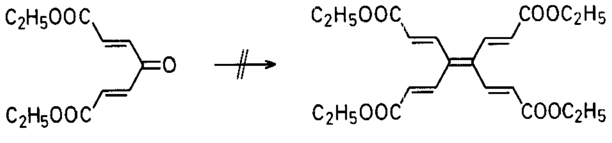
Synthesis of Tetrakis[2-ethoxycarbonyl-*trans*-ethenyl]ethene

Luciano Lombardo[1], Franz Sondheimer*

Chemistry Department, University College London, 20 Gordon Street, London WC1H OAJ, England

We describe a synthesis of tetrakis[2-ethoxycarbonyl-*trans*-ethenyl]ethene (**2**), an interesting cross-conjugated tetra-ester which was required as a potential starting material for the synthesis of *o*-fused annulenoannulenes[2,3]. An obvious direct approach to **2** involves the readily available diethyl *trans,trans*-penta-1,4-dien-3-one-1,5-dicarboxylate (**1**)[4] as a precursor. Unfortunately, all attempts to convert **1** to **2** (e.g. by the Barton-Kellogg[5,6] or the McMurry[7] methods) were unsuccessful. A less direct route to **2** was therefore developed.



1 **2**

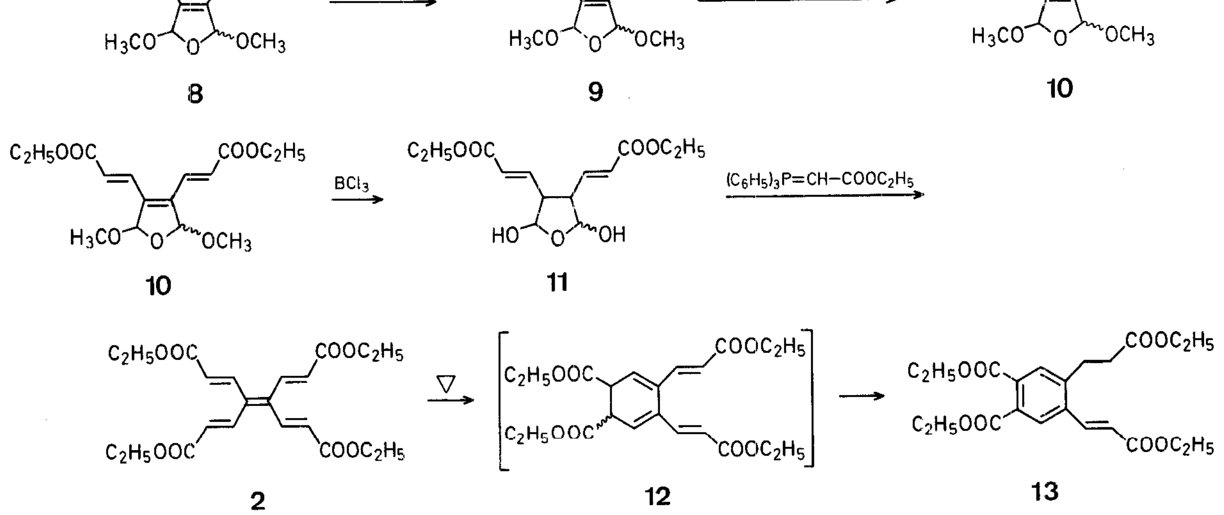
The starting material was furan-3,4-dicarboxaldehyde (**4**), which was prepared most conveniently in 55% yield by oxidation of 3,4-bis[hydroxymethyl]furan (**3**)[8] with the chromic anhydride/pyridine complex[9]. This method is superior to the previously reported ones[2,8,10]. Reaction of **4** with trimethyl orthoformate and methanol in the presence of *p*-toluenesulphonic acid led quantitatively to the bis[dimethylacetal] **5**. This substance was converted in 59% yield to a stereoisomeric mixture (~3:2, as determined by the ^{1}H-N.M.R. spectrum) of the tetra-acetal **6** by treatment with bromine in methanol at −20 °C[11].

Hydrolysis of one of the two dimethylacetal groupings of **6** was brought about smoothly by treatment with *p*-toluenesulphonic acid in aqueous acetone at room temperature. The resulting stereoisomeric monoaldehyde **7**, formed in quantitative yield, was then subjected to Wittig reaction with ethoxycarbonylmethylenetriphenylphosphorane[12] in dichloromethane at room temperature, whereby the α,β-unsaturated ester **8** (stereoisomeric mixture) was obtained smoothly. Compound **8** was not purified, but the other dimethylacetal grouping in this substance was now hydrolysed by means of *p*-toluenesulphonic acid in aqueous acetone at 35–40 °C, a reaction which led to 94% (based on **7**) of a stereoisomeric mixture of the aldehydo-esters **9**. A second Wittig reaction of **9** with ethoxycarbonylmethylenetriphenylphosphorane[12] in dichloromethane at room temperature then gave the stereoisomeric dimethoxy-diesters **10** in 71% yield.

It is of interest that the successful conversion of the acetal **6** to the diester **10** involved successive hydrolyses of each of the two dimethylacetal groupings in **6**. Attempts to simplify the procedure by bringing about the hydrolysis of both dimethylacetal functions of **6** to give the corresponding dicarboxaldehyde directly were unsatisfactory, and led to complex mixtures of products.

Treatment of the dimethoxy-diester **10** with boron trichloride[13] in dichloromethane at −5 °C caused cleavage of both methoxy groups, and quantitatively gave a stereoisomeric mixture of the dihydroxy-diesters **11**. Wittig reaction with an excess of ethoxycarbonylmethylenetriphenylphosphorane[12] in boiling benzene then gave the required tetra-ester **2** in 18% yield. In addition, the benzenoid tetra-ester **13** was obtained in 13% yield.

The tetra-ester **13** was presumably derived from **2** by an initial 6π electrocyclic disrotatory ring closure to give the 1,2-dihydrobenzene derivative **12**, followed by the shift of two hydrogens. This was confirmed by heating the tetra-ester **2** in pyridine at 110 °C for 2 h, a reaction which led to **13** as sole product.



Furan-3,4-dicarboxaldehyde (4):

A solution of 3,4-bis[hydroxymethyl]furan[8] (3; 29 g) in dichloromethane (50 ml) is added to a stirred solution of chromic anhydride/pyridine complex[9] (350 g) in dichloromethane (2 l) cooled in an ice bath during 2 h. A further quantity of chromic anhydride/pyridine complex (150 g) is then added at room temperature with stirring during 1.5 h. Ether (1 l) is added, and the mixture is filtered through a short column of alumina (act.: IV). Evaporation of the filtrate to dryness and crystallisation of the residue from ethyl acetate/petroleum ether (b.p. 40–60 °C) gives **4**; yield: 15.4 g (55%); needles, m.p. 76–77 °C.

^{1}H-N.M.R. ($CDCl_3$, cf. Refs.[8, 10]) $\delta = 10.18$ (s, 2H); 8.15 ppm (s, 2H).

Furan-3,4-dicarboxaldehyde Bis(dimethylacetal) (5):

A solution of **4** (23.1 g) and *p*-toluenesulphonic acid (0.1 g) in trimethyl orthoformate (70 ml) and methanol (120 ml) is heated at 35 °C for 20 h. Evaporation under reduced pressure gives **5**, a clear colourless liquid; yield: 40.1 g (100%); a small sample is distilled; b.p. 60–62 °C/0.07 torr.

$C_{10}H_{16}O_5$	calc.	C 55.54	H 7.46
(216.1)	found	55.33	7.40

M.S.: *m/e* = 216 (M^+); 185 ($M^+ - OCH_3$).

I.R. (KBr): $\nu = 1195$; 1170; 1135; 1110; 1090; 1050 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 7.43$ (s, 2H), 5.45 (s, 2H); 3.33 ppm (s, 12H).

2,5-Dimethoxy-2,5-dihydrofuran-3,4-dicarboxaldehyde Bis[dimethylacetal] (6):

A solution of bromine (30.4 g, 0.19 mol) in methanol (120 ml) is added during 30 min to a solution of **5** (41.0 g, 0.19 mol) in ether (150 ml) and methanol (150 ml) cooled to −25 °C by means of a Dry Ice-acetone bath (internal temperature ~ −20 °C). The solution is then kept at −15 °C for a further 2 h, slowly allowed to reach room temperature during 20 h, and cooled to −70 °C. Gaseous ammonia is passed through the solution at such a rate that the internal temperature does not exceed −50 °C until the solution is slightly basic (pH paper). The solution is evaporated under reduced pressure, ether is added to the residue, and the mixture is filtered through a short column of alumina (act.: IV). Evaporation of the solvent under reduced pressure and subsequent distillation through a 10″ Vigreux column gives unchanged **5** (4.0 g, b.p. 60–62 °C/0.07 torr), followed by **6**, a clear colourless liquid; yield: 31.0 g (59%); b.p. 91–94 °C/0.03 torr.

$C_{12}H_{22}O_7$	calc.	C 51.79	H 7.97
(278.3)	found	51.73	7.82

M.S.: *m/e* = 278 (M^+); 247 ($M^+ - OCH_3$); 216 ($M^+ - 2 \times OCH_3$).

I.R. (KBr): $\nu = 1165$; 1130; 1120; 1110; 1050 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 5.87$, 5.58 (s, 2:3, 2H); 5.32 (s, 2H); 3.47, 3.43, 3.40, 3.38 ppm (s, 18H).

2,5-Dimethoxy-2,5-dihydrofuran-3,4-dicarboxaldehyde Mono[dimethylacetal] (7):

A solution of **6** (12.05 g) and *p*-toluenesulphonic acid (0.01 g) in acetone (200 ml) and water (1 ml) is allowed to stand at room temperature for 48 h. The solvent is evaporated under reduced pressure, the residue is redissolved in acetone (200 ml), and allowed to stand for a further 48 h. Evaporation of the solvent under reduced pressure gives **7**, a clear colourless liquid; yield: 10.0 g (99%); a small sample is distilled; b.p. 92–96 °C/0.08 torr.

$C_{10}H_{16}O_6$	calc.	C 51.72	H 6.94
(232.2)	found	51.34	7.02

M.S.: *m/e* = 232 (M^+), 201 ($M^+ - OCH_3$); 172 ($M^+ - OCH_3 - CHO$).

I.R. (KBr): $\nu = 1687$; 1676; 1200; 1165; 1130; 1085; 1060 cm^{-1}.

^{1}H-N.M.R. ($CDCl_3$): $\delta = 10.28$ (m, 1H); 6.03 (d, $J = 4$ Hz), 5.85 (d, $J = 4$ Hz), 5.80 (s), 5.57 (s) (total 2H); 5.30 (s, 1H); 3.52 (s), 3.50 (s), 3.37 (s), 3.33 (s) ppm (total 12H).

2,5-Dimethoxy-4-(2-ethoxycarbonyl-*trans*-ethenyl)-2,5-dihydrofuran-3-carboxaldehyde (9):

A solution of ethoxycarbonylmethylenetriphenylphosphorane[12] (6.5 g, 18.7 mmol) in dichloromethane (30 ml) is added during 30 min to a stirred solution of **7** (4.25 g, 18.3 mmol) in dichloromethane (30 ml) at room temperature. The solution is allowed to stand for a further 30 min and is then evaporated under reduced pressure. The residue is washed with ethyl acetate/petroleum ether (b.p. 40–60 °C), 1:19, and the washings are filtered through a short column of alumina (act.: IV). Evaporation under reduced pressure then gives crude **8** as a clear colourless liquid; yield: 5.47 g (99%).

A solution of crude **8** (5.3 g) and *p*-toluenesulphonic acid (0.1 g) in acetone (100 ml) is heated at 35 °C for 10 h. The solvent is evaporated under reduced pressure, the residue is redissolved in acetone (100 ml), and the solution is heated at 40 °C for 16 h. The solvent is again evaporated, and the residue is heated in acetone (100 ml) at 40 °C for a further 5 h. The solvent is evaporated under reduced pressure, the residue is dissolved in ethyl acetate/petroleum ether (b.p. 40–60 °C), 2:3, and filtered through a short column of alumina (act.: IV). Evaporation under reduced pressure gives **9** as an orange oil which crystallised on standing; yield: 4.25 g (94%, based on **7**); crystallisation of a small sample from ether/petroleum ether (b.p. 40–60 °C) produces light yellow crystals; m.p. 89–99 °C.

$C_{12}H_{16}O_6$	calc.	C 56.24	H 6.29
(256.2)	found	56.09	6.41

M.S.: *m/e* = 256 (M^+); 227 ($M^+ - CHO$ or CH_2CH_3); 225 ($M^+ - OCH_3$).

I.R. (KBr): $\nu = 1720$; 1675; 1210; 1185; 1105; 980 cm^{-1}.

U.V. (ethanol): $\lambda_{max} = 257$ nm ($\varepsilon = 20$, 100).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 10.20$ (s, 1H); 7.95, 6.55 (ABq, 2H, $J = 16$ Hz); 6.20 (d, $J = 4$ Hz), 6.08 (d, $J = 4$ Hz), 5.93 (s), 5.85 (s) (total 2H); 4.32 (q, 2H, $J = 7$ Hz); 3.60–3.40 (m, 6H); 1.33 ppm (t, 3H, $J = 7$ Hz).

2,5-Dimethoxy-3,4-bis[2-ethoxycarbonyl-*trans*-ethenyl]-2,5-dihydrofuran (10):

A solution of ethoxycarbonylmethylenetriphenylphosphorane[12] (5.6 g, 16.1 mmol) in dichloromethane (20 ml) is added during 15 min to a stirred ice-cooled solution of **9** (4.1 g, 16.0 mmol) in dichloromethane (30 ml). The solution is allowed to stand at room temperature for 30 min and is then evaporated under reduced pressure. The residue is washed with ethyl acetate/petroleum ether (b.p. 40–60 °C), 1:19, and the washings are filtered through a short column of alumina (act.: IV). Evaporation under reduced pressure and crystallisation of the residue from ether/petroleum ether (b.p. 40–60 °C) gives **10** as crystals; yield: 3.7 g (71%); m.p. 95–99 °C.

$C_{16}H_{22}O_7$	calc.	C 58.88	H 6.80
(326.3)	found	58.83	6.89

M.S.: *m/e* = 326 (M^+); 297 ($M^+ - CH_2CH_3$); 295 ($M^+ - OCH_3$); 281 ($M^+ - OCH_2CH_3$).

I.R. (KBr): $\nu = 1730$; 1715; 1185; 1100; 975 cm^{-1}.

U.V. (ethanol): $\lambda_{max} = 276$ sh ($\varepsilon = 14700$), 289 sh (25400), 301 (32900), 315 nm (25100).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 7.65$, 6.35 (ABq, 4H, $J = 16$ Hz); 6.07, 5.83 (s, 2H); 4.32 (q, 4H, $J = 7$ Hz); 3.47, 3.40 (s, 6H); 1.33 ppm (t, 6H, $J = 7$ Hz).

2,5-Dihydroxy-3,4-bis[2-ethoxycarbonyl-*trans*-ethenyl]-2,5-dihydrofuran (11):

A solution of boron trichloride[13] (0.35 ml) in dichloromethane (3.5 ml) is added dropwise during 35 min to a stirred solution of **10** (1.0 g) in dichloromethane (20 ml) cooled in a Dry Ice-acetone bath. The bath is allowed to warm to −5 °C during 40 min and is then kept at this temperature for a further 30 min. Tetrahydrofuran (150 ml) and water (20 ml) are added, and the mixture is stirred at room temperature for 45 min. Solid sodium hydrogen carbonate (~0.5 g) is added in order to neutralize the liberated acid, and the mixture is allowed to stand at room temperature for 40 h. Ether (200 ml) is added and the organic layer is separated, washed with brine, dried with magnesium sulphate, and evaporated under reduced pressure. Trituration of the residue with ether/petroleum ether (b.p. 40–

60 °C), 1:4, gives **11** as a colourless solid; yield: 0.91 g (100%); crystallisation of a sample from tetrahydrofuran/petroleum ether (b.p. 40–60 °C) gives crystals; m.p. 121–131 °C.

$C_{14}H_{18}O_7$	calc.	C 56.37	H 6.08
(298.2)	found	56.11	6.20

M.S.: *m/e* 298 (M^+); 280 ($M^+ - H_2O$).

I.R. (KBr): $\nu = 3360$; 1715; 1695; 1190; 1090; 970 cm^{-1}.

U.V. (ether): $\lambda_{max} = 275$ sh ($\varepsilon = 13600$); 288 (25200); 301 (33800); 314 nm (25500).

^{1}H-N.M.R. ($CDCl_3/THF$-d_8, 1:1): $\delta = 7.74$, 6.65 (ABq, 4H, $J = 16$ Hz); 6.33, 6.02 (s, 2H); 5.40 (br s, 2H); 4.32 (q, 4H, $J = 7$ Hz); 1.33 ppm (t, 6H, $J = 7$ Hz).

Tetrakis[2-ethoxycarbonyl-*trans*-ethenyl]ethene (2) and 1,2-Bis[ethoxycarbonyl]-4-(2-ethoxycarbonylethyl)-5-(2-ethoxycarbonyl-*trans*-ethenyl)-benzene (13) from 11:

A solution of **11** (0.66 g, 2.2 mmol) and ethoxycarbonylmethylenetriphenylphosphorane[12] (3.3 g, 9.5 mmol) in benzene (20 ml) is boiled under reflux for 2 h. The mixture is concentrated and chromatographed on a column of silica gel (100 g, act.: III). Elution with ethyl acetate/petroleum ether (b.p. 40–60 °C), 1:9, gives an oil (0.23 g), which partially crystallises on standing. The column is stripped by elution with ethyl acetate/methanol (1:1), the solvents are evaporated under reduced pressure, and the residue in benzene (20 ml) is boiled under reflux for 2 h with ethoxycarbonylmethylenetriphenylphosphorane[12] (3.0 g, 8.6 mmol). Chromatography as before yields a further amount of crude product (0.16 g). Crystallisation of the combined crude products from ether leads to **2** as colourless crystals; yield: 0.165 g (18%); m.p. 112–114 °C.

$C_{22}H_{28}O_8$	calc.	C 62.84	H 6.71
(420.4)	found	63.04	6.75

M.S.: *m/e* = 420 (M^+); 375 ($M^+ - OCH_2CH_3$).

I.R. (KBr): $\nu = 1722$; 1712; 1305; 1185; 1170; 970 cm^{-1}.

U.V. (ether): $\lambda_{max} = 255$ ($\varepsilon = 20800$); 330 nm (28900).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 7.61$, 6.13 (ABq, 8H, $J = 16$ Hz); 4.28 (q, 8H, $J = 7$ Hz); 1.33 ppm (t, 12H, $J = 7$ Hz).

The mother liquids remaining after crystallisation of **2** are chromatographed on a column of alumina (100 g, act.: IV). Elution with ethyl acetate/petroleum ether (b.p. 40–60 °C), 1:9, gives **13** as a viscous oil; yield: 0.12 g (13%); the analytical sample is obtained by distillation over a Bunsen burner at 0.1 torr.

$C_{22}H_{28}O_8$	calc.	C 62.84	H 6.71
(420.4)	found	62.88	6.73

M.S.: *m/e* 420 (M^+); 375 ($M^+ - OCH_2CH_3$); 330 ($M^+ - 2 \times OCH_2CH_3$).

I.R. (KBr): $\nu = 1720$; 1300; 1250; 1210; 1180; 980 cm^{-1}.

U.V. (ethanol): $\lambda_{max} = 228$ ($\varepsilon = 21600$); 279 nm (24600).

^{1}H-N.M.R. ($CDCl_3$): $\delta = 7.95$ (s, 1H); 7.62 (s, 1H); 7.99, 6.51 (ABq, 2H, $J = 16$ Hz); 4.63–3.97 (complex m, 8H); 3.17, 2.60 (t of A_2B_2 system, 4H); 1.50–1.12 ppm (complex m, 12H).

Thermolysis of 2 to 13:

A solution of **2** (10 mg) in pyridine (0.5 ml) is heated at 110 °C under a reflux condenser for 2 h. Evaporation under reduced pressure gives an oil (10 mg), the I.R. and ^{1}H-N.M.R. spectra of which are identical in every respect to those of **13**.

We thank the Science Research Council and the Royal Society for financial support.

Received: May 12, 1980

---

[1] Present address: Research School of Chemistry, The Australian National University, Box 4 P.O., Canberra, A.C.T. 2600, Australia.

[2] See: T. M. Cresp, F. Sondheimer, *J. Am. Chem. Soc.* **99**, 194 (1977).

[3] M. Nakagawa, *Angew. Chem.* **91**, 215 (1979); *Angew. Chem. Int. Ed. Engl.* **18**, 202 (1979).

[4] See: F. Straus, *Ber. Dtsch. Chem. Ges.* **37**, 3293 (1904).
N. E. Rowland, *M. Phil. Thesis*, University of London, 1972.

[5] D. H. R. Barton, B. J. Willis, *J. Chem. Soc. Perkin Trans. 1* **1972**, 305.

[6] J. Buter, S. Wassenaar, R. M. Kellogg, *J. Org. Chem.* **37**, 4045 (1972).

[7] See: J. E. McMurry, *Acc. Chem. Res.* **7**, 281 (1974).
J. E. McMurry, M. P. Fleming, K. L. Kees, L. R. Krepski, *J. Org. Chem.* **43**, 3255 (1978), and references cited there.

[8] M. J. Cook, E. J. Forbes, *Tetrahedron* **24**, 4501 (1968).

[9] J. C. Collins, W. H. Hess, F. J. Frank, *Tetrahedron Lett.* **1968**, 3363.

[10] J. A. Elix, M. V. Sargent, F. Sondheimer, *J. Am. Chem. Soc.* **92**, 973 (1970).

[11] See: N. Elming, *Adv. Org. Chem.* **2**, 67 (1960).

[12] O. Isler, H. Gutmann, M. Montavon, R. Rüegg, G. Ryser, P. Zeller, *Helv. Chim. Acta* **40**, 1242 (1957).

[13] See: T. G. Bonner, N. M. Saville, *J. Chem. Soc.* **1960**, 2851.
T. G. Bonner, E. J. Bourne, S. McNally, *J. Chem. Soc.* **1960**, 2929.
S. D. Géro, *Tetrahedron Lett.* **1966**, 591.