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Notes

Effects of 5-*tert*-Butyl and 5-Methyl Group Substitution on the Reactivity and Dimerization Products of Furan-Based *o*-Quinodimethanes[1]

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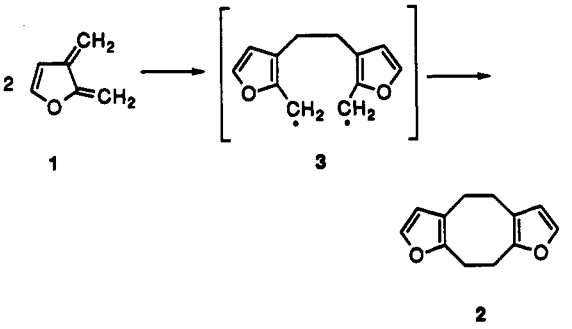
Introduction

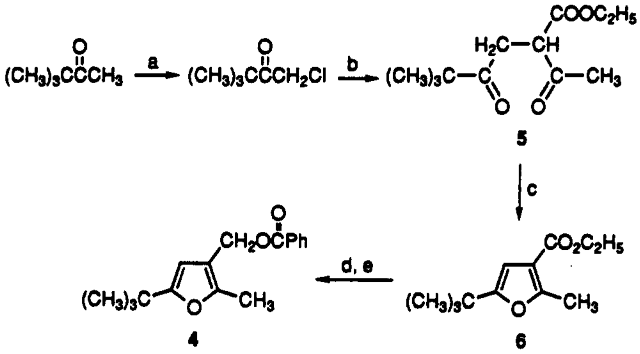
We have proposed that dimerization of the parent furan-based *o*-quinodimethane (*o*-QDM), 1, which gives a high yield of the head-to-head [4 + 4] dimer 2,[2] proceeds by a stepwise mechanism via diradical intermediate 3.[3,4] This mechanism is strongly supported by the results of a secondary deuterium kinetic isotope effect study[3] and by the results of a study of the effects of *tert*-butyl substitution on the ends of the reactive diene system.[4] Also, the observation that the 2-α-methyl furan-based *o*-QDM gives a dimer derived from the proposed diradical intermediate by an intramolecular hydrogen-atom transfer offers further support for the two-step mechanism.[5]



(1)

There are many reasonable relative orientations of the two *o*-QDM moieties in the transition state of the rate-determining first step of the dimerization but these can be divided into two classes: endo orientations, which have the two rings face to face, and exo orientations, which have the two rings away from each other. It is conceivable that the very rapid rate of dimerization of *o*-QDMs results from some special interaction of the π electrons of the two dimerizing monomers which would require an endo orientation. If endo orientations are important, a bulky substituent on the ring should retard the rate of dimerization. In an attempt to probe this point, we have studied the dimerization products and kinetics of the 5-*tert*-butyl furan-based *o*-QDM, and, as a model compound, the 5-methyl derivative. The results of this study are presented and discussed herein.

Scheme 1[a]

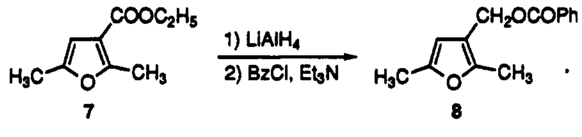


[a] (a) HCl, NaClO$_3$; (b) CH$_3$COCHCO$_2$C$_2$H$_5$$^-Na^+$; (c) 180 °C; (d) LiAlH$_4$; (e) PhCOCl, Et$_3$N.

Results

Synthesis of (2-Methyl-3-furyl)methyl Benzoates. The synthetic route to (5-*tert*-butyl-2-methyl-3-furyl)methyl benzoate (4) is outlined in Scheme 1. 1-Chloro-3,3-dimethyl-2-butanone,[6] obtained from the chlorination of 3,3-dimethyl-2-butanone, was allowed to react with the sodium salt of ethyl acetoacetate to give ethyl 2-(3,3-dimethyl-2-butanoyl)acetoacetate (5). Cyclization of 5, effected by heating to 180 °C, produced 6, which was reduced by lithium aluminum hydride and the resulting alcohol was converted to 4 by treatment with benzoyl chloride and triethylamine.[2]

Ethyl 2,5-dimethyl-3-furoate (7), prepared as described by Dann et al.,[7] was reduced by lithium aluminum hydride and the resulting alcohol was converted to (2,5-dimethyl-3-furyl)methyl benzoate (8) by treatment with benzoyl chloride and triethylamine.[2]



Preparation of 2,3-Bis(methylene)-2,3-dihydrofurans. The furan-based *o*-QDMs 9 and 10 were prepared by the flash vacuum pyrolysis (FVP) of benzoates 4 and 8, respectively. It was found that in order to obtain monomers in good yield it is important to control the temperature of the cooling condenser in addition to the pyrolysis temperature. For example, the FVP of 4 gave 9 as the major product collected in the liquid-nitrogen-cooled trap when the sample head temperature was 100 °C, the pyrolysis temperature was between 540 to 560 °C, and the cooling condenser temperature was between −5 to 0 °C. At higher pyrolysis temperatures some undesired products were also generated, possibly from fragmentation of the *tert*-butyl group of 9. When the temperature of the

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[1] Based on work by C.-H. Chou and T. J. Cassady in partial fulfillment of the requirements for the Ph.D. degree at Iowa State University.

[2] Trahanovsky, W. S.; Cassady, T. J.; Woods, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 6691.

[3] Chou, C.-H.; Trahanovsky, W. S. *J. Am. Chem. Soc.* **1986**, *108*, 4138.

[4] Trahanovsky, W. S.; Huang Y.-c. J; Leung, M.-k. *J. Org. Chem.* Submitted.

[5] Leung, M.-k.; Trahanovsky, W. S. *J. Am. Chem. Soc.* Submitted.

[6] Iimura, F. *Nippon Kagaku Zasshi* **1957**, *78*, 48; *Chem. Abstr*, **1957**, *53*, 5185d. *Beilsteins Handbuch der Organische Chemie, 1*, IV 3313.

[7] Dann, O.; Distler, H.; Merkel, H. *Chem. Ber.* **1952**, *85*, 457.

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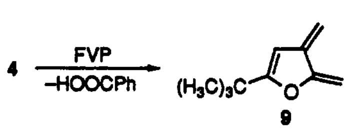

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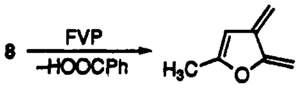

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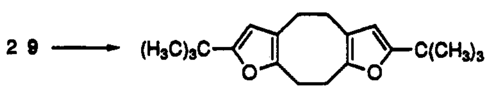
cooling condenser was below -10 °C, much of **9** was trapped by the condenser and eventually polymerized before it could be isolated.

Rate Constants were determined as described previously.[3] The dimerization of **9** gave a high yield of [4 + 4] dimer **11**. The second-order rate constants for the



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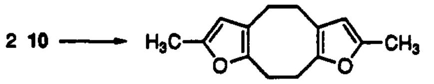
dimerization of **9** at various temperatures are presented in Table 1. The dimerization of **10** gave a high yield of [4 + 4] dimer **12**. The second-order rate constants for the

Table 1. Temperature Dependence of the Rate Constant, k_9, for the [4 + 4] Dimerization of 5-*tert*-Butyl-2,3-bis(methylene)-2,3-dihydrofuran (9)

temp, °C	k_9,[a] L mol^{-1} s^{-1}
−5.0	$(1.300 \pm 0.037) \times 10^{-3}$
−9.0	$(9.219 \pm 0.136) \times 10^{-4}$
−15.0	$(5.071 \pm 0.129) \times 10^{-4}$
−20.0	$(3.209 \pm 0.120) \times 10^{-4}$
−26.0	$(1.880 \pm 0.049) \times 10^{-4}$

[a] Rate constants, k_9, were measured in 1:1 CS_2CDCl_3.



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dimerization of **10** at various temperatures are presented in Table 2.

Table 2. Temperature Dependence of the Rate Constant, k_{10}, for the [4 + 4] Dimerization of 5-Methyl-2,3-bis(methylene)-2,3-dihydrofuran (10)

temp, °C	k_{10},[a] L mol^{-1} s^{-1}
−9.0	$(1.204 \pm 0.034) \times 10^{-3}$
−12.0	$(8.913 \pm 0.275) \times 10^{-4}$
−15.0	$(5.876 \pm 0.147) \times 10^{-4}$
−20.0	$(4.497 \pm 0.118) \times 10^{-4}$
−28.0	$(1.927 \pm 0.052) \times 10^{-4}$
−33.0	$(1.210 \pm 0.016) \times 10^{-4}$
−39.0	$(6.714 \pm 0.163) \times 10^{-5}$

[a] Rate constants, k_{10}, were measured in 1:1 $CS_2/CDCl_3$.

Plots of log k versus $1/T$ for both sets of data were very good and in Table 3 are presented second-order rate constants at −15 °C and the activation parameters for the dimerization of the unsubstituted *o*-QDM **1**, **9**, and **10**.

Table 3. Rate Constants at −15 °C and Activation Parameters for the Dimerization of 1,[a] 9, and 10

o-QDM	k at −15 °C, M^{-1} s^{-1}	ΔH,‡ kcal mol^{-1}	ΔS,‡ cal K^{-1} mol^{-1}
1[a]	$(2.27 \pm 0.17) \times 10^{-3}$	10.2 ± 0.3	-30.9 ± 1.2
9	$(5.27 \pm 0.18) \times 10^{-4}$	11.6 ± 0.3	-29.2 ± 0.9
10	$(6.70 \pm 0.49) \times 10^{-4}$	11.1 ± 0.3	-29.9 ± 1.3

[a] Data from ref 3.

Discussion

The data in Table 3 show that a 5-*tert*-butyl group retards the rate of dimerization of furan-based *o*-QDMs by a small factor, 4.3 at −15 °C. This retardation cannot be explained by a steric effect since the 5-methyl group, a much smaller group but one which models the electronic effects of the *tert*-butyl group, has almost the same effect on the rate of dimerization as the *tert*-butyl group; the ratio of the dimerization rate constant for dimerization of the parent to that of the 5-methyl derivative is 3.4 at −15 °C.

Recent kinetic and product studies are consistent with the proposal that furan-based *o*-QDMs dimerize by a two-step mechanism which involves rate-determining formation of a diradical intermediate followed by rapid cyclization of the diradical (shown in eq 1 for the parent system).[3–5] The comparable effects of the 5-*tert*-butyl and 5-methyl groups indicate that the ring systems of the two *o*-QDM moieties in the transition state of the first step are not close enough to allow the *tert*-butyl groups to interact. These results are consistent with orientations of the two *o*-QDM moieties which have the two rings away from each other, orientations that can be called exo.

The rate of dimerization of benzene-based *o*-QDMs is also only slightly affected by bulky groups on the ring[8] and these results further support the idea that there are not strong ring–ring interactions in the transition state of the rate-determining step of the dimerization of *o*-QDMs.

The Hammett σ values for the *p*-*tert*-butyl and *p*-methyl groups are −0.20 and −0.17, respectively.[9] These values indicate that both groups have comparable, weak electron-donating characteristics. Thus the data in Table 3 show that the rate of dimerization of furan-based *o*-QDMs is slightly retarded by electron-donating substituents. Using 2σ since two monomers are involved in the rate-determining step, a Hammett ρ value of 1.6 would account for the observed rate changes.

Experimental Section

Some general methods have been described previously.[3]

(5-*tert*-Butyl-2-methyl-3-furyl)methyl Benzoate (4). To a stirred solution of 50.0 g (0.499 mol) of 3,3-dimethyl-2-butanone in 125 mL of concentrated hydrochloric acid at 0 °C was added dropwise a solution of 17.75 g (0.167 mol) of sodium chlorate in 50 mL of water. After stirring at 0 °C for 1 h, the reaction mixture was extracted with ether (5 × 50 mL). The combined organic layers was washed with saturated sodium bicarbonate (3 × 50 mL) and water (2 × 50 mL). After the extract was dried and concentrated, distillation of the residue gave 32.80 g (0.244 mol; 48.8%) of 1-chloro-3,3-dimethyl-2-butanone: bp 172–174 °C [lit.[6] bp 170–173 °C]; IR (thin film) 1725, 1470, 1400, 1370, 1060, 1005 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.30 (s, 2 H), 2.24 (s, 9 H).

To a stirred solution of 23.8 g (0.156 mol) of the sodium salt of ethyl acetoacetate and 2.0 g of sodium iodide in 200 mL of acetone was added dropwise 21.0 g (0.156 mol) of 1-chloro-3,3-dimethyl-2-butanone over a 10-min period. The mixture was heated to reflux for 10 h. After removal of the acetone by simple distillation, 120 mL of water was added and the layers were separated. The aqueous layer was extracted with ether (3 × 70 mL). The combined organic layers was washed with saturated

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(8) Trahanovsky, W. S.; Macias, J. R. *J. Am. Chem. Soc.* **1986**, *108*, 6820.

(9) Chapman, N. B.; Shorter, J. *Correlation Analysis in Chemistry*; Plenum Press: New York, 1978; Chapter 10.

sodium chloride (3 × 30 mL) and dried ($MgSO_4$). After removal of the solvent, 25.1 g (0.110 mol; 78%) of crude ethyl 2-(3,3-dimethyl-2-butanoyl)acetoacetate (**5**) was isolated. Ester **5** was heated at 180 °C for 1 h to eliminate a molecule of water and cyclize to form ethyl 5-*tert*-butyl-2-methyl-3-furoate (**6**). The crude product was purified by vacuum distillation to yield 16.03 g (76.2 mmol; 69.3%) of **6**: bp 67–68 °C (0.01 mm); IR (thin film) 1710, 1610, 1584, 1355, 1290, 1245, 1230, 1200, 1105, 1060 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.20 (s, 1 H), 4.27 (q, J = 7.0 Hz, 2 H), 2.55 (s, 2 H), 1.35 (t, J = 7.0 Hz, 3 H), 1.25 (s, 9 H).

To a stirred slurry of 2.73 g (71.8 mmol) of $LiAlH_4$ in 100 mL of dry ether ($LiAlH_4$) at 0 °C was slowly added a solution of 15.10 g (71.8 mmol) of **5** in 50 mL of dry ether. The mixture was stirred at room temperature for 10 h and a standard workup[10] gave 11.46 g (68.1 mmol; 95.4%) of (5-*tert*-butyl-2-methyl-3-furyl)methyl alcohol: bp 60–61 °C (0.01 mm): IR (thin film) 3500, 1630, 1575, 1455, 1355, 1280, 1215, 1180, 1090, 990 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 5.95 (s, 1 H), 4.43 (s, 2 H), 2.25 (s, 3 H), 1.73 (br, 1 H), 1.27 (s, 9 H). Without further purification 8.00 g (47.6 mmol) of the alcohol was converted to **4** using the procedure previously described.[2] The benzoate was purified by column chromatography on silica gel (5% ether in hexanes) followed by distillation, yielding 11.65 g (42.8 mmol; 90%) of **4**: bp 124–125 °C (0.025 mm); IR (thin film) 1715, 1600, 1570, 1450, 1360, 1310, 1260, 1100, 1090, 1060, 1020, cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.3–8.0 (m, 2 H), 7.7–7.3 (m, 3 H), 5.97 (s, 1 H), 5.13 (s, 2 H), 2.34 (s, 3 H), 1.26 (s, 9 H); ^{13}C NMR ($CDCl_3$) δ 166.56, 162.22, 148.68, 132.75, 130.53, 129.66, 128.25, 114.60, 103,77, 58.91, 32.37, 29.06, 11.62; exact mass *m/e* 272.14087, calcd for $C_{17}H_{20}O_3$ 272.14125. Anal. Calcd: C, 74.97; H, 7.41. Found: C, 74.77; H, 7.24.

(2,5-Dimethyl-3-furyl)methyl Benzoate (8). Ethyl 2,5-dimethyl-3-furoate (**7**) was prepared as described[7] in 40% yield: bp 86–88 °C (12 mm) [lit.[7] bp 100–105 °C (12 mm)]; IR (thin film) 1715, 1625, 1595, 1405, 1285, 1235, 1205, 1080 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.26 (s, 1 H), 4.30 (q, J = 7.0 Hz, 2 H), 2.54 (s, 3 H), 2.26 (s, 3 H), 1.36 (t, J = 7.0 Hz, 3 H); exact mass *m/e* 168.07851, calcd for $C_9H_{12}O_3$ 168.07865. To a stirred slurry of 2.26 g (59.5 mmol) of $LiAlH_4$ in 200 mL of dry ether ($LiAlH_4$) at 0 °C was slowly added a solution of 10.0 g (59.5 mmol) of **7** in 50 mL of dry ether. After the mixture was stirred at room temperature for 10 h, a standard workup[10] gave 7.13 g (56.5 mmol; 95%) of (2,5-dimethyl-3-furyl)methyl alcohol: bp 90–91 °C (25 mm); IR (thin film) 3350, 1645, 1590, 1260, 1215, 1000 cm^{-1}; ^{1}H NMR ($CDCl_3$) (δ 5.90 (s, 1 H), 4.37 (s, 2 H), 2.24 (s, 6 H), 1.97 (br, 1 H). Without further purification, the alcohol was converted to benzoate **8** in 92% yield using the method previously described.[2] Purification by column chromatography on silica gel (5% ether in hexanes) followed by distillation yielded 11.4 g (49.4 mmol; 83% isolated yield from ethyl 2,5-dimethyl-3-furoate) of **8**: bp 107–108 °C (0.025 mm); IR (thin film) 1720, 1645, 1610, 1590, 1455, 1275, 1180, 1100, 1070 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.2–7.9 (m, 2 H), 7.7–7.2 (m, 3 H), 5.98 (s, 1 H), 5.10 (s, 2 H), 2.30 (s, 3 H), 2.22 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.50, 149.92, 148.90, 132.75, 130.37, 129.56, 128.20, 115.09, 107.29, 57.70, 13.25, 11.51; exact mass *m/e* 230.09455, calcd for $C_{14}H_{14}O_3$ 230.09430. Anal. Calcd: C, 73.01; H, 6.13. Found: C, 72.82; H, 5.85.

Pyrolysis of (5-*tert*-Butyl-2-methyl-3-furyl)methyl Benzoate (4). For kinetic study, a quantity of about 200 mg (0.735 mmol) of **4** was pyrolyzed each time at 540–560 °C and 10^{-4} Torr with the cooling condenser at −5 to 0 °C. The pyrolysate was collected in 3.0 mL of 1:1 $CS_2/CDCl_3$ and ^{1}H NMR spectral data were recorded at low temperature for **9**: ^{1}H NMR (1:1 $CS_2/CDCl_3$) δ 5.39 (s, 1 H), 5.08 (s, 1 H), 4.75 (m, 2 H), 4.57 (m, 1 H), 1.16 (s, 9 H). Quantitative ^{1}H NMR analysis indicated that pyrolysis of **4** gave 47% yield of **9**, which, in the temperature range of −30 to −5 °C, dimerized quantitatively (>95%) to **11**: mp[11] 122–123 °C; ^{1}H NMR (1:1 $CS_2/CDCl_3$) δ 5.61 (s, 2 H), 2.97 (s, 4 H), 2.69 (s, 4 H), 1.21 (s, 18 H); ^{13}C NMR (1:1 $CS_2/CDCl_3$) δ 161.19, 147.81, 118.12, 105.83, 32.37, 29.22, 25.97, 25.16.

Pyrolysis of (2,5-Dimethyl-3-furyl)methyl Benzoate (8). For kinetic study, a quantity of about 300 mg (1.30 mmol) of **8** was pyrolyzed each time at 610–630 °C and 10^{-4} Torr with the cooling condenser at −5 to 0 °C. The pyrolyzate was collected in 3.0 mL of 1:1 $CS_2/CDCl_3$ and ^{1}H NMR spectral data were recorded at low temperature for **10**: ^{1}H NMR (1:1 $CS_2/CDCl_3$) δ 5.44 (m, 1 H), 5.07 (m, 1 H), 4.75 (m, 2 H), 4.58 (m, 1 H), 2.00 (s, 3 H). Quantitative ^{1}H NMR analysis indicated that pyrolysis of **8** gave a 91% yield of **10**, which, in the temperature range of −40 to -10 °C, dimerized quantitatively (>95%) to **12**: mp[12] 64 °C; IR ($CHCl_3$)[12] 1605, 1570, 1062, 895, 740 cm^{-1}; ^{1}H NMR (1:1 $CS_2/CDCl_3$) δ 5.64 (m, 2 H), 2.97 (s, 4 H), 2.69 (s, 4 H), 2.18 (s, 6 H); ^{13}C NMR (1:1 $CS_2/CDCl_3$) δ 149.01, 148.00, 118.64, 109.40, 25.95, 24.98, 13.35; exact mass[12] *m/e* 216.11477, calcd for $C_{14}H_{16}O_2$ 216.11503.

Acknowledgment. This work was supported by the U.S. Department of Energy, Office of Basic Energy Sciences, Division of Chemical Sciences, under Contract W-7405-ENG-82.

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(10) Fieser, L. F.; Fieser, M. *Reagents for Organic Synthesis*; Wiley: New York, 1967; Vol. 1, p 584.

(11) A sample that had been purified by flash chromatography on silica gel (5% ether in hexanes) was used for the melting point determination.

(12) Crystallization of a *ca.* 1-g sample of **12** from freshly-distilled petroleum ether gave fluffy white needles. This sample was used for the mp, IR, and exact mass determinations.