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THE CONDENSATION OF METHYL KETONES WITH FURAN

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In its reaction with certain dienophiles, furan, like pyrrole, does not undergo the typical Diels-Alder addition. Pyrrole reacts with maleic anhydride to form 2-pyrrolesuccinic acid (1). Likewise, furan reacts with acrolein (in the presence of sulfur dioxide) yielding 3-furylpropanal and 2,5-furandipropanal (2). Acid catalysts (including sulfuric and hydrochloric acids) are effective in the addition of furan to 3-buten-2-one yielding 2,5-*bis*(3-oxobutyl)furan. The same ketone with 2-methylfuran yields 4-(5-methylfuryl)-2-butanone (3).

Addition to carbon-oxygen unsaturation also occurs. Chloral reacts with furan to form 1-furyl-2,2,2-trichloroethanol (4). Likewise, reaction of furfuryl alcohol with methanal yields polymeric 2,5-furandimethanol (5) and diethyl 5,5′-methylene*bis*(2-furoate) is obtained from ethyl 2-furoate and methanal (6). The success of these methylolation reactions shows that furans should undergo the Mannich condensation. Holdren (7) prepared substances such as 5-(N-morpholinomethyl)furfuryl alcohol by this method.

In view of these reactions we were not surprised to find that furan reacts with some methyl ketones in the presence of hydrochloric acid, but the products which we obtained were unexpected. Although neither acetophenone nor pinacolone reacts, five other methyl ketones form high molecular weight condensation products with furan. These condensation products, which are listed in Table I, are called anhydrotetramers because the analytical data show that they contain four units each of furan and ketone minus four units of water. Alternatively, the anhydrotetramers may be formed either from one equivalent each of ketone and a substituted 2,2′-methylene*bis*(5-furfurylfuran) (VI) or from two equivalents each of ketone and a substituted difurylmethane. Since these compounds have been found in the reaction system from furan and a ketone it is probable that they are the progenitors of the anhydrotetramer in each instance.

The progenitor which has been isolated from the reaction of butanone and furan is 2,2-difurylbutane (II; R = Me,R_1 = Et) according to its chemical analysis and properties; it is oxidized to ethylmethylmalonic acid. The 2,2-difurylpropane (II. R,R_1 = Me) from acetone and furan has been investigated more thoroughly. Analysis and chemical properties confirm the proposed structure; oxidation with alkaline permanganate yields dimethylmalonic acid, while nitration typical for furans yields 2,2-*bis*(5-nitrofuryl)propane. Furthermore, II (R,R_1 = Me) has been synthesized by stepwise condensation of 2-furyl-2-propanol with furan.

The condensation of acetone with furan is typical of the other ketones. The yields of 2,2-difurylpropane (II; R,R_1 = Me) and the anhydrotetramer (V; R,R_1,R_2 = Me) vary according to the furan:acetone ratio. Additionally, a low-melting solid, thought to be 2,5-*bis*(dimethylfurfuryl)furan (III; R,R_1 = Me)

TABLE I

ANHYDROTETRAMERS OF 2-FURYL-2-ALKANOLS

Ketone	Product							
	m.p., °C.	Yield, %	M.W. Found	Mol. Formula (M.W.)	Analysis			
					Calc'd		Found	
					C	H	C	H
Acetone	243	18.5	423	$C_{28}H_{32}O_4$ (432)	77.78	7.46	78.14	7.57
Butanone	174	11.5	473	$C_{32}H_{40}O_4$ (488)	78.56	8.25	78.58	8.24
Methyl *n*-propyl ketone	148	5.5	502	$C_{36}H_{48}O_4$ (544)	79.38	8.86	79.30	8.62
Methyl isobutyl ketone	241	6.3	—	$C_{40}H_{56}O_4$ (600)	79.95	9.39	80.04	9.46
Methyl *n*-amyl ketone	198	6.1	589	$C_{44}H_{64}O_4$ (656)	80.46	9.82	80.60	9.69
Pinacolone	No reaction							
Acetophenone	No reaction							

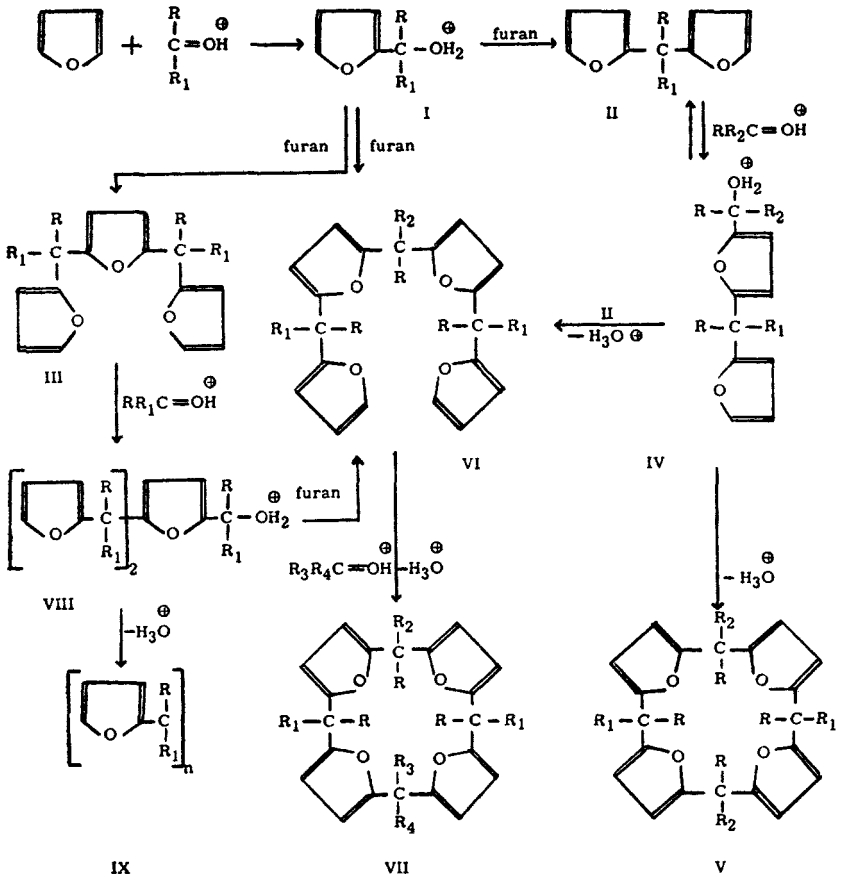
TABLE II

EFFECT OF MOLECULAR RATIO OF FURAN:ACETONE ON YIELD OF II, III, AND V

Molecular Ratio Furan: Acetone	Yield, %		
	II	III	V
1:5	0.0	0.0	18.5
1:2	.0	.0	18.0
1:1	.0	32	2.5
2:1	20.5	27	1.0

is found among the products. Variation in yield of these three products with respect to the ratio is shown in Table II, but the percentages should not be construed as indicative of the complete reaction systems. The low yields may partly be accounted for by unavoidable evaporation and by ring fission of furan, when it is in excess, and by formation of substances like mesityl oxide when the acetone is in excess. However, another diversion of reagents from formation of II, III, and V is found in the presence of viscous oils such as the one remaining after II and III are distilled from the system prepared from furan and acetone. This residue probably consists of polymeric material IX; (R,R_1 = Me) where n is so large that the terminal furyl group is not shown. Actually, a small yield of a product boiling higher than III has been isolated which contains an additional polymeric repeating unit according to its analysis and chemical reactions. This 2,2′-isopropylidene*bis* [5-(dimethylfurfuryl)furan] (VI; R,R_1,R_2 = Me) might be thought to form from III and protonated acetone *via* VIII and furan, but there is no positive evidence for this mechanism.

Presumably 2,2-difurylpropane (II; R,R_1 = Me) is formed from one equiva-



lent each of furan and the conjugate acid (I; R,R_1 = Me) of 2-furyl-2-propanol, obtained either by protonation of the alcohol or else from furan and protonated acetone. It follows then that one equivalent of furan and two of the conjugate acid (I; R,R_1 = Me) should lead to 2,5-*bis*(dimethylfurfuryl)furan (III; R,R_1 = Me).

The composition of the anhydrotetramers (Table I) indicates that they should each be obtainable by loss of two equivalents of water from the addition product of a ketone and the difurylalkane derived from it. This condensation has been effected when acetone and 2,2-difurylpropane (II; R,R_1 = Me) are treated with hydrochloric acid. It may be assumed that this reaction proceeds *via* the protonated addition product IV (R,R_1,R_2 = Me) which then condenses to the anhydrodimer of IV (anhydrotetramer of I) with loss of two equivalents of hydronium ion.

It is apparent that anhydrotetramers should also be formed by treatment of 2,2′-isopropylidene*bis*[5-(dimethylfurfuryl)furan] (VI; R,R_1,R_2 = Me) with a protonated ketone if hydronium ion is eliminated. Indeed the anhydrotetramer VII (R,R_1,R_2,R_3,R_4 = Me), identical with that obtained from furan or from

II with acetone and hydrochloric acid is obtained when VI is treated with the same reagents. Furthermore, VI must react as a unit and not by reversion to its constituent parts. The integrity of VI is demonstrated by treating it with either butanone (to give VII; R,R_1,R_2,R_3 = Me; R_4 = Et) or 3-pentanone (to give VII; R,R_1,R_2 = Me; R_3,R_4 = Et). A mixture of products, which would be expected if VI decomposed to furan and acetone, is not apparent. Actually, the crude melting point of the mixed anhydrotetramer from 3-pentanone differs by only a few degrees from that of the purified product. Reaction of VI with benzaldehyde, methanal, ethanal, and propanal also occurs but the products have not yet been purified.

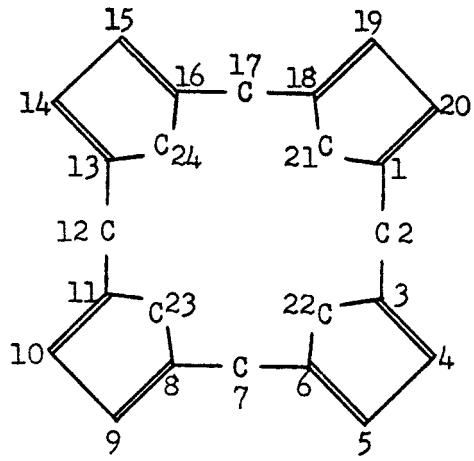
The elimination of hydronium ion during formation of the anhydrotetramers may occur in two ways. Firstly, a linear condensation polymer may be formed which is terminated by an alkene linkage. Secondly, a cyclic anhydrotetramer (V or VII) analogous with a porphyrinogen (9) would be obtained if the final condensation involved ring closure.

The anhydrotetramers from furan and ketones seem to have the porphyrinogen type of structure. The reaction is analogous with that of Rothemund (10) who obtained a low yield of porphyrin from pyrrole and menthanal. Likewise, Calvin, *et al.* (11–13) have found that benzaldehyde reacts with pyrrole to give tetraphenylporphyrin and its dihydroanalog in 4–11% yield.

It is unfortunate that a name for the anhydrotetramers can not be derived by analogy with the porphyrinogens. Such a derivation seems to be impossible since no syllable in the latter term expresses the presence of the pyrrole nucleus. Since we anticipate that anhydrotetramers will be prepared containing ring systems other than that of furan we are reluctant to name the anhydrotetramers as furan derivatives. Therefore, we suggest the name "Quaterene" to describe a closed system of four methylene-bridged 1,4-disubstituted cyclopentadienes. The nucleus is numbered as shown in the accompanying diagram. Thus, the anhydrotetramer V (R,R_1,R_2 = Me) becomes 2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetroxaquaterene. If, in future, an anhydrotetramer were to be synthesized from three thiophene and one furan intermediates involving butanone the compound would be 2,7,12,17-tetraethyl-2,7,12,17-tetramethyl-21-oxa-22,23,24-trithiaquaterene. Of course the establishment of this name must require more rigorous proof than that of analogical similarity with the porphyrinogens.

The cyclic structure of the tetroxaquaterenes has been demonstrated by treatment either of 2,2-difurylpropane (II; R,R_1 = Me) with butanone or, alternatively, of 2,2-difurylbutane (II; R = Me, R_1 = Et) with acetone. If the condensations gave linear anhydrotetramers of I then these alternatives would lead to two products, differing according to whether the terminal groups were isopropenyl or isobutenyl. On the other hand, the two alternatives would give only one structural entity (V; R,R_1 = Me; R_2 = Et) if it were cyclic. Actually, the products from the alternative reactions are identical and uncontaminated with the products listed in Table I.

Although V can not be structurally isomeric in the organic chemical sense of

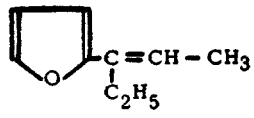


QUATERENE NUCLEUS

this term it may be seen that two geometrical isomers should exist when R and R_1 are methyl while R_2 is ethyl. Examination of the products has shown that these isomers are present in the ratio of 1 to 8. Surprisingly, the isomer in preponderance, which might be expected to have the *trans-* configuration, melts lower (178°) than the minimal geoisomer (m.p. 204°). Despite this disparity in respect of melting points the isomer melting at 178° evidently is the *trans-* form since its electric moment is zero. On the other hand, the isomer melting at 204° shows a moment in benzene solution of 0.77D. This value is approximately that expected if methyl groups were on one side, and ethyl groups on the other side of the plane defining the resultant of atoms in this quaterene.

In view of these results one might expect that each of the quaterenes except the first one listed in Table I would exist as four geoisomers. However, only one form of each has been isolated. A search for other isomers is being made. In view of the alternate formation of the quaterenes by paths shown to lead to V or VII the search is important. The existence of only one form might imply that the path to V is most favorable because of a configurational influence compelling the two enantiomers of one of the diastereomeric forms of IV to combine preferentially with one another.

When 2,5-*bis*(dimethylfurfuryl)furan (III; R,R_1 = Me) is treated with acetone and hydrochloric acid the protonated addition product VIII (R,R_1 = Me) seems to combine with itself, because a definite crystalline product (m.p. 177°) and an indefinite product (m.p. 112–118°) are obtained which are distinct from V (R,R_1,R_2 = Me). The observed molecular weight of the indefinite product (at least 800–900) probably designates it as a linear anhydropolymer. The definite crystallinity of the minor product together with its analysis and molecular weight (650) suggests that it may be the cyclic anhydrohexamer, IX (R,R_1 = Me n = 6). While this does not preclude the possibility that VI is formed from III under the conditions of concentration used with furan and acetone it is also



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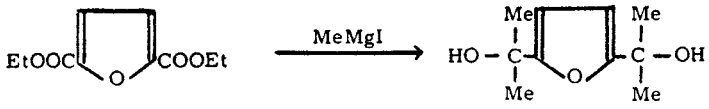

XI XII

possible that VI arises preferentially from II *via* the supposed intermediate IV (R, R_1, R_2 = Me). These questions may be answered by the study of geometric isomerism mentioned above.

The reactions of furans with methyl ketones have been described in this report as metathetical reactions of the conjugate protonic acids of intermediate tertiary alcohols, but they might also have been described as transformations of carbonium ions (liberating protons) or as interadditions of alkenes. It is of interest in this connection to observe that the quaterene type reported here is probably not entirely new.

When Hale, McNally, and Pater (14) treated ethyl furoate with ethyl iodide Grignard reagent they obtained, instead of the expected tertiary alcohol, 3-furyl-3-pentanol, a compound melting at 249° which they designated as 3-furyl-2-pentene (X). They did not report a molecular weight determination. We have repeated their preparation and find, by molecular weight determination, that the product is a tetramer of X. In consideration of the structure proofs for V it is probable that $(X)_4$ is 2,2,7,7,12,12,17,17-octaethyl-21,22,23,24-tetroxaquaterene. This result is of further interest because we have been unable to effect the synthesis of $(X)_4$ by reaction of furan with 3-pentanone and hydrochloric acid. Instead an oil is formed which has not been characterized. Thus far, we have been able to prepare quaterenes only from methyl ketones when furan is the other reagent.

The intermediates in our condensations have been assumed to be protonated tertiary alcohols but the conjugate acid of a di-*tert*-alcohol is not entirely excluded by our facts. However, the alternative is improbable. We have synthesized 2,5-diisopropylolfuran (XII) from methyl iodide Grignard reagent and diethyl 2,5-furandicarboxylate (XI), prepared by an improved synthesis (15). When XII is treated with furan and hydrochloric acid only resins are formed.

We are grateful to du Pont of Canada for generous supplies of furan and to the Science Service Laboratories, London, Ontario, for infrared spectrograms. We acknowledge technical aid from Misses G. Chisholm and L. Schlomer.

EXPERIMENTAL

All melting points have been corrected against reliable standards. Molecular weights were determined by the Rast method. X-ray diffraction data are recorded as relative intensities I/I_1 at spacings in Å using CuK_α radiation, nickel filtered.

2,2-Difurylpropane. II (*R*, R_1 = *Me*) *from furan and acetone.* In a three-necked 2-l. flask, fitted with a reflux condenser and stirrer were placed 340 g. (5.0 moles) of furan, 150 ml. of commerical absolute ethanol, and 100 ml. of 37% hydrochloric acid solution. To this mixture was added dropwise while stirring, 146 g. (2.5 moles) of acetone. The addition of acetone was complete after 35 minutes. No heat was evolved but the reaction mixture slowly took on a reddish tinge. Stirring was continued for 18 hours at 25°. When stirring was discontinued the mixture separated into two phases. The upper pink aqueous phase was separated from the lower orange organic phase. The organic phase was washed with 5% aqueous sodium bicarbonate until neutral, dried over magnesium sulfate, and fractionally distilled under diminished pressure.

The first fraction was a colorless oil boiling at 73–76°/5–6 mm. It weighed 90.4 g. (20.5%) and had n_D^{20} 1.4966, d_4^{20} 1.043. MR_D Calc'd: 51.16. Found: 49.43. m.p. −12°.

Anal. Calc'd for $C_{11}H_{12}O_2$: C, 74.0; H, 6.87; Mol. wt., 176.

Found: C, 74.9; H, 7.09; Mol. wt., 189.

2,5-bis (Dimethylfurfuryl) furan. III (*R*,R_1 = *Me*). A second fraction from the preceding distillation boiled at 120–123°/1 mm. It was a colorless liquid weighing 97.8 g. (27%) which crystallized in the receiver, m.p. 47.0–47.5°.

Crystallization from absolute methanol did not improve the melting point.

Anal. Calc'd for $C_{18}H_{20}O_2$: C, 76.1; H, 7.09; Mol. wt., 284.

Found: C, 75.8; H, 6.94; Mol. wt., 285.

2,2'-Isopropylidenebis [5-(dimethylfurfuryl)furan]. VI (*R*,R_1,R_2 = *Me*). A third fraction from the preceding distillation boiled at 163–167°/1 mm. The product was a viscous pale yellow oil which weighed 24.1 g. (7.5%). n_D^{20} 1.5172, d_4^{20} 1.030, MR_D Calc'd: 116.1; Found: 115.1.

Anal. Calc'd for $C_{25}H_{28}O_4$: C, 76.5; H, 7.19; Mol. wt., 392.

Found: C, 76.4; H, 7.26; Mol. wt., 418.

2,2,7,7,12,12,17,17-Octamethyl-21,22,23,24-tetroxaquaterene. V (*R*,R_1,R_2 = *Me*). (a) *From 2,2-difurylpropane and acetone.* When 1.33 g. (0.0076 mole) of 2,2-difurylpropane was dissolved in 10 ml. of commercial absolute ethanol and treated with 0.44 g. (0.0076 mole) of acetone and 3 ml. of 37% hydrochloric acid a clear solution resulted. After 15 minutes the solution became cloudy. Within three hours crystals began to form. After standing for 13 days the crystals were filtered off, and washed with 10 ml. of absolute ethanol to free them from oily impurities, leaving 1.06 g. (65%) of crude product, m.p. 155–225°. Crystallization from benzene (25 ml./g.) gave 0.60 g. (37.5%) of small white rectangles m.p. 243°. X-ray pattern: [10] 6.19; [4] 3.22; [3] 11.0, 4.74, 4.33; [2] 9.40, 5.05, 4.47, 2.46, 1.99. Electric moment in benzene, zero, since $P_\infty = P_{e+a}$ (calc'd) = 119.8 ± 0.2.

Anal. Calc'd for $C_{28}H_{32}O_4$: C, 77.8; H, 7.46; Mol. wt., 432.

Found: C, 78.1; H, 7.57; Mol. wt., 423.

(b) *From 2,2'-isopropylidenebis [5-(dimethylfurfuryl)furan].* VI (*R*,R_1,R_2 = *Me*). When 1.0 g. (0.0025 mole) of VI (R,R_1,R_2 = Me) and 1.6 g. (0.025 mole) of acetone were dissolved in 5 ml. of commercial absolute ethanol and about 20 ml. of dry hydrogen chloride gas was bubbled in, the solution turned pale red in color. Within 15 minutes a white granular solid began to precipitate. After standing for 22 hours the mixture was filtered and the residue was washed with 5 ml. of absolute ethanol. There remained on the filter 0.89 g. (82%) of crude, m.p. 220–235°. Crystallization from benzene gave 0.57 g. (53%) of white rectangles, m.p. 243°. A mixture melting point with V (R,R_1,R_2 = Me), described in the preceding experiment, was not depressed.

Oxidation of 2,2-difurylpropane. II (*R*,R_1 = *Me*). When 1.76 g. (0.01 mole) of 2,2-difurylpropane was stirred with 15.8 g. (0.10 mole) of potassium permanganate dissolved in 225 ml.

of water, heat was evolved over a period of two hours. Stirring was continued for another 21 hours at room temperature. At the end of this time all the permanganate had been consumed. After filtering off the manganese dioxide, the filtrate was acidified with hydrochloric acid and continuously extracted with 100 ml. of ether for 26 hours. The ether solution was dried over sodium sulfate. After flashing off the ether there remained 0.73 g. (55%) of white granular solid, m.p. 187–189°. Crystallization from ether-benzene solution gave beautiful rhombs, m.p. 192.5–193.0°. A mixture melting point with authentic dimethylmalonic acid showed no depression.

2,2-bis(5-Nitrofuryl)propane. A solution of 1.76 g. (0.01 mole) of 2,2-difurylpropane in 4 ml. of acetic anhydride, chilled to 0°, was added dropwise over a period of eight minutes to a stirred solution of 6 ml. of 93% nitric acid in 10 ml. of acetic anhydride. The nitrating mixture was maintained at −5° throughout the addition and for 45 minutes thereafter. Only slight evolution of oxides of nitrogen occurred during the reaction, indicating very little oxidation. The reaction mixture then was poured onto 75 g. of chipped ice. An orange-colored oil separated, which slowly changed to a mushy solid on standing for 3½ hours at room temperature. This material was washed with 50 ml. of water and then with 50 ml. of 5% aqueous sodium bicarbonate solution. Crystallization from methanol (30 ml./g.) yielded 0.66 g. (25%) of pale yellow plates, m.p. 133–135°. A second crystallization from methanol including treatment with decolorizing charcoal (Norit A) gave yellow plates, m.p. 135.0–135.5°.

Anal. Calc'd for $C_{11}H_{10}N_2O_6$ (266.21): C, 49.6; H, 3.78; N, 10.53.
Found: C, 50.0; H, 3.85; N, 10.33.

Anhydrohexamer of 2-furyl-2-propanol. IX ($R,R_1 = Me; n = 6$). When 2.84 g. (0.0088 mole) of 2,5-*bis*(dimethylfurfuryl)furan was dissolved in 25 ml. of acetone and 5 ml. of 37% hydrochloric acid, two phases separated within five minutes. The mixture was stirred at room temperature for 14 hours. At the end of this time a white solid, weighing 0.86 g. and melting at 100–102°, had separated. The solid, when crystallized from acetone, melted at 112–118°. Subsequent crystallization did not improve its melting point. Its molecular weight was of the order of 800–900.

When the acetone was evaporated from the filtrate, needles, mixed with an oil, resulted. Crystallization from acetone yielded 0.25 g. (8.8%) of white needles m.p. 177°. A second crystallization from acetone did not raise the melting point but the crystal habit changed to rhombs. Crystallization from acetone-methanol again gave needles of the same melting point.

Anal. Calc'd for $C_{42}H_{48}O_6$: C, 77.8; H, 7.46; Mol. wt., 649.
Found: C, 78.0; H, 7.62; Mol. wt., 650.

2,2-Difurylpropane from 2-furyl-2-propanol and furan. When 20.0 g. (0.159 mole) of 2-furyl-2-propanol was treated with 1.5 ml. of 37% hydrochloric acid, heat was evolved and a white solid formed. After cooling, the mixture was treated with 10.8 g. (0.159 mole) of furan. The mixture was stirred at room temperature for two hours, during which time the solid disappeared. After neutralizing with solid sodium carbonate, the reaction product was extracted with ether. The ether extract was dried over sodium sulfate. After flashing off the ether, 10.22 g. (36.5%) of a colorless oil, b.p. 85–90° at 13 mm. was obtained. This oil was shown to be 2,2-difurylpropane by its physical constants and by oxidation with permanganate to dimethylmalonic acid.

2,2-Difurylbutane. A solution containing 68 g. (1.0 mole) of furan and 36 g. (0.50 mole) of butanone in 30 ml. of commercial absolute ethanol was treated with 60 ml. of 37% hydrochloric acid solution. The mixture was stirred for seven hours. Heat was evolved over the whole period and the mixture became cherry-red. The resulting two phase system was diluted with 500 ml. of water and neutralized with solid sodium carbonate. The mixture was steam-distilled and the resulting oil was taken up in ether. After drying the ether solution over magnesium sulfate, the ether was flashed off. The residual pale yellow oil distilled between 68–70° at 2 mm. The product, a colorless oil, weighed 15.6 g. (15%), n_D^{20} 1.4970, d_4^{20} 1.033.

Anal. Calc'd for $C_{12}H_{14}O_2$: C, 75.8; H, 7.37; Mol. wt., 190.
Found: C, 75.4; H, 7.37; Mol. wt., 187.

2,7,12,17-Tetraethyl-2,7,12,17-tetramethyl-21,22,23,24-tetroxaquaterene. V (R = *Me*; R_1,R_2 = *Et*). A solution of 1.0 g. (0.0052 mole) of 2,2-difurylbutane and 3.0 g. (0.033 mole) of butanone in 10 ml. of commercial absolute ethanol was treated with dry hydrogen chloride gas. Within two minutes a white precipitate appeared. After five minutes the reaction was stopped and the precipitate was filtered off. Crystallization from ethanol gave 0.45 g. (37%) of white needles, m.p. 174°. This condensation may also be carried out using 37% hydrochloric acid solution.

Anal. Calc'd for $C_{22}H_{40}O_4$: C, 78.6; H, 8.25; Mol. wt., 488.
Found: C, 78.6; H, 8.24; Mol. wt., 473.

2,12-Diethyl-2,7,7,12,17,17-hexamethyl-21,22,23,24-tetroxaquaterene. V (R,R_1 = *Me*; R_2 = *Et*) (a) *From 2,2-difurylpropane and butanone.* A solution of 1.76 g. (0.010 mole) of 2,2-difurylpropane and 1.44 g. (0.020 mole) of butanone in 10 ml. of commercial absolute ethanol was treated with 3 ml. of 37% hydrochloric acid. A clear solution resulted. Upon standing for six hours at 25° an oil separated. White needles began forming in this oil after another 17 hours. When two days had elapsed the mixture was filtered and the remaining oil was expressed from the white solid which weighed 0.22 g. but was too sticky for a melting point determination. The expressed oil was returned to the filtrate from the original reaction mixture and after another five days an additional 0.40 g. of white needles was obtained. When the combined crude products were successively leached with 15-ml. portions of boiling methanol five fractions were obtained of which the first three, 0.32 g., melted at 178–179°; the fourth, 0.07 g. melted at 178–183°; while the fifth fraction, 0.03 g., melted at 202.0–202.5°. Further crystallization from methanol and methanol-acetone solutions gave two pure products, one melting at 178.5° and the other at 204° in the ratio of about 8:1.

trans- V, m.p. 178.5°.

Anal. Calc'd for $C_{30}H_{36}O_4$: C, 78.2; H, 7.88; Mol. wt., 461.
Found: C, 78.7; H, 8.03; Mol. wt., 457.

cis- V, m.p. 204°.

Anal. Calc'd for $C_{30}H_{36}O_4$: C, 78.2; H, 7.88; Mol. wt., 461.
Found: C, 78.5; H, 7.85; Mol. wt., 450.

(b) *From 2,2-difurylbutane and acetone.* A solution of 97.7 g. (0.51 mole) of 2,2-difurylbutane and 60 g. (1.02 moles) of acetone (purified with potassium permanganate) in 750 ml. of commercial absolute ethanol was treated with 162 ml. of 37% hydrochloric acid. A clear solution resulted. After standing for nine days at room temperature the resulting crystalline solid was filtered off and washed with 200 ml. of absolute ethanol. The crude weighed 33.0 g. (28%), m.p. 172–181°. The combined filtrate and washings were set aside and after another six days a further crop of crystals weighing 11.4 g. and melting at 175–185° was obtained. A third crop of crystals weighing 6.3 g. and melting at 172–185° was obtained after a further eight days. The over-all yield was 50.7 g. (43%). After treating the remaining reaction mixture, from which the crystalline product had been removed, with water, 40.5 g. of a mixture of a thick oil and crystals was recovered, from which more product undoubtedly could have been obtained.

From the 50.7 g. of crude product there was separated, by means of boiling methanol leaches, 1.9 g. of a compound melting at 204° and 8.3 g. of a compound melting at 178.5°. The remainder was left as a mixture of the two isomers.

A mixture melting point of this compound melting at 204° with the compound melting at 204°, described in the preceding experiment, was not depressed. Both samples, m.p. 204°, gave identical X-ray patterns: [10] 10.39, 5.73; [9] 4.69, 4.11; [7] 5.16, 3.90 [6] 6.21. Similarly a mixture melting point of this compound melting at 178.5° with the compound melting at 178.5° described in the preceding experiment was not depressed. Again both samples, m.p. 178.5°, gave identical X-ray patterns: [10] 10.04, 5.79, 4.99, 4.50; [8] 3.50.

Both isomers (*cis* and *trans*) in carbon tetrachloride or carbon disulfide solution (20%)

gave indistinguishable infrared absorption spectra (cell thickness 0.5 mm.), the principal bands of which are shown as follows:

Wave No., cm.$^{-1}$ and Transmittance, %					
cm.$^{-1}$	%	cm.$^{-1}$	%	cm.$^{-1}$	%
3100	83	1383	40	1112	25
2970	15	1375	56	1100	35
2930	30	1300	74	1020	12
2870	48	1265	54	957	25
1657	77	1241	63	777	5
1600	82	1210	32	730	60
1548	83	1158	24	712	62
1465	46	1130	55	670	84

The identity of these spectra is surprising in view of the difference in electric moments described below. Actually, slight differences are apparent in the spectra obtained from mulls or from potassium chloride pellets. Thus absorption at 707 cm^{-1} is observed in the compound melting at 204° but not in that melting at 178°. Furthermore, the transmittance at 780 cm^{-1} for the latter compound is shifted to 770 cm^{-1} in the spectrum of the higher-melting isomer. Of course these differences may be due to crystal form.

Electric moments of compounds melting at 178.5° and 204°. The total polarizations, P_∞, of the two compounds were determined on a heterodyne beat frequency oscillator apparatus in benzene solution (16). Since difficulty was encountered in pelleting the compound melting at 178.5°, the values for P_{e+a} could not be determined directly but, instead, were calculated from atomic refraction data. The electric moments were calculated from the equation:

$$\mu = 0.01281 \times 10^{-18} [(P_\infty - R_D)T]^{\frac{1}{2}}$$
$$= 0.00D \text{ for the compound m.p. } 178.5°$$
$$= 0.77D \text{ for the compound m.p. } 204°$$

17-Ethyl-2,2,7,7,12,12,17-heptamethyl-21,22,23,24-tetroxaquaterene. VII (R,R_1,R_2,R_3 = *Me;* R_4 = *Et*). A solution of 1.0 g. (0.0025 mole) of 2,2′-isopropylidene*bis*-[5-(dimethylfurfuryl)furan] (VI) and 1.6 g. (0.022 mole) of butanone in 10 ml. of commercial absolute ethanol was treated with 25 ml. of dry gaseous hydrogen chloride. Within one hour fine needles began to separate. After 22 hours the crystalline product was filtered off and washed with 5 ml. of absolute ethanol. The crude product weighed 0.83 g. (74%) m.p. 185–193°. Crystallization from absolute ethanol (60 ml./g.) gave 0.58 g. (52%) of coarse shiny needles, m.p. 195.0–195.5°.

Anal. Calc'd for $C_{29}H_{34}O_3$: C, 78.0; H, 7.67; Mol. wt., 446.
Found: C, 77.8; H, 7.67; Mol. wt., 450.

17,17-Diethyl-2,2,7,7,12,12-hexamethyl-21,22,23,24-tetroxaquaterene. VII (R,R_1,R_2 = *Me;* R_3,R_4 = *Et*). A solution of 1.0 g. (0.0025 mole) of VI (R,R_1,R_2 = Me) and 1.6 g. (0.019 mole) of 3-pentanone (E.K. 1330) in 10 ml. of commercial absolute ethanol was treated with 25 ml. of dry gaseous hydrogen chloride. Within 20 minutes fine white needles began to separate. After 19 hours the crystals were filtered off and washed with 3 ml. of absolute ethanol. The crude product, 0.70 g. (61%) m.p. 204–206°, was crystallized from absolute ethanol (115 ml./g.) giving 0.54 g. (47%) of very fine white needles m.p. 209.0–209.5°.

Anal. Calc'd for $C_{30}H_{36}O_4$: C, 78.2; H, 7.88; Mol. wt., 461.
Found: C, 78.6; H, 7.65; Mol. wt., 477.

2,5-Furandicarboxylic acid. A mixture of 200 g. (0.95 mole) of mucic acid (Pfanstiehl C.P.) and 100 g. of 96% sulfuric acid was placed in a two liter three-necked balloon flask and heated externally with an oil-bath. After 20 minutes the temperature of the mixture reached 128°, sulfur dioxide was evolved, and the temperature rose rapidly to 155°. The contents of the flask were cooled to 130° and maintained at this temperature for another 20 minutes. The mixture by this time was black. After cooling to room temperature the black

mass was treated with 800 ml. of water, and warmed for ten minutes on the steam-bath while stirring. After standing for a day at room temperature the mixture was filtered and the filtrate was discarded. The filter cake was treated with 3200 ml. of boiling water and sufficient barium hydroxide was added to render the mixture alkaline. The mixture then was filtered while hot, using Celite on the filter. The cake was finally washed with 200 ml. of hot water containing one per cent barium hydroxide. The combined filtrates were cooled to room temperature and acidified with hydrochloric acid. After standing overnight the precipitated crude 2,5-furandicarboxylic acid was filtered off and dissolved in 1200 ml. of water containing sufficient ammonia to render the final solution alkaline. This straw-colored solution was treated with 6 g. of decolorizing charcoal (Norit), heated to boiling, and filtered through a 3-mm.—deep bed of Celite on the Büchner. The pale yellow filtrate was cooled to 25° and acidified with hydrochloric acid. After standing for two hours the white 2,5-furandicarboxylic acid was filtered off and dried to a constant weight of 41 g. (27.6%).

2,5-Diisopropylolfuran. XII. An ether solution of 0.25 mole of methylmagnesium iodide was prepared in the usual manner. To this solution, cooled by means of an ice-salt bath, was added dropwise 10.6 g. (0.05 mole) of diethyl 2,5-furandicarboxylate dissolved in 30 ml. of dry ether. During the addition the reaction mixture was stirred vigorously. After the addition was completed, the reaction mixture was stirred for 1½ hours and then stored in the refrigerator overnight. The resulting yellow mixture was decomposed by pouring onto 150 g. of chipped ice and then carefully acidifying with 25% acetic acid solution. The resulting pale yellow solution was continuously extracted with ether for 24 hours. The resulting ether extract was dried over potassium carbonate and the ether was flashed off leaving a thick golden yellow oil. This oil distilled at 95–115° at 2 mm. The distillate, a very pale yellow oil which weighed 5.2 g. (56%) crystallized in the receiver. Crystallization from hexane gave 2.7 g. (40%) of white needles, m.p. 70–71°. The compound is readily soluble in water.

Anal. Calc'd for $C_{10}H_{16}O_2$: C, 65.2; H, 8.76.

Found: C, 65.0; H, 8.75.

Attempted condensation of 2,5-diisopropylolfuran (XII) *with furan.* When a solution of 0.92 g. (0.005 mole) of 2,5-diisopropylolfuran in 10 ml. of commercial absolute ethanol was treated with 0.34 g. (0.005 mole) of furan at room temperature there was no sign of reaction. However, when 0.5 ml. of 37% hydrochloric acid was added to the solution a turquoise green color developed immediately and within seven minutes an orange precipitate began to settle out. After 24 hours 0.64 g. of orange resin of indefinite melting point was obtained. Attempts to isolate a definite compound from the resin by fractional crystallization failed. The same type of resin was obtained when furan was omitted from the reaction.

3-Furyl-3-pentanol. To 0.10 mole of ethylmagnesium iodide in 75 ml. of anhydrous ether was added slowly a solution of 7.0 g. (0.05 mole) of ethyl furoate in 25 ml. of anhydrous ether. The rate of addition was adjusted so that the ether in the reaction mixture refluxed gently. After the addition was complete the yellowish mixture was stirred at room temperature for an additional 15 hours. The yellow mixture then was poured onto 150 g. of crushed ice and sufficient 25% acetic acid solution added to dissolve the magnesium hydroxide. The ice-cold mixture was extracted twice with 50-ml. portions of ether in addition to the ether already present. The resulting ether solution was washed free from acid with 10% sodium carbonate solution and dried over calcium chloride. When the ether was removed under reduced pressure at room temperature there remained 7.2 g. (96%) of golden yellow oil, presumably crude 3-furyl-3-pentanol.

2,2,7,7,12,12,17,17-Octaethyl-21,22,23,24-tetroxaquaterene. X_4. (14). The crude 3-furyl-3-pentanol was placed in a petri dish in a vacuum desiccator containing phosphorus pentoxide as a desiccant and the pressure was maintained at 15 mm. After seven days at room temperature the oil had been converted to an impure white solid. The white solid was purified by crystallization from ethyl acetate, giving a final yield of 0.70 g. (11%) of white rhombs m.p. 249–250°, mol. wt. calc'd, 545; found, 544. It is interesting to note that the compound undergoes a transition from needles to rhombs during the process of crystalli-

zation. This phenomenon was also noted in the case of 2,2,7,7,12,12,17,17-octamethyl-21,22,23,24-tetroxaquaterene.

SUMMARY

1. Polycondensation occurs when furan and some methyl ketones are treated with hydrochloric acid. Typically with acetone the products are (a) 2,2-difurylpropane, (b) 2,5-*bis*(dimethylfurfuryl)furan, (c) 2,2′-isopropylidene*bis*[5-(dimethylfurfuryl)furan], and (d) an anhydrotetramer of 2-furyl-2-propanol as well as some higher polymer. The ratio of product yields may be altered by the ratio of reagents used.

2. The anhydrotetramers have been shown to be cyclic since when one is prepared from a symmetriacl difurylalkane and an unsymmetrical ketone (or *vice versa*) the same two products are formed. These products are *cis*- and *trans*- geoisomers with electric moments of 0.77D and zero respectively. These cyclic anhydrotetramers have been generally named tetroxaquaterenes.

3. A tetroxaquaterene can not be prepared from 2,5-*bis*(dimethylfurfuryl)-furan and a ketone with hydrochloric acid. Instead, a polymer and what seems to be an anhydrohexamer are obtained.

4. Unsymmetrical tetroxaquaterenes are obtained when 2,2′-isopropylidene-*bis*[5-(dimethylfurfuryl)furan] is treated with aldehydes and ketones. Typical is 17-ethyl-2,2,7,7,12,12,17-heptamethyl-21,22,23,24-tetroxaquaterene from butanone.

5. The dehydration product of 2-furyl-3-pentanol, formerly thought to be an alkene, is probably 2,2,7,7,12,12,17,17-octaethyl-21,22,23,24-tetroxaquaterene.

6. It has been shown that 2,5-diisopropylolfuran is not an intermediate in the condensation of furan with acetone.

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