(s, H-2). Irradiation at τ 8.3 changed the doublet at τ 6.05 to a singlet and altered the multiplet at τ 6.15–6.4. Irradiation at τ 4.4 altered the H-2′ signal.

For analysis compound (**6**) was dried at 60° under reduced pressure for 1 h.

Anal. Calcd. for $C_{12}H_{17}N_5O_5 \cdot H_2O$: C, 43.70; H, 5.75; H, 21.20. Found: C, 43.40; H, 5.60; N, 21.41.

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Ring enlargement through acyloin condensation of cycloalkane-1,2-dicarboxylic esters

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Cycloalkane-1,2-dicarboxylic esters of 11-, 12-, and 13-membered rings were prepared from cyclododecanone. Acyloin condensation of these esters in the presence of trimethylchlorosilane followed by acidic hydrolysis afforded 13-, 14-, and 15-membered cycloalkane-1,2-diones in 71–74% yields. The diketones were reduced by treatment with triethyl phosphite and alkali hydroxide into corresponding acyloins.

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Acyloin condensation in the presence of trimethylchlorosilane was first reported by Schräpler and Rühlmann (1) and later extended to the preparation of four membered cyclic acyloins by Rühlmann (2) and Bloomfield (3). Bloomfield further discussed thermal ring-opening of intermediary cyclobutene-1,2-diol disilyl ethers being controlled by the Woodward–Hoffmann rule.[1]

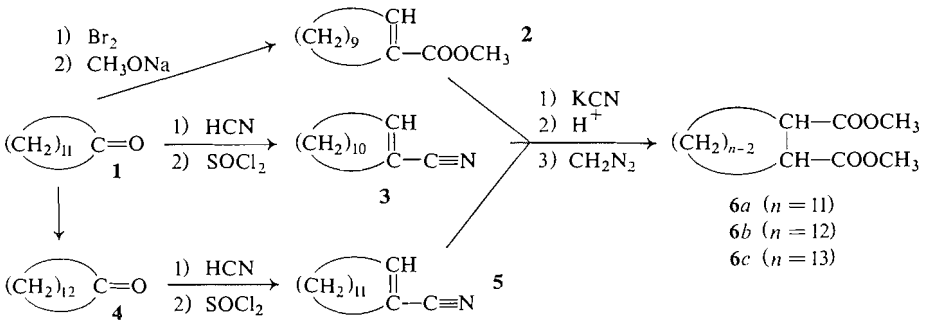
We now wish to report that this procedure, when applied to large ring cycloalkane-1,2-dicarboxylic esters, constitutes a convenient method for ring enlargement affording cycloalkane-1,2-diones under the incorporation of two side-chain carbons into the rings.[2,3]

Experiments were conducted with 11-, 12-, and 13-membered cycloalkane-1,2-dicarboxylic esters (**6***a–c*), all of which were hitherto unknown compounds and prepared from cyclododecanone (**1**) as a common starting material as shown in Scheme 1. The 11-membered unsaturated ester **2** (7) and the 12-membered unsaturated nitrile **3** (8*b*) have already been obtained from cyclo-

[1]For the valence-isomerization of cyclobutenes, see ref. 4.

[2]Brannock *et al.* (5) and Scharf *et al.* (6) reported similar ring enlargements through thermal ring-opening of bicyclic cyclobutene derivatives.

[3]Dr. Bloomfield kindly suggested to us that the application of this procedure to the diester available from cycloalkanone enamine and dimethyl acetylenedicarboxylate (5) can add four carbon atoms into the starting ring.



SCHEME 1

dodecanone (**1**) in good yields. Cyclotridecanone (**4**) required in the preparation of 13-membered nitrile **5** is now readily accessible from **1** or its precursor 1,5,9-cyclododecatriene (8).

The α,β-unsaturated ester and nitriles were all converted into corresponding diesters (**6***a–c*) by hydrocyanation, acidic hydrolysis, and final esterification with diazomethane. The diesters (**6**) were characterized by correct elemental analyses, infrared (i.r.) absorption spectra, and nuclear magnetic resonance (n.m.r.) spectra (see Experimental). Each diester would naturally form a mixture of *cis* and *trans* isomers but the separation has not been attempted. As described below, both of the *cis* and *trans* isomers of the intermediates **7** derived from the respective isomers of **6** should be able to undergo ring-opening to **8** to give the same products after hydrolysis, when *n* is sufficiently large.

The acyloin condensation of **6** (see Scheme 2) was performed by following the procedure of Bloomfield (3) in the presence of trimethylchlorosilane in xylene at 110–120°. The reaction was completed by heating to reflux in order to ensure the ring-opening of intermediary cyclobutenes **7** into 1,3-dienes (**8**). Acidic hydrolysis of the reaction mixture gave 1,2-diketones (**9**) in 71–74% yields. The structures of the diketones **9** were ascertained by elemental analyses, i.r., visible absorption spectra, n.m.r., and by reduction to the known cyclic acyloins (**10**).

Reduction of **9** was attained by alkaline hydrolysis of the adducts of **9** with triethyl phosphite in 74–79% yields.

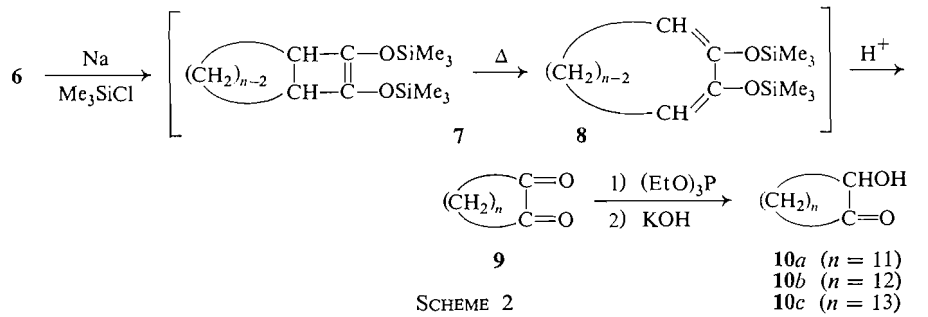
Since the cyclic acyloins (**10**) can be easily reduced to cycloalkanones (9) this reaction sequence would constitute another route to larger ring ketones including cyclotetradecanone and exaltone that are useful as musk odor substances.

Experimental

All temperatures are uncorrected. Nuclear magnetic resonance spectra were obtained on JOEL C-60-H spectrometer in CCl_4 solutions with tetramethylsilane as an internal reference. Chemical shifts are given in p.p.m. from this reference, together with the multiplicity of signals indicated in an abbreviated form: s for singlet, t for triplet, and m for multiplet, respectively. Gas–liquid chromatography was conducted on SE-30 on Chromosorb W (10%) with hydrogen as a carrier gas at 150–190°.

Dimethyl Cycloundecane-1,2-dicarboxylate (6a)

A solution of methyl cycloundecene-1-carboxylate (**2**) (7) (105 g, 0.5 mole) in ethanol (500 ml) was added to potassium cyanide (97.5 g, 1.5 mole) dissolved in water (225 ml) and the whole mixture was heated at reflux for



SCHEME 2

40 h. After cooling, the mixture was diluted with water (300 ml) and washed with ether. The aqueous layer was acidified with dilute hydrochloric acid and extracted with ether. The organic layer was washed with water, dried (Na_2SO_4), and concentrated *in vacuo*. The residual semisolid was dissolved in acetic acid (830 ml) and concentrated hydrochloric acid (450 ml) and the solution was heated at reflux for 40 h. After cooling and dilution with water, the mixture was extracted with ether several times. The extracts were combined, washed with water, and concentrated *in vacuo*. The resulting solid was immediately esterified with diazomethane to give dimethyl ester (**6***a*). Vacuum distillation gave pure **6***a* (47.3 g, 35% yield based on **2**) as a colorless oil, b.p. 128–134°/0.2 mm Hg. Gas–liquid chromatography showed a single peak. Infrared (neat): 1740, 1190, 1160 cm^{-1} ($COOCH_3$). Nuclear magnetic resonance: δ 3.60 s (6 H), 2.75 m (2 H), 2.0–1.0 m (18 H, a peak at 1.45).

Anal. Calcd. for $C_{15}H_{26}O_4$: C, 66.6; H, 9.7. Found: C, 66.4; H, 9.8.

Dimethyl Cyclododecane-1,2-dicarboxylate (6b)

To a solution of cyclododecene-1-carbonitrile (**3**) (8*b*) (50 g, 0.26 mole) in ethanol (500 ml) was added potassium cyanide (80 g, 1.23 mole) dissolved in water (200 ml) and the whole mixture was heated at reflux for 42 h. After cooling, the reaction mixture was diluted with water. Acidification with dilute hydrochloric acid and salting-out gave white powdery precipitates which were separated by filtration and dissolved in acetic acid (1100 ml) and concentrated hydrochloric acid (750 ml). The resulting solution was heated at reflux for 16 h, cooled, diluted with water, and extracted with ether several times. The extracts were, combined, washed with water, dried (Na_2SO_4), and concentrated *in vacuo* to give solid cyclododecane-1,2-dicarboxylic acid which was esterified with diazomethane without further purification into dimethyl ester (**6***b*). Distillation *in vacuo* afforded pure **6***b* as a colorless solid (57.3 g, 77% yield based on **3**), b.p. 116–118°/0.03 mm Hg, m.p. 54–56°. Gas–liquid chromatography gave a single peak. Infrared (Nujol): 1740, 1190, 1160 cm^{-1} ($COOCH_3$). Nuclear magnetic resonance: δ 3.60 s (6 H), 2.70 m (2 H), 2.0–1.0 m (20 H, a peak at 1.40).

Anal. Calcd. for $C_{16}H_{28}O_4$: C, 67.6; H, 9.9. Found: C, 67.4; H, 9.9.

Cyclotridecene-1-carbonitrile (5)

Hydrocyanic acid (35 ml) was added to a mixture of cyclotridecanone (**4**) (8) (27.5 g, 0.14 mole), triethylamine (3 ml), and ether (50 ml) under stirring in the course of 1 h at room temperature. After stirring at room temperature for 3 h, the mixture was heated at reflux for 1 h. The reaction mixture was cooled, acetic acid (4 ml) added, and the whole washed with water, dried (Na_2SO_4), and concentrated *in vacuo* to give crude cyclotridecanone cyanohydrine (33 g) as a pale-yellow solid. Thionyl chloride (50 g, 0.41 mole) was added dropwise to the crude cyanohydrine dissolved in benzene (70 ml) under stirring at 60° during 2 h. Then the reaction temperature was raised to 75–80° and stirring was continued until no evolution of hydrogen chloride was observed. Vacuum distillation of the reaction mixture gave **5** (24 g, 83% yield based on **4**) as a yellow oil. Redistillation afforded an analytically pure sample as an almost colorless oil, b.p. 102–107°/0.2 mm Hg. Infrared (neat): 2240 cm^{-1} C≡N). Nuclear magnetic resonance: δ 6.05 t (1 H), 2.6–1.9 m (4 H), 1.9–1.1 m (18 H, a peak at 1.30).

Anal. Calcd. for $C_{14}H_{23}N$: C, 81.9; H, 11.3; N, 6.8. Found: C, 81.6; H, 11.2; N, 6.4.

Dimethyl Cyclotridecane-1,2-dicarboxylate (6c)

The unsaturated nitrile **5** was converted into dimethyl ester **6***c* in the same way as described for the preparation of **6***b*. The ester **6***c* was obtained in 56% yield as a colorless solid, b.p. 137–142°/0.08 mm Hg, m.p. 95–97°. Infrared (Nujol): 1740, 1190, 1160 cm^{-1} ($COOCH_3$). Nuclear magnetic resonance: δ 3.65 s (6 H), 2.7 m (2 H), 2.0–1.0 m (22 H, a peak at 1.40).

Anal. Calcd. for $C_{17}H_{30}O_4$: C, 68.4; H, 10.1. Found: C, 68.3; H, 10.2.

Cycloalkane-1,2-diones (9a–c)

General Procedure

A mixture of dimethyl cycloalkane-1,2-dicarboxylate (**6**) (0.04 mole), trimethylchlorosilane (21.7 g, 0.2 mole), and xylene (20 ml) was added dropwise to metallic sodium (5.7 g, 0.24 mole) dispersed in xylene (60 ml) with vigorous stirring at 110–120° under nitrogen atmosphere in the course of 3 h. Stirring was continued at 110–120° for 6 h, and then at reflux temperature for 3 h. After cooling and filtration of inorganic substances, the filtrate was concentrated *in vacuo* to give a viscous oil, which was dissolved in ethanol (140 ml). The resulting solution was added with water (25 ml) and with concentrated hydrochloric acid (4 ml) and the mixture was heated at reflux for 15 min under nitrogen atmosphere. After cooling and dilution with water, the mixture was extracted with ether. The extracts were combined, washed with water, dried (Na_2SO_4), and distilled *in vacuo* to afford **9** as a golden yellow oil or solid. The yields and physical properties were as follows. There was no spectral evidence indicating the presence of enol tautomer.

Cyclotridecane-1,2-dione (9a)

Product was obtained in 71% yield, b.p. 94–97°/2 mm Hg, infrared (neat): 1710 cm^{-1} (C=O), nuclear magnetic resonance: δ 2.70 diffused t (4 H), 2.0–1.0 m (18 H, a peak at 1.25), visible and ultraviolet absorption spectra (in *n*-hexane): log ε_{max} 1.33 (446 mμ), 3.22 (267 mμ). The abnormal absorption in the ultraviolet region might possibly be ascribed to the presence of a trace of inseparable impurity. Biacetyl and cyclodecane-1,2-dione show absorptions of log ε_{max} 1.2 (276 mμ, in cyclohexane) and 1.43 (270 mμ, in ethanol), respectively (10).

Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.2; H, 10.5. Found: C, 74.4; H, 10.6.

Cyclotetradecane-1,2-dione (9b)

Product was obtained in 73% yield, b.p. 88–93°/0.03 mm Hg, m.p. 37–38° (from *n*-hexane), infrared (Nujol): 1710 cm^{-1} (C=O), nuclear magnetic resonance: δ 2.70 diffused t (4 H), 2.0–1.0 m (20 H, a peak at 1.25), visible and ultraviolet absorption spectra (in *n*-hexane): log ε_{max} 1.37 (443 mμ), 1.53 (278 mμ).

Anal. Calcd. for $C_{14}H_{24}O_2$: C, 75.0; H, 10.8. Found: C, 75.2; H, 10.8.

Cyclopentadecane-1,2-dione (9c)

Product was obtained in 74% yield, b.p. 86–92°/0.02 mm Hg, m.p. 35–37° (from *n*-hexane), infrared (Nujol): 1710 cm^{-1} (C=O), nuclear magnetic resonance: δ 2.75

diffused t (4 H), 2.0–1.0 m (22 H, a peak at 1.25), visible and ultraviolet absorption spectra (in *n*-hexane): log ε_{max} 1.31 (442 mμ), 1.58 (276 mμ).

Anal. Calcd. for $C_{15}H_{26}O_2$: C, 75.6; H, 11.0. Found: C, 75.3; H, 11.0.

*2-Hydroxycycloalkanones (**10a–c**)*

General Procedure

1,2-Diketones (**9**) (0.03 mole) dissolved in benzene (20 ml) was added to a stirred mixture of triethyl phosphite (6.1 g, 0.04 mole) and benzene (16 ml) in the course of 15 min at room temperature under nitrogen atmosphere. The whole mixture was then heated at reflux for 1 h, and concentrated *in vacuo*. The residual oil was mixed with ethanol (75 ml), water (60 ml), and potassium hydroxide (6.7 g, 0.12 mole) and the mixture was stirred at room temperature for 3 h. After dilution with water, the mixture was extracted with chloroform. The extracts were combined, washed, dried and concentrated. Purification of the residual solid by vacuum distillation and recrystallization from *n*-hexane gave analytically pure samples of acyloins **10**. The yields, melting points, etc. were as follows.

*2-Hydroxycyclotridecanone (**10a**)*

Product was obtained in 79% yield, m.p. 44–45° (reported (11) m.p. 45–46°), infrared (Nujol): 3400 (OH), 1710 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_{24}O_2$: C, 73.5; H, 11.4. Found: C, 73.5; H, 11.4.

*2-Hydroxycyclotetradecanone (**10b**)*

Product was obtained in 78% yield, m.p. 82–83° (reported (11) m.p. 84–85°), infrared (Nujol): 3530 (OH), 1705 cm^{-1} (C=O).

Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.3; H, 11.6. Found: C, 74.4; H, 11.5.

*2-Hydroxycyclopentadecanone (**10c**)*

Product was obtained in 74% yield, m.p. 55–56° (reported (11) m.p. 57–58°), infrared (Nujol): 3450 (OH), 1710 cm^{-1} (C=O).

Anal. Calcd. for $C_{15}H_{28}O_2$: C, 75.0; H, 11.7. Found: C, 75.1; H, 11.8.

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Separation and identification of methyl ethers of D-glucose and D-glucitol by gas–liquid chromatography[1]

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The separation by gas–liquid chromatography of the methyl ethers of D-glucose and of D-glucitol is described.

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In view of the importance of methyl ether derivatives in the determination of polysaccharide structure it is considered of value to publish details of their separation by gas–liquid chromatography as methyl glycosides and glycitol ethers, and as their acetyl derivative. Details of the separation of methyl ethers of arabinose (1) and of xylose have already been given (2). We now publish details of the separation of the methyl ethers of D-glucose and of D-glucitol.

All separations were made on a Pye–Argon

[1]Abstracted from the Ph.D. thesis of H. G. Jones, Queen's University, Kingston, Ontario, 1964.