalkanone). The nonconsumed ketone can be recycled. Esterification of acids **2a—e** with methanol and ethanol was carried out under classic conditions of sulfuric acid catalysis. The resulting esters **3a,b,e,f** were used in the

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Table 1. Metathesis reaction of alkyl ω-alkenoates **3a—f**

Entry	Reagent	[Re] (%)*	Sn/Re	Product	Conversion of esters (%) **3a—f**	Yield of ethene (%)
1	**3a**	19	1 : 1	**4a**	34	32
2	**3a**	9	1 : 1	**4a**	50	48
3	**3a**	9	1 : 2	**4a**	64	66
4	**3a**	12	1 : 2	**4a**	67	64
5	**3b**	12	1 : 0.5	**4b**	59	54
6	**3b**	12	1 : 1	**4b**	92	90
7	**3b**	9	1 : 1	**4b**	91	89
8	**3f**	9	1 : 1	**4f**	64	62
9	**3f**	9	1 : 1	**4f**	52	50
10	**3c**	12	1 : 1	**4c**	8	10
11	**3d**	12	1 : 1	**4d**	0	0
12	**3e**	9	1 : 1	**4e**	79	81

* The rhenium content of the catalyst (Re_2O_7—B_2O_3/Al_2O_3 in entries 2—8 and 10—12 and Re_2O_7/Al_2O_3 in entries 1 and 9). The B_2O_3 content of the catalyst was 5%.

metathesis reaction over a Re catalyst to give dialkyl alkenedioates **4a,b,e,f** (Table 1).

Similar diesters and the corresponding dibasic acids are used in organic synthesis, *e.g.*, in the synthesis of pheromones.[6] Symmetrical (with respect to the position of the double bond) alkenedioic acid esters can be obtained in several ways: (1) catalytic decomposition of not easily accessible diazo esters,[7] (2) multistep synthesis from ω-chloroalkynes and ω-bromo-α-chloroalkanes (the synthesis includes replacement of the Cl atoms by cyano groups, their hydrolysis, and hydrogenation of the triple bond),[8] (3) electrolysis of alkanoic acid esters with participation of butadiene (isomeric alkenedioic and alkadienedioic acids are by-products),[9] and (4) oxidative dehydrodimerization of cycloalkanones into bicycloalkane-2,2′-diones followed by their reaction with H_2O_2 and thermolysis of the resulting peroxides. The last method[10] also gives rise to isomeric alkenedioic acids.

Among the existing approaches to the synthesis of esters **4**, metathesis has been employed in the template intramolecular cyclization of dihexenoyl derivatives of diamines and diglycols and the resulting macrocycles have been converted into the target compound **4b** (see Ref. 11).

The route to diesters **4** we propose is experimentally simple and the starting reagents are accessible. The metathesis of esters **3a—f** is the most important step of the synthesis. Reactions were carried out over Re_2O_7/Al_2O_3 and Re_2O_7—B_2O_3/Al_2O_3 in combination with $SnMe_4$ as an activator. The results obtained are summarized in Table 1. The conversions of esters **3a,b,e** containing no alkyl substituents in the side chain into the target products **4a,b,e** were 65—90% (reaction conditions were not optimized). The α-methyl group with respect to the double bond in ester **3c** strongly hinders the metathesis reaction; ester **3d** containing the *tert*-butyl group does not undergo metathesis at all. The alkoxy group of the ester fragment also affects the metathesis: the conversion of methyl hex-5-enoate **3b** is appreciably higher than that of ethyl ester **3f**. A variation in the rhenium content from 9 to 12% virtually does not affect the activity of the catalyst; the B_2O_3-free catalyst is less effective (see Table 1).

According to NMR and GLC data, dialkyl alkenedioates **4a,b,e,f** are mixtures of the *cis*- and *trans*-isomers in the ratio ~1 : 4. This ratio was confirmed by calculations performed with the Panic program for the six-spin system $CH_2CH{=}CHCH_2$ in ester **4a**. A satisfactory agreement of experimental and theoretical spectra was obtained for the *trans*-isomer with the characteristic coupling constant J_{trans} = 15.16 Hz.

Experimental

GLC-analysis was carried out on an LKhM-80 chromatograph (flame ionization detector, column 3000×3 mm, 6% SE-30 on Chromosorb´e W (60—80 mesh)). ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 instrument (200.13 and 50.32 MHz, respectively).

Commercial starting ketones **1a—e** (97—98% purity; Across, Lancaster) were used as purchased. ω-Alkenoic acids **2a—e** were synthesized by oxidation of ketones **1a—e** with 30% H_2O_2—$FeSO_4$ according to a known procedure;[3] **2a**: b.p. 86—87 °C (15 Torr); **2b**: b.p. 93—95 °C (14 Torr); **2c**: b.p. 102—104 °C (15 Torr); **2d**: b.p. 141—143 °C (14 Torr); **2e**: b.p. 116—117 °C (15 Torr). Esters **3a—f** were obtained by esterification of acids **2a—e** with methanol or ethanol in the presence of 98% H_2SO_4.

When preparing the catalysts Re_2O_7—B_2O_3/Al_2O_3 and Re_2O_7/Al_2O_3 containing 9 or 12% Re and 5% B_2O_3, NH_4ReO_4 (Aldrich) was used as a precursor of the active phase.[12]

The carrier B_2O_3/Al_2O_3 was prepared by impregnation of γ-Al_2O_3 (S_{sp} = 196 $m^2\ g^{-1}$, grain size 0.3—0.6 mm, d = 0.56 g cm^{-3}) with aqueous H_3BO_3 followed by drying in a drying box at 150 °C. The activator $SnMe_4$ was synthesized as described earlier[12] and stored over molecular sieves in argon.

Metathesis reaction. Hexane (5 mL) distilled over sodium in an argon atmosphere and Re_2O_7—B_2O_3/Al_2O_3 or Re_2O_7/Al_2O_3 (0.47 g (9% Re) or 0.35 g (12% Re), which corresponds to $2.4 \cdot 10^{-3}$ mol of rhenium (see Table 1), were placed in a flask connected to a gas burette. Then a required amount of $SnMe_4$ ($2.4 \cdot 10^{-3}$ or $4.8 \cdot 10^{-3}$ mol, depending on the given Re : Sn ratio) in hexane (1.0 mL) was added and the mixture was stirred with a magnetic stirring bar at 20 °C for 1 h. Ester **3** ($12 \cdot 10^{-2}$ mol; Re : **3** = 1 : 50) in hexane (5 mL) was added and the volume of evolved ethene was measured. After the evolution of ethene ceased, the reaction mixture was filtered, the solid phase was washed with hexane, and the hexane and nonconsumed ester **3** were removed. The residue was diester **4** (GLC and NMR data).

4-Methylhex-5-enoic acid (2c) (see Ref. 13). ^{1}H NMR ($CDCl_3$), δ: 1.02 (d, 3 H, Me, J = 6.70 Hz); 1.64 (m, 2 H, CH_2CH_2CO); 2.17 (m, 1 H, CHMe); 2.34 (t, 2 H, CH_2COO, J = 7.72 Hz); 5.02 (m, 2 H, $CH{=}CH_2$); 5.64 (m, 1 H, $CH{=}CH_2$); 10.60 (br.s, 1 H). ^{13}C NMR ($CDCl_3$), δ: 20.12 (CMe), 31.01, 31.93 (CH_2CH_2), 37.39 (CHMe), 113.84 ($CH{=}CH_2$), 143.20 ($CH{=}CH_2$), 180.50 (C=O).

4-*tert*-Butylhex-5-enoic acid (2d) (see Ref. 14). ^{1}H NMR ($CDCl_3$), δ: 0.88 (s, 9 H, CMe_3); 1.30—1.70 (wm, 2 H, CH_2CH_2CO); 1.92 (m, 1 H, CH); 2.1—2.50 (wm, 2 H, CH_2CO); 5.00 (m, 2 H, $CH{=}CH_2$); 5.53 (m, 1 H, $CH{=}CH_2$); 11.30 (br.s, 1 H). ^{13}C NMR ($CDCl_3$), δ: 27.63 (Me_3), 32.57 (CMe_3), 32.86 (CH_2CO), 54.75 ($CHCMe_3$), 117.15 ($CH{=}CH_2$), 139.05 ($CH{=}CH_2$), 180.85 (C=O).

Methyl pent-4-enoate (3a) (see Ref. 15). ^{1}H NMR ($CDCl_3$), δ: 2.44 (m, 4 H, CH_2CH_2); 3.67 (s, 3 H, OMe); 5.0 (m, 2 H, $CH{=}CH_2$); 5.8 (wm, 1 H, $CH{=}CH_2$). ^{13}C NMR ($CDCl_3$), δ: 27.31 ($CH_2CH{=}$); 32.92 ($CH_2C{=}O$); 51.42 (OMe); 115.34 ($CH{=}CH_2$); 135.92 ($CH{=}CH_2$); 173.41 (C=O).

Methyl hex-5-enoate (3b) (see Ref. 16). ^{1}H NMR ($CDCl_3$), δ: 1.8 (m, 2 H, CCH_2C, J = 7.3 Hz); 2.10 (quint, 2 H, $CH_2C{=}$, J = 7.3 Hz); 2.31 (t, 2 H, $O{=}CCH_2$, J = 7.2 Hz); 3.66 (s, 3 H, OMe). ^{13}C NMR ($CDCl_3$), δ: 24.1 (CCH_2C); 32.44 ($CH_2CH{=}$); 33.64 ($CH_2C{=}O$), 50.95 (OMe), 115.41 ($CH{=}CH_2$), 136.61 ($CH{=}CH_2$), 173.32 (C=O).

Methyl 4-methylhex-5-enoate (3c) (see Ref. 17). ^{1}H NMR ($CDCl_3$), δ: 0.95 (d, 3 H, Me, J = 6.72 Hz); 1.58 (m, 2 H, CH_2CH_2CO); 2.09 (m, 1 H, CHMe); 2.25 (t, 2 H, CH_2CO, J = 7.74 Hz); 3.61 (s, 3 H, OMe); 4.93 (m, 2 H, $CH{=}CH_2$); 5.58 (m, 1 H, $CH{=}CH_2$). ^{13}C NMR ($CDCl_3$), δ: 19.96 (CCH_3); 31.23, 31.77 (CH_2CH_2); 37.36 (CHMe); 51.30 (OMe); 113.47 ($CH{=}CH_2$); 143.24 ($CH{=}CH_2$); 174.30 (C=O).

Methyl 4-*tert*-butylhex-5-enoate (3d) (see Ref. 18). ^{1}H NMR ($CDCl_3$), δ: 0.86 (s, 9 H, CMe_3); 1.3—1.8 (wm, 2 H, CH_2CH_2CO); 1.90 (m, 1 H, $CHCMe_3$); 2.00—2.40 (wm, 2 H, CH_2CO); 3.64 (s, 3 H, OMe); 5.00 (m, 2 H, $CH{=}CH_2$); 5.50 (m, 1 H, $CH{=}CH_2$). ^{13}C NMR ($CDCl_3$), δ: 23.82 (CH_2CH_2CO), 27.69 (Me_3), 32.44 (CMe_3), 31.94 (CH_2CO), 50.84 (OMe), 54.83 ($CHCMe_3$), 116.89 ($CH{=}CH_2$), 140.04 ($CH{=}CH_2$), 178.79 (C=O).

Methyl hept-6-enoate (3e) (see Ref. 19). ^{1}H NMR ($CDCl_3$), δ: 1.9 (m, 2 H, $CH_2CH_2CH_2CO$); 2.1 (m, 2 H, $CH_2CH_2CH_2CO$); 2.35 (wm, 4 H, CH_2); 3.60 (s, 3 H, OMe); 4.96 (m, 2H,$CH{=}CH_2$); 5.75 (m, 1 H, $CH{=}CH_2$). ^{13}C NMR ($CDCl_3$), δ: 24.0 ($CH_2CH_2CH_2CH_2CO$), 33.3 ($CH_2CH_2CH_2CH_2CO$), 38.3 ($CH_2C{=}O$), 51.4 (OMe), 115.4 ($CH{=}CH_2$), 136.6 ($CH{=}CH_2$), 173.4 (C=O).

Ethyl hex-5-enoate (3f) (see Ref. 20). ^{1}H NMR ($CDCl_3$), δ: 1.7 (quint, 2 H, CCH_2C, J = 7.3 Hz); 2.06 (quint, 2 H, $CH_2C{=}$, J = 7.2 Hz); 2.28 (t, 2 H, $O{=}CCH_2$, J = 7.3 Hz); 4.10 (m, 2 H, OCH_2Me, J = 7.1 Hz); 4.98 (m, 2 H, $CH_2{=}C$); 5.74 (m, 1 H, CH=C). ^{13}C NMR ($CDCl_3$), δ: 14.50 (Me), 24.0 (CCH_2C), 32.98 ($CH_2CH{=}$), 33.50 ($CH_2C{=}O$), 60.10 (OCH_2Me), 115.22 ($CH{=}CH_2$), 137.64 ($CH{=}CH_2$), 173.50 (C=O).

Dimethyl *Z,E*-oct-4-enedioate (4a) (see Ref. 21). ^{1}H NMR ($CDCl_3$), δ: 2.30 (m, 4 H, CH_2CH_2); 3.55 (s, 3 H, OMe); 5.45 (m, 1 H, CH=C). ^{13}C NMR ($CDCl_3$), δ: 27.50 ($CH_2CH{=}$), 33.63 ($CH_2C{=}O$), 51.15 (OMe), 128.76 (*cis*-CH=CH), 129.19 (*trans*-CH=CH), 173.11 (C=O).

Dimethyl *Z,E*-dec-5-enedioate (4b) (see Ref. 22). ^{1}H NMR ($CDCl_3$), δ: 1.68 (quint, 2 H, CCH_2C, J = 7.46 Hz); 2.20 (m, 2 H, $CH_2CH{=}$); 2.30 (t, 2 H, $O{=}CCH_2$, J = 7.46 Hz); 3.67 (s, 3 H, OMe); 5.38 (m, 1 H, CH=C). ^{13}C NMR ($CDCl_3$), δ: 24.62 (CCH_2C); 31.84 ($CH_2CH{=}$); 34.01 ($CH_2C{=}O$); 51.46 (OMe); 129.50 (*cis*-CH=CH); 130.00 (*trans*-CH=CH); 174.50 (C=O).

Dimethyl *Z,E*-dodec-6-enedioate (4e) (see Ref. 10). ^{1}H NMR ($CDCl_3$), δ: 1.35 and 1.58 (m, 4 H, CCH_2CH_2C); 1.98 (m, 2 H, $CH_2CH{=}$); 2.30 (t, 2 H, $O{=}CCH_2$, J = 7.2 Hz); 3.63 (s, 3 H, OMe); 5.37 (m, 1 H, CH=C). ^{13}C NMR ($CDCl_3$), δ: 24.33, 28.75, 31.79 (3 CH_2); 33.50 ($CH_2C{=}O$); 51.00 (OMe), 129.28 (*cis*-CH=CH), 129.79 (*trans*-CH=CH), 173.68 (C=O).

Diethyl *Z,E*-dec-5-enedioate (4f) (see Ref. 23). ^{1}H NMR ($CDCl_3$), δ: 1.20 (m, 3 H, CH_2CH_3); 1.70 (q, 2 H, CCH_2C, J = 7.3 Hz); 2.04 (q, 2 H, $CH_2CH{=}CH$, J = 7.2 Hz); 2.30 (t, 2 H, $O{=}CCH_2$, J = 7.2 Hz); 4.10 (q, 2 H, OCH_2Me, J = 7.1 Hz); 5.29 (m, 1 H, CH=C).

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References

1. V. L. Antonovskii, *Organicheskie perekisnye initsiatory* [*Organic Peroxide Initiators*], Khimiya, Moscow, 1972, 134 (in Russian).
2. A. I. Rakhimov, *Khimiya i tekhnologiya organicheskikh peroksidnykh soedinenii* [*The Chemistry and Technology of Organic Peroxides*], Khimiya, Moscow, 1979, 163 (in Russian).
3. A. V. Aleksandrov, Ph.D. (Chem.) Thesis, Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow, 1986, 163 pp. (in Russian).
4. G. I. Nikishin, A. V. Aleksandrov, A. V. Ignatenko, and E. K. Starostin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1984, 2628 [*Bull. Acad. Sci. USSR*, *Div. Chem Sci.*, 1984, **33**, 2407 (Engl. Transl.)].
5. E. K. Starostin, A. V. Ignatenko, M. A. Lapitskaya, K. K. Pivnitskii, and G. I. Nikishin, *Izv. Akad. Nauk, Ser. Khim.*, 2001, 797 [*Russ. Chem. Bull.*, *Int. Ed.*, 2001, **50**, 833].
6. G. Yu. Ishmuratov, R. Ya. Kharisov, V. N. Odinokov, and G. A. Tolstikov, *Usp. Khim.*, 1995, **64**, 580 [*Russ. Chem. Rev.*, 1955, **64**, 541 (Engl. Transl.)].
7. S. Hauptmann and K. Hizschberg, *J. Pract. Chem.*, 1966, **34**, 55.
8. B. W. Baker, R. W. Kiezstead, P. P. Linstead, and B. C. L. Weedon, *J. Chem. Soc.*, 1954, 1804.
9. M. Ya. Fioshin, A. I. Kamneva, L. A. Mirkind, L. A. Salmin´, and A. G. Kornienko, *Neftekhimiya*, 1962, **11**, 557 [*Petroleum Chemistry*, 1962, **11** (Engl. Transl.)].
10. E. G. E. Hawkins and R. Large, *J. Chem. Soc.*, *Perkin Trans. 1*, 1974, **21**, 2561.
11. M. Arisawa, H. Kaneko, A. Nishida, and M. Nakagawa, *J. Chem. Soc.*, *Perkin Trans. 1*, 2002, 959.
12. D. B. Furman, R. V. Dmitriev, A. P. Barkova, and M. A. Vasil´ev, *Neftekhimiya*, 2004, **44**, 131 [*Petroleum Chemistry*, 2004, **44** (Engl. Transl.)].

13. K. Mori, T. Suguro, and S. Masuda, *Tetrahedron Lett.*, 1978, 3447.
14. T. Fujisawa, K. Umezu, and M. Kawashima, *Chem. Lett.*, 1984, 1795.
15. H. Hoberg, Y. Peres, C. Kruger, and Yi-H. Tsay, *Angew. Chem.*, 1987, **99**, 799.
16. M. Scarborough and A. B. Smith, *Tetrahedron Lett.*, 1977, 4361.
17. S. Aouagi, Y. Shishido, and Ch. Kabayash, *Tetrahedron Lett.*, 1991, **32**, 4325.
18. H. Inoue, Sh. Mikata, and T. Suzuki, *Liebigs Ann. Chem.*, 1994, 901.
19. L. A. Arnold, R. Naasz, A. J. Minnaard, and V. L. Feringa, *J. Org. Chem.*, 2002, **67**, 7244.
20. S. F. Wnuk, J. M. Rios, J. Khan, and Ya-Li Hsu, *J. Org. Chem.*, 2000, **65**, 4169.
21. C. Baker, *Tetrahedron Lett.*, 1977, **5**, 441.
22. D. J. Cram and N. I. Allinger, *J. Am. Chem. Soc.*, 1956, **78**, 2518.
23. H. G. Thomas and F. Thonnessen, *Chem. Ber.*, 1979, **112**, 2786.

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