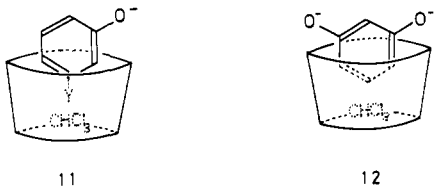

11 12

Figure 4. Ternary molecular complex composed of β-CD, chloroform, and **1d** or **1e** (**11**) and that composed of β-CD, chloroform, and **1b** (**12**). Y = CH_3 (for **1d**) and $C(CH_3)_3$ (for **1e**).

the molecular conformation between chloroform and the phenol by β-CD due to competition with the phenol in binding with β-CD.

Comparison of Catalytic Activities of α-CD and β-CD. The lower selectivity in the reaction using α-CD than that in the reaction using β-CD comes from weaker regulation of the molecular conformation of phenol or its derivative with respect to chloroform in the ternary molecular complex. The penetration of phenols in the cavity of α-CD is shallower than that in the cavity of β-CD. For example, the center of the aromatic ring of **1a** is located at the height of +2.0 Å from the plane comprised of seven H-3 atoms in the ternary molecular complex **8** of β-CD. In the ternary molecular complex composed of α-CD, chloroform, and **1a**, however, the height is larger than +3.5 Å since no chemical shift changes were observed for either α-CD or **1a**.[17] In the selective catalyses by α-CD, the transition state should involve the ternary molecular complex composed of α-CD, phenol, and dichlorocarbene.

The above argument is consistent with the larger f_p value for the reaction using α-CD than that in the reaction using β-CD. The increase of the activation energy due to the requirement for the change of the molecular conformation of dichlorocarbene and phenols in the cavity, a sterically restricted reaction field, prior to the transformation should be smaller for α-CD showing shallower penetration.

Effects of Meta Substituents of Phenols on Selective Catalyses by CDs. The structures of the ternary molecular complexes, formed in the reaction between chloroform with phenols possessing substituents at the meta position of the hydroxyl group, are shown in Figure 4. In the ternary molecular complex **11** for **1d** or **1e**, phenols penetrate the cavity from the side involving the apolar substituents at the meta position. The low selectivity of the reaction at the para position for these phenols is attributable to smallness of geometric discrimination between the para and the ortho carbon atoms in the acttack of dichlorocarbene.

In the reaction of a symmetrically substituted phenol, **4c**, which possesses the alkyl groups at the 3, 4, and 5 positions, **4c** probably penetrates in the cavity from the side involving the methyl group at the 4 position rather than from the side involving the methyl group at the 3 or 5 position, resulting in a selective reaction at the 4 position.

In the case of **1b**, the polar property of the phenoxide ion at the meta position requires the inclusion of the part of the aromatic ring involving the C-5 atom in the cavity, as shown in **12**. Thus, dichlorocarbene predominantly attacks at the C-4 or C-6 atom without the attack at the C-2 atom, producing **2b** in 100% selectivity.

These arguments are consistent with the importance of geometry of inclusion complexes in the CD-accelerated cleavages of esters.[1,14,18]

Acknowledgment. This work is partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education in Japan.

Registry No. **1a**, 108-95-2; **1b**, 108-46-3; **1c**, 95-48-7; **1d**, 108-39-4; **1e**, 585-34-2; **2a**, 123-08-0; **2b**, 95-01-2; **2c**, 15174-69-3; **2d**, 41438-18-0; **2e**, 84694-00-8; **4a**, 106-44-5; **46**, 92-69-3; **4c**, 527-54-8; **4d**, 1125-78-6; **5a**, 6611-78-5; **5b**, 78227-72-2; **5c**, 5682-84-8; **5d**, 84694-01-9; α-CD, 10016-20-3; β-CD, 7585-39-9; dichlorocarbene, 1605-72-7; β-CD-**1a**, 84694-02-0; β-CD-**1a**-$CHCl_3$, 84694-03-1.

(17) Komiyama, M.; Hirai, H. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2053.

(18) Bergeron, R. J.; Channing, M. A. *J. Am. Chem. Soc.* **1979**, *101*, 2511.

Short Syntheses of Furan and Catechol Derivatives. A Synthesis of Hydrourushiol[1,2]

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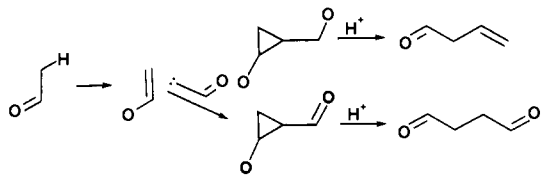
Contribution from the Departments of Chemistry, Indiana University, Bloomington, Indiana 47401, and Rice University, Houston, Texas 77001. *Received July 2, 1982*

Abstract: The copper-catalyzed decomposition of ethyl diazopyruvate in enol ethers is shown to yield alkoxydihydrofuroates, whose exposure to acid leads to ethyl α-furoates. The latter are also the products of the copper-induced interaction of ethyl diazopyruvate with acetylenes. The conversion of one furoate into a furan and another into a furanoid terpene system is described. The Fêtizon oxidation of primary β-alkoxycyclopropylcarbinols is shown to give alkoxydihydrofurans. The formation of a masked, 1,2,5-triketo system by the copper-assisted decomposition of 1-diazo-3,3-dimethoxy-2-butanone in *n*-butyl vinyl ether and subsequent acid-catalyzed unraveling of the resultant β-alkoxycyclopropyl ketone are portrayed. Ring scission of the intermediate in methanolic acid at elevated temperature yields veratrole. Utilization of this new method of synthesis of aromatic compounds of the catechol type in the synthesis of hydrourushiol is illustrated.

The reaction sequences depicted in eq 1 have served for some



(1)

time as the basis of a general procedure for the preparation of γ-difunctionalized organic substances and their use in natural product synthesis.[7] The most vital step in this general method

(1) Based on work described first in the Ph.D. Dissertations of B. L. Buckwalter and M. E. Alonso, Indiana University, 1973 and 1974, respectively.

(2) The work was presented by E.W. in a plenary lecture at the Sixième Colloque de Chimie Heterocyclique, Mulhouse, France, July 1–3, 1980. Wenkert, E. *Heterocycles* **1980**, *14*, 1703.

(3) E.W. and M.E.A. gratefully acknowledge partial support of the work at Rice University by the Robert A. Welch Foundation.

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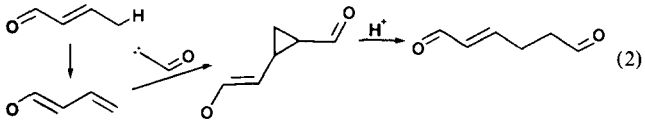
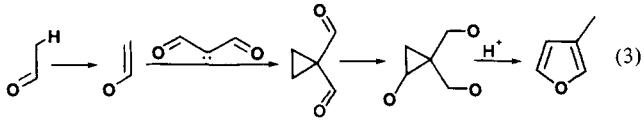
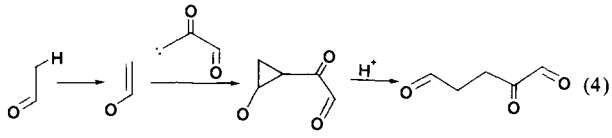
of synthesis has been the formation of the β-oxycyclopropylketo intermediate, usually conducted by thermal, copper-assisted decomposition of α-diazocarbonyl compounds in the presence of enol derivatives. After the procedure had become established, there was initiated a study of the consequence of the structure modification of each of the two reacting components of the cyclopropanation process by the introduction of new functional groups conjugated with the reaction sites. Thus it was found that the use of conjugated dienol derivatives in place of simple enol ethers or esters opened a path to olefinic 1,6-diketo systems (eq 2)[8] and


(2)

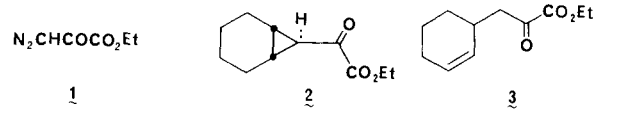
replacement of the α-diazoketo moiety by an α-diazo-β-dicarbonyl system led to the development of a facile terpenoid furan synthesis (eq 3).[9]


(3)

It was now of interest to investigate the effect of the replacement of diazoacetic ester or diazomethyl ketones by an α-diazo-α-dicarbonyl compound in the cyclopropanation reaction on the assumption of the two-step cyclopropane formation unraveling process being a route for the production of 1,2,5-triketo systems (eq 4). Since the 1,4-diketones (eq 1) had served as excellent

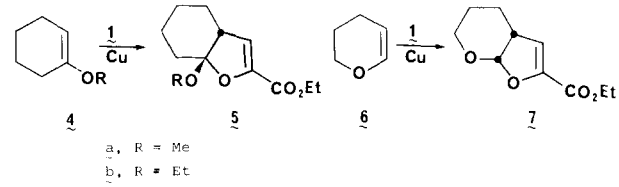

(4)

precursors of cyclopentenones, it was hoped that the triketones would lead readily to polyfunctional, six-membered ring compounds. The new investigation commenced with the use of ethyl diazopyruvate (**1**)[10] as the model α-diazo-α-diketo substance.


1 **2** **3**

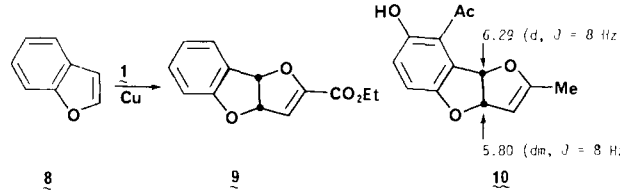
Diazopyruvic Ester. In the sole previous study of the copper-catalyzed reaction of ethyl diazopyruvate (**1**) with unsaturated substances, the diazo compound had been exposed to indole and *N*-methylpyrrole and the products had been shown to be arylpyruvic esters.[11,12] In order now to ascertain whether the diazo compound reacts with simple olefins in a conventional manner, it was exposed first to cyclohexene. Heating of a xylene solution of the mixture over copper yielded the acylnorcarane **2** and a small quantity of the cyclohexenylpyruvic ester **3**.[12b,13] Diazopyruvic ester **1** thus had revealed itself as a fairly normal α-diazocarbonyl compound. However, as the following experiments with polarized olefins indicate, the reagent interacted with enol ethers in quite unexpected fashion.

Copper-promoted reactions of ethyl diazopyruvate (**1**) with 1-alkoxycyclohexenes (**4**) and dihydropyran (**6**) produced no


4 **5** **6** **7**

a, R = Me
b, R = Et

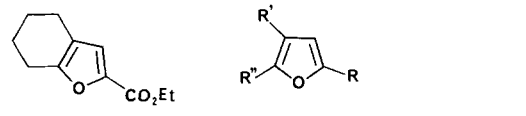
cyclopropanes, but only dihydrofurans (**5** and **7**, respectively). Thus in an unsymmetrical electronic environment of the olefin, the diazopyruvate-derived carbenoid exhibits its dipolarophilic nature, perhaps, inter alia, to overcome the energetically unfavorable coulombic repulsion of two vicinal carbonyl groups by masking the α-keto unit in enol form. The regiochemistry of the unusual reactions was in accord with expectations for polarized, nucleophilic olefins, and the product stereochemistry was expected to reflect cis fusion of the bicycles. Benzofuran (**8**), an enol ether


6.29 (d, J = 8 Hz)
5.80 (dm, J = 8 Hz)

8 **9** **10**

system of more complex olefin polarization, underwent a copper-catalyzed reaction with ethyl diazopyruvate (**1**), yielding ester **9**. The structure of this product was determined by ^{1}H NMR spectral means: comparison of the data with those reported for model **10**[14] and the absence of the ca. 100 ppm ^{13}C NMR signal characteristic of an acetal methine, i.e., the functional group expected for the alternate dihydrofuran structure.

Pyrolytic or acid-induced elimination of alcohol from the ketals **5** yielded ester **11**, thus making the **4** → **5** → **11** pathway an


11

12a, R = CO_2Et, R' = R" = Et
b, R = CO_2Et, R' = n-Bu, R" = H
c, R = CO_2Et, R' = H, R" = n-Bu
d, R = CO_2H, R' = R" = Et
e, R = H, R' = R" = Et

example of a facile, two-step route for α-furoic ester synthesis. An even shorter procedure emanated from the reactions of the diazocarbonyl reagent with acetylenes. A copper-assisted reaction of ester **1** with 3-hexyne yielded ethyl 4,5-diethylfuroate (**12a**), and a reaction with 1-hexyne led to 4- and 5-*n*-butylfuroic esters

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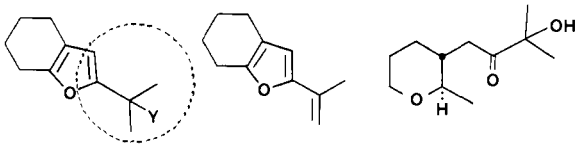
(5) 1971–1974 holder of a predoctoral fellowship from the Instituto Venezolano de Investigaciones Cientificas, Caracas, Venezuela.
(6) 1970–1972 holder of a postdoctoral fellowship from the Consejo Nacional de Investigaciones Cientificas y Tecnicas, Republica Argentina.
(7) Wenkert, E. *Acc. Chem. Res.* **1980**, *13*, 27.
(8) Wenkert, E.; Goodwin, T. E.; Ranu, B. C. *J. Org. Chem.* **1977**, *42*, 2137.
(9) Wenkert, E.; Alonso, M. E.; Buckwalter, B. L.; Chou, K. J. *J. Am. Chem. Soc.* **1977**, *99*, 4778.
(10) Its reactions proceed also with methyl diazopyruvate, but the greater crystallinity and lower solubility (in most solvents used for cyclopropanation reactions) of the methyl ester reduce its efficiency in reaction rate and product yield.
(11) Šorm, F.; Ratusky, J. *Chem. Listy* **1957**, *51*, 1091.
(12) Since the completion of the present work,[1] there have appeared the following publications on metal-catalyzed reactions between diazopyruvic esters and olefins: (a) Galluci, R. R.; Jones, M., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 7704. (b) Bien, S.; Segal, Y. *J. Org. Chem.* **1977**, *42*, 1685, 3983. (c) Mueller, L. G.; Lawton, R. G. *Ibid.* **1979**, *44*, 4741. (d) Alonso, M. E.; Jano, S. P.; Hernandez, M. I. *Ibid.* **1980**, *45*, 5299. (e) Wenkert, E.; Halls, T. D. J.; Kwart, L. D.; Magnusson, G.; Showalter, H. D. H. *Tetrahedron* **1981**, *37*, 4017.
(13) Whereas ester **3** appears to be an allylic carbon–hydrogen insertion product of the carbenoid moiety derived from diazopyruvic ester **1**, it may be the product of the pyrolytic ring opening of an intermediate endo-substituted norcarane (cf., inter alia: Wenkert, E.; de Sousa, J. R. *Synth. Commun.* **1977**, *7*, 457). This possible origin of ester **3** is in accord with the isolation of exo isomer **3** as the sole cyclopropane product despite the known propensity of cyclohexenes to yield exo and endo isomer mixtures (cf., inter alia: Wenkert, E.; Mueller, R. A.; Reardon, E. J., Jr.; Sathe, S. S.; Scharf, D. J.; Tosi, G. *J. Am. Chem. Soc.* **1970**, *92*, 7428).
(14) Eugster, C. H.; Kuser, P.; Frauenfelder, E. *Helv. Chim. Acta* **1971**, *54*, 969.

(**12b** and **12c**).[15] The lack of regiochemical control in the latter case suggested that the new α-furoic ester synthesis is most efficient with the use of symmetrical acetylenes or enol ethers as starting materials.

In view of the ease of alkaline hydrolysis of furoic esters and pyrolytic decarboxylation of the resultant furoic acids, e.g., **12a** → **12d** → **12e**, the above furoic ester synthesis constitutes also a rapid, new route to furans. Furthermore, the carbalkoxy group of the furoic esters represents an excellent substituent for elaboration into side chains common to furanoid natural products. Thus, for example, treatment of ester **11** with methyllithium, dehydration of the furfuryl alcohol **13a** with acetic anhydride, and reduction of the resultant olefin (**14**) with diimide yielded the α-isopropylfuran **13b**, part of whose structure (see portion encircled



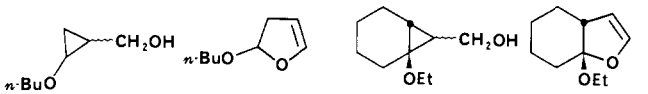
13a, Y = OH; **b**, Y = H **14** **15**

by the dotted lines) represents an isoprene unit found frequently among natural products in such furanoid form and in various oxidation states.

An attempt to convert a carbethoxy function into an isopropyl group at the alkoxydihydrofuroate instead of furoic ester stage failed, but afforded an interesting result. Exposure of ester **7** to methylmagnesium iodide yielded ketol **15**.[16] Not only had the ester been converted into a dimethylcarbinol moiety but the acetal enol ether unit had undergone scission via enolate displacement by the Grignard reagent.

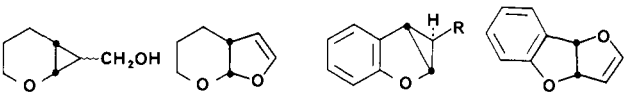
2-Oxy-2,3-dihydrofurans by Oxidative Rearrangement of β-Oxycyclopropylcarbinols. At an early stage of the investigations involving the preparation and scission of β-oxycyclopropylketo systems (eq 1),[7] a study of the chemistry of β-oxycyclopropanecarboxaldehydes was contemplated. However this inquiry was sidetracked by the discovery of an unexpected oxidative rearrangement during attempts to prepare the aldehydes by Fêtizon oxidation of β-oxycyclopropylcarbinols. The following discussion of these observations illustrates a new, facile method of 2-oxy-2,3-dihydrofuran synthesis and hence, in principle, of another furan synthesis.[17,18]

Oxidation of carbinols **16**,[20] prepared by the thermal decomposition of ethyl diazoacetate in *n*-butyl vinyl ether over copper and subsequent reduction of the resultant stereoisomer mixture



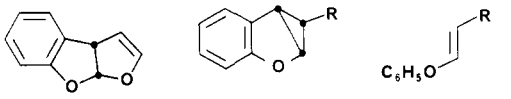
16 **17** **18** **19**

of β-*n*-butoxycyclopropanecarboxylates with lithium aluminum hydride, with silver carbonate on Celite in refluxing benzene yielded heterocycle **17**. Similar Fêtizon oxidations of alcohols **18**[21] and **20**,[22] derived in the two-step procedure from **4b** and **6**, respectively, led to bicycles **19** and **21**, respectively.



20 **21** **22a**, R = CH_2OH; **b**, R = CHO **23**

Fêtizon oxidation of the benzofuran-derived alcohol **22a**[23] afforded tricycle **23** in poor yield, whereas Collins oxidation of the alcohol yielded aldehyde **22b**. On the assumption of the dihydrofuran formation during the Fêtizon oxidations being the possible consequence of a two-reaction sequence, alcohol oxidation and subsequent silver-induced isomerization of the resultant aldehyde, aldehyde **22b** was exposed to silver salts. Interaction of **22b** with the Fêtizon reagent under conditions of the normal oxidation gave intractable material, while the milder reaction environment of a benzene solution of silver tetrafluoroborate at room temperature for 12 h led to the recovery of mostly starting aldehyde. However, isomerization in a refluxing tetrahydrofuran solution of silver tetrafluoroborate produced a ca. 2:3 mixture of tricycles **23** and **24** in poor yield. It thus seems likely that the



24 **25a**, R = CH_2OH; **b**, R = CHO **26a**, R = H; **b**, R = C_6H_5

dihydrofuran formation does not take place by the aforementioned two-step scheme, at least not exclusively. An attempt to intercept an aldehyde in the oxidation of endo alcohol **25a** failed when its Collins oxidation liberated a ca. 12:1 mixture of **23** and **24** in high yield.

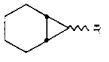
As the above data indicate, the oxidation behavior of the benzofuran-derived β-oxycyclopropylcarbinols differed markedly from that of the alcohols obtained from simpler enol ethers. Whereas the latter alcohols had suffered cyclopropane cleavage on Fêtizon oxidation in such a manner as to liberate α-oxydihydrofurans, both the Fêtizon oxidation of exo alcohol **22a** and the Collins oxidation of its endo isomer (**25a**) had led preponderantly to a β-oxydihydrofuran, and even the Lewis acid catalyzed rearrangement of the exo aldehyde **22b** had yielded the latter product to an appreciable degree. Since in the benzofuran-derived alcohols both the aromatic nucleus and the oxygen can affect the course of the cyclopropane fission, the formation of dihydrofuran **23** implies participation of the benzene ring in stabilization of the transition state of the bond-breaking step, presumably with characteristics of a benzyl radical in the Fêtizon oxidation[24] and benzyl cation in the silver ion induced rearrangement. However, not only did the presence of the benzene ring alter the site of cyclopropane cleavage but also it lowered electron availability from the oxygen for transition-state stabilization, as a consequence of

(15) Despite previous reports of acylcyclopropene formation in reactions of acetylenes (D'yakonov, I. A.; Komendatov, M. I.; Smirnova, T. S. *Zh. Org. Khim.* **1969**, *5*, 1742 and preceeding publications referred therein), no such products were detected in the present reactions.

(16) The stereochemistry of **15** was determined by ^1H NMR spectroscopy, i.e., comparison of the H-2–H-3 coupling constant with that of *cis*- and *trans*-2-methoxy-3-ethyltetrahydropyran (Wenkert, E.; Buckwalter, B. L.; Sathe, S. S. *Synth. Commun.* **1973**, *3*, 261).

(17) For two applications of this reaction scheme in natural products synthesis, see ref 9 and 12e.

(18) The presence of a β-oxy substituent on the cyclopropylcarbinol is obligatory for successful dihydrofuran formation. Thus, for example, the Fêtizon oxidation of carbinol ii, prepared by the copper-catalyzed decompo-



i, R = CO_2Et
ii, R = CH_2OH
iii, R = CHO

sition of ethyl diazoacetate in cyclohexene and subsequent lithium aluminum hydride reduction of the resultant ester i,[19a] yielded exclusively aldehyde iii[19b] (Wenkert, E.; Alonso, M. E., unpublished observation). Furthermore, the latter refused to undergo isomerization into a dihydrofuran on exposure to silver fluoroborate in benzene solution.

(19) (a) Berson, J. A.; Hand, E. S. *J. Am. Chem. Soc.* **1964**, *86*, 1978 and references cited therein. (b) Garin, D. L. *J. Org. Chem.* **1971**, *36*, 1697.

(20) Julia, M.; Baillarge, M. *Bull. Soc. Chim. Fr.* **1966**, 743.

(21) Wenkert, E.; McPherson, C. A.; Sanchez, E. L.; Webb, R. L. *Synth. Commun.* **1973**, *3*, 255.

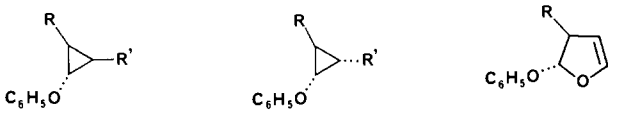
(22) Novak, J.; Ratuskỳ, J.; Šneberk, V.; Šorm, F. *Collect. Czech. Chem. Commun.* **1957**, *22*, 1836. Paul, R.; Tchelitcheff, S. *C. R. Hebd. Seances Acad. Sci.* **1957**, *244*, 2806. Literature citation in ref 16.

(23) Wenkert, E.; Alonso, M. E.; Gottlieb, H. E.; Sanchez, E. L. *J. Org. Chem.* **1977**, *42*, 3945.

(24) Kakis, F. J. *J. Org. Chem.* **1973**, *38*, 2536. Kakis, F. J.; Fêtizon, M.; Douchkine, N.; Golfier, M.; Mourgues, P.; Prange, T. *Ibid.* **1974**, *39*, 523.

the oxy substituent being a phenoxy group rather than, as heretofore, an alkoxy function must have contributed to the anomalous cyclopropane behavior. In order to gain more insight into this problem, an investigation of the chemistry of cyclopropanes derived from phenyl vinyl (**26a**) and phenyl β-styryl ethers (**26b**) was undertaken.

Copper-catalyzed decomposition of ethyl diazoacetate in phenoxyethylene (**26a**) yielded a mixture of stereoisomeric esters **27a** and **28a**, the former of which was reduced with lithium aluminum hydride. Fētizon oxidation of the resultant alcohol **27b**

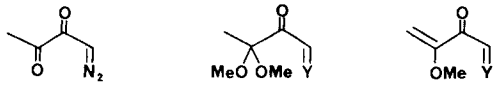


27a, R = H, R' = CO_2Et **28a**, R = H, R' = CO_2Et **29a**, R = H
b, R = H, R' = CH_2OH **b**, R = C_6H_5, R' = CO_2Me **b**, R = C_6H_5
c, R = H, R' = CHO
d, R = C_6H_5, R' = CO_2Me
e, R = C_6H_5, R' = CH_2OH
f, R = C_6H_5, R' = CHO

gave aldehyde **27c** accompanied by a minimal amount of dihydrofuran **29a**. This nearly total suppression of α-oxydihydrofuran production illustrates the power of the benzene ring attached to the oxygen in reducing the latter's propensity of directing the path of the Fētizon oxidation and helps partly to explain the anomalous behavior of the oxidative rearrangement of the benzofuran-derived cyclopropylcarbinols (vide supra). However, the observation of an isomerization into dihydrofuran **29a** occurring on treatment of aldehyde **27c** with silver tetrafluoroborate in benzene solution, albeit slowly, showed oxygen participation in cationic rearrangements despite the *O*-phenyl group. This fact is also in agreement with the benzofuran-based cyclopropane data, i.e., silver ion catalyzed isomerization of aldehyde **22b** producing more dihydrofuran **24** than **23** (vide supra).

Decomposition of diazoacetic ester over copper in a methylcyclohexane solution of (*E*)-β-phenoxystyrene afforded an ester mixture, whose alkaline hydrolysis and subsequent esterification with diazomethane produced esters **27d** and **28b**. Reduction of the former with lithium aluminum hydride, followed by Fētizon oxidation of the resultant alcohol (**27e**), a slow reaction, gave aldehyde **27f** as the only isolable product. Isomerization of the latter by silver tetrafluoroborate in benzene solution was a slow process and led to furanoid compound **29b**. The lack of dihydrofuran formation in the Fētizon oxidation of alcohol **27e** and the exclusivity of production of an α-oxydihydrofuran (**29b**) in the silver ion induced transformation of aldehyde **27f** despite the presence of a phenyl group capable of participation in cyclopropane unraveling processes stand in stark contrast to the behavior of like starting compounds in the benzofuran series. It thus seems reasonable to assume that the anomalous behavior of the latter substances (compounds **22**) may be associated with the ease of benzene π-orbital overlap with the p orbital of the rupturing, vicinal, cyclopropane carbon–carbon bond in rigid tricycles with geometrically proper orbital orientation in either radical or cationic cyclopropane scission processes. In the absence of this structural constraint, the cyclopropane-attached benzene ring of compounds **27e** and **27f** has little other than steric effect on the oxidation or rearrangement reactions.

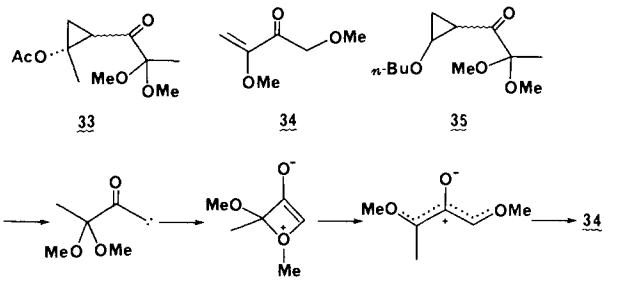
Diazobiacetyl Derivatives. In continuation of the study of copper-catalyzed decomposition of diazopyruvic ester (vide supra), it became of interest to investigate like reactions with a ketone equivalent of this ester. The first choice of a diazodiketone reagent, diazobiacetyl **30**, proved to be difficult to prepare mainly because



30 **31** **32**
a, Y = H_2
b, Y = N_2

of lack of ready access to its precursor, pyruvyl chloride.[25] Hence it was decided to synthesize two derivatives of diazobiacetyl (**30**) in which one of the keto groups was to be masked either as a ketal (**31b**) or as an enol ether (**32b**). The diazoketones could be obtained from the biacetyl monoketal **31a**[26] and the biacetyl enol ether **32a**, prepared by acid-catalyzed elimination of methanol from the ketal **31a**[27] on application of the Yates–Regitz scheme of α-keto diazotization.[28] Thus base-catalyzed condensation of ketones **31a** and **32a** with ethyl formate and subsequent treatment of the resultant hydroxymethylene ketone salts with *p*-toluenesulfonyl azide yielded diazo products **31b** and **32b**, respectively. An alternate, more efficient preparation of the latter compound followed the following, more traditional route: conversion of methyl pyruvate into methyl α-methoxyacrylate[29] by ketalation followed by acid-induced methanol elimination and sequential alkaline hydrolysis of the ester, treatment of α-methoxyacrylic acid with thionyl chloride, and exposure of the resultant acid chloride to diazomethane. Unfortunately diazo ketone **32b** proved to be a poor cyclopropanating reagent in view of its borderline stability at room temperature and its production of intractable material on copper-assisted interaction with enol ethers.[30]

Whereas the ketal diazo ketone **31b** became a valuable reagent, it underwent an undesired side reaction, especially during cyclopropanations with enol derivatives of low reactivity. Thus, for example, decomposition of the diazo compound **31b** over copper in isopropenyl acetate afforded ketoester **33** in poor yield and the



33 **34** **35**

side product as the major reaction product. Formation of the latter was suppressed totally when the reaction was executed photochemically in the presence of benzophenone as sensitizer. On the other hand, the side product became the sole end product of a copper-catalyzed decomposition of diazo ketone **31b** in benzene solution without added enol derivative. Spectroscopic structure analysis showed the substance to be 1,3-dimethoxy-3-buten-2-one (**34**). Its most probable genesis is outlined in the following mechanistic portrayal (copper association of the intermediates being omitted) reminiscent of the acid-catalyzed transformation of 1-diazo-3-methyl-3-(*p*-phenyl)phenoxy-2-butanone into 3-methyl-1-(*p*-phenyl)phenoxy-3-buten-2-one.[31]

(25) Whereas there existed at the time of the present study[1] reports on the preparation of this compound by traditional means of acid chloride formation (Klimenko, E. *Chem. Ber.* **1870**, *3*, 465. Bekurts, H.; Otto, R. *Ibid.* **1878**, *11*, 386. Bernton, A. *Ibid.* **1925**, *58*, 661. Carrē, P.; Julien, P. *C. R. Hebd. Seances Acad. Sci.* **1936**, *202*, 1521. Kharasch, M. S.; Brown, H. C. *J. Am. Chem. Soc.* **1942**, *64*, 329. Wieland, Th.; Köppe, H. *Liebigs Ann. Chem.* **1954**, *588*, 15. Tanner, D. D.; Das, N. C. *J. Org. Chem.* **1970**, *35*, 3972), the procedures yielded irreproducible results and frequently acetyl chloride as the product. Since the completion of the present investigation, pyruvyl chloride has been prepared by the latter of two recent reports (Häusler, J.; Schmidt, U. *Chem. Ber.* **1974**, *107*, 145. Ottenheijm, H. C. J.; de Man, J. H. M. *Synthesis* **1975**, 163) and exposed to ethereal diazomethane solution (with or without triethylamine added). Unfortunately these attempts to obtain diazobiacetyl failed either at the preparation step or the subsequent cyclopropanation stage (Wenkert, E.; Woodgate, P. D., unpublished observations).

(26) Braude, E. A.; Timmons, C. J. *J. Chem. Soc.* **1953**, 3131.

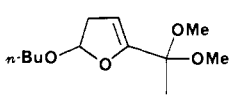
(27) An in-house procedure first developed in 1970 (Wenkert, E.; Smith, R. A. J., unpublished observations). Cf. also: Brodsky, L.; Agosta, W. C. *J. Org. Chem.* **1974**, *39*, 2928.

(28) Regitz, M.; Meinz, F. *Chem. Ber.* **1968**, *101*, 2622 and earlier references therein.

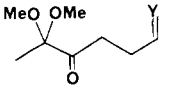
(29) Baker, J. W. *J. Chem. Soc.* **1942**, 520.

(30) If this result implies polymer formation, i.e., intermolecular interaction of a copper carbenoid with its own enol ether moiety, it must be due to the terminal position of the double bond. A more substituted enol ether α-diazocarbonyl system, e.g., 1-diazo-3-methoxy-3-penten-2-one, undergoes ready cyclopropanation of enol ethers without undue polymer formation (Wenkert, E.; Buckwalter, B. L., unpublished observations).

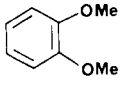
Decomposition of diazo ketone **31b** in *n*-butyl vinyl ether over copper yielded cyclopropyl ketone **35**. Longer reaction time or elevated temperature isomerized the product into dihydrofuran **36**. Isomerization was also the consequence of attempted pu-



36



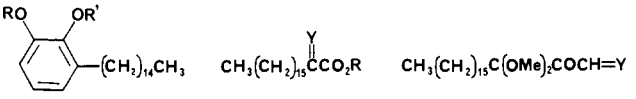
37a, Y = O
b, Y = $(OMe)_2$



38

rification of ketone **35** by chromatography on silica gel, although this acid-induced process was accompanied by the traditional hydrolytic ring scission of the β-oxycyclopropylcarbonyl system (eq 1) and led to γ-ketoaldehyde **37a** as a second product. When the three-membered-ring unraveling was carried out in methanolic acid, one of the two products isolated was the ketoacetal ketal **37b**, a substance that could be obtained also by acetalation of aldehyde **37a** with trimethyl orthoformate in acidic methanol solution. The other compound produced by the cyclopropane cleavage process in methanolic medium proved surprisingly to be veratrole (**38**). The latter substance was the sole, high-yield product of the reaction of ketone **35** in refluxing methanolic acid for short time. This fascinating result indicated that the triketohexane system, masked in various forms (**35**, **37b**, or others), is capable of undergoing facile, intramolecular, acid-induced aldol condensation. Furthermore, this experience had uncovered a simple, two-step procedure for the synthesis of catechol derivatives from acyclic precursors.

Synthesis of Hydrourushiol.[32] The ease of synthesis of the catechol system recommended the procedure for use in the construction of catechol-based natural products. One such naturally occurring substance is hydrourushiol (3-pentadecylcatechol, **39a**),



39a, R = R' = H
b, R = Me, R' = H
c, R = H, R' = Me
d, R = R' = Me

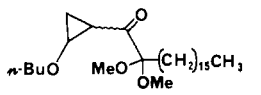
40a, R = H, Y = H_2
b, R = H, Y = H,Br
c, R = H, Y = H,OH
d, R = Me, Y = H,OH
e, R = Me, Y = O
f, R = Me, Y = $(OMe)_2$

41a, Y = H_2
b, Y = N_2

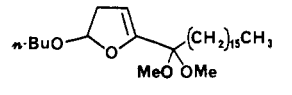
one of several vesicant constituents of, inter alia, the lac tree (*Rhus vernicifera*) of Japan,[32] poison ivy (*Rhus toxicodendron*) of North America,[32] and the manzanillo tree (*Rhus striata*) of Venezuela.[33] This compound and/or its methyl ethers were chosen as a goal of the next synthesis, and a reaction scheme was started with the natural substance stearic acid (**40a**).

Treatment of α-hydroxystearic acid (**40c**)[34] (prepared by the sequential bromination of stearic acid (**40a**) with bromine and phosphorus tribromide, hydrolysis of the acid bromide, and exposure of the resultant α-bromostearic acid (**40b**) to aqueous alkali) with diazomethane and oxidation of the hydroxyester **40d** with chromic acid in acetic acid liberated methyl α-oxostearate (**40e**), whose interaction with trimethyl orthoformate in acidic methanol furnished methyl α,α-dimethoxystearate (**40f**) (62% overall yield). Reaction of the latter with 2 equiv of methyllithium yielded the ketal ketone **41a** (91% yield),[35] whose submission to the Yates–Regitz method of diazo group transfer (vide supra)[28] led to the needed diazo ketone **41b** (67% yield).

Decomposition of the diazo ketone in *n*-butyl vinyl ether over copper yielded the cyclopropylketone **42** and to a minor extent dihydrofuran **43**. When the mixture was heated in acidic



42



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methanol for a short time, it gave hydrourushiol monomethyl ether (35% yield).[36] The product could be shown to be 2-methoxy-6-pentadecylphenol (**39b**), a substance obtained earlier by the partial ether scission of hydrourushiol dimethyl ether (**39d**) with hydrogen iodide[37] or by the platinum-catalyzed hydrogenation of the product of partial alkylation of urushiol with dimethyl sulfate in sodium ethoxide solution,[32b,37] rather than its isomer **39c** by ^{13}C NMR spectroscopy. The methoxy carbon shift of 55.9 ppm for the product was in accord with the 55–56 ppm value for *O*-methyl groups of 2,3-disubstituted anisoles and in contrast to the 60–61 ppm shift of such groups in 2,6-disubstituted anisoles.[38,39]

In view of the recorded hydrolyses of hydrourushiol methyl ethers,[32,37] the above construction of phenol **39b** constitutes a total synthesis of hydrourushiol (**39a**).

Experimental Section

Melting points were determined on a Reichert micro hotstage and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 137 spectrophotometer, and ^1H NMR spectra of deuteriochloroform solutions (unless noted otherwise) with Me_4Si as internal standard (δ = 0 ppm) were taken on Varian EM-360 and HR-220 spectrometers. Low- and high-resolution mass spectra were obtained on Varian CH-7 and A.E.I. MS-9 spectrometers, respectively. Analytical and preparative GC experiments were carried out on Varian Aerograph 1200 (flame ionization detector, nitrogen carrier gas) and Varian Aerograph Autoprep (thermal conductivity detector, helium carrier gas) chromatographs, respectively. Analytical TLC experiments utilized Woelm alumina G and Merck silica gel G plates, while preparative TLC was performed on Merck alumina PF-254. For column chromatography, Woelm neutral alumina and G.F. Smith silica (50–200 mesh) were used as adsorbants.

Ethyl *exo*-Bicyclo[4.1.0]heptyl-7-glyoxylate (2) and Ethyl 2-Cyclohexenylpyruvate (3). A solution of 500 mg of ethyl diazopyruvate (**1**) in 7 mL of cyclohexene and 10 mL of xylene was added dropwise over a 5-h period to a stirring suspension of 110 mg of copper bronze in 2 mL of cyclohexene under nitrogen at 100 °C and the heating continued for 15 min. Filtration of the hot reaction mixture through Celite, vacuum removal of starting olefin and solvent, and distillation of the product at 110–120 °C (1 torr) yielded 421 mg of colorless oil, consisting (by GC analysis) of two components in 19:1 ratio. GC separation (10-ft 10% SE-30 column, 150 mL/min flow rate) gave ester **2** as major component: IR (neat) C=O 1725 (s), 1700 (s) cm^{-1}; ^1H NMR δ 1.28 (m, 2, H-1, H-6), 1.34 (t, 3, J = 7 Hz, Me), 1.6–2.0 (m, 8, methylenes), 2.54 (t, 1, J = 4 Hz, H-7), 4.29 (q, 2, J = 7 Hz, OCH_2); mass spectrum, m/e 196 (M^+, 1), 123 (base), 95 (55). Anal. ($C_{11}H_{16}O_3$) C, H.

The minor component was ester **3**: IR (neat) C=O 1740 (s), 1725 (s), C=C 1645 (w) cm^{-1}; ^1H NMR δ 1.2–2.1 (m, 7, methylenes, meth-

(31) Nelson, N. A. *J. Org. Chem.* **1973**, *38*, 3798.

(32) For previous syntheses of hydrourushiol or its ethers, see: (a) Majima, R.; Nakamura, I. *Chem. Ber.* **1915**, *48*, 1597, 1607. (b) Backer, H. J.; Haack, N. H. *Recl. Trav. Chim. Pays-Bas* **1938**, *57*, 225. (c) Wasserman, D.; Dawson, C. R. *J. Org. Chem.* **1943**, *8*, 73. (d) Mason, H. S. *J. Am. Chem. Soc.* **1945**, *67*, 1538. (e) Dawson, C. R.; Wasserman, D.; Keil, H. *Ibid.* **1946**, *68*, 534. (f) Vithayathil, P. J.; Dawson, C. R. *J. Org. Chem.* **1958**, *23*, 1443. (g) Loev, B.; Dawson, C. R. *Ibid.* **1959**, *24*, 981. (h) Boehme, W. *J. Am. Chem. Soc.* **1960**, *82*, 498. (i) Yukawa, Y.; Hanabusa, A. *Chem. Ind. (London)* **1961**, 23. (j) Murakami, M.; Chen, J.-C. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 263. References 32h and 32j illustrate syntheses from acyclic precursors.

(33) Nakano, T.; Medina, J. D.; Hurtado, I. *Planta Med.* **1970**, *18*, 260.

(34) Hell, C.; Sandomsky, J. *Chem. Ber.* **1891**, *24*, 2388. Ucciani, E.; Morot-Sir, F.; Naudet, N. *Bull. Soc. Chim. Fr.* **1967**, 1913. Ucciani, E.; Siouffi, A. M.; Naudet, N. *Ibid.* **1967**, 2018.

(35) Cf.: Majetich, G.; Grieco, P. A.; Bongers, S.; Erman, M. G.; Langs, D. A. *J. Org. Chem.* **1981**, *46*, 209.

(36) Mass spectral analyses revealed a trace of dimethyl ether **39d** in the crude product mixture.

(37) Majima, R.; Takayama, G. *Chem. Ber.* **1920**, 1907.

(38) Wenkert, E.; Gottlieb, H. E.; Gottlieb, O. R.; da S. Pereira, M. O.; Formiga, M. D. *Phytochemistry* **1976**, *15*, 1547. Castelão, J. F.; Gottlieb, O. R.; de Lima, R. A.; Mesquita, A. A. L.; Gottlieb, H. E.; Wenkert, E. *Ibid.* **1977**, *16*, 735. Wenkert, E.; Gottlieb, H. E. *Ibid.* **1977**, *16*, 1811.

(39) The formation of a guaiacol in the methanolysis of cyclopropyl ketone **42** in contrast to the production of veratrole (**38**) in the methanolysis of model ketone **35** and the exclusivity of formation of guaiacol **39b** from a starting ketone expected (in the absence of any methoxy group exchange) to yield guaiacol **39c** require explanation. Whereas without firm data on the site and speed of methoxy-group scrambling prior to aromatization a mechanistic analysis is tenuous at best, it is tempting to suggest that as in the **35** → **38** conversion, the primary product of the methanolysis of ketone **42** is also a veratrole (**39d**) and that as in the hydrogen iodide catalyzed **39d** → **39b** transformation,[37] the drastic condition of the present methanolysis cause demethylation of the central methoxy group of diether **39d** also. (For complete O-demethylation of **39d** by hydrochloric acid in water or acetic acid see ref 32d.)

ine), 1.35 (t, 3, J = 7 Hz, Me), 2.77 (m, 2, $COCH_2$), 5.47 (dd, 1, J = 2, 10 Hz, olefinic H-2), 5.71 (dtd, 1, J = 2, 5, 10 Hz, olefinic H-3); mass spectrum, m/e 196 (M^+, 4), 168 (11), 123 (74), 95 (34), 81 (base). Exact mass: m/e 196.1105; calcd for $C_{11}H_{16}O_3$: 196.1099.

Ethyl 7a-Methoxy-3a,4,5,6,7,7a-hexahydrobenzofuran-2-carboxylate (5a). A solution of 500 mg of ethyl diazopyruvate (**1**) in 7 mL of 1-methoxycyclohexene (**4a**) and 3 mL of xylene was added dropwise over a 5-h period to a stirring mixture of 100 mg of copper bronze and 2 mL of 1-methoxycyclohexene under nitrogen at 110 °C and the heating continued for 30 min. Work up as above and distillation at 110 °C (1.5 torr) led to 570 mg (73%) of ester **5a**: IR (neat) C=O 1745 (s), C=C 1660 (w), 1630 (m) cm^{-1}; ^1H NMR δ 1.1–2.5 (m, 8, methylenes), 1.31 (t, 3, J = 7 Hz, Me), 2.71 (td, 1, J = 4, 8 Hz, allyl H), 3.30 (s, 3, OMe), 4.24 (q, 2, J = 7 Hz, OCH_2), 6.01 (d, 1, J = 4 Hz, olefinic H); mass spectrum, m/e 226 (M^+, 10), 194 (36), 28 (base). Exact mass: m/e 226.1200; calcd for $C_{12}H_{18}O_4$: 226.1205.

Ethyl 4,5,6,7-Tetrahydrobenzofuran-2-carboxylate (11). Pyrolysis of ester **5b**, prepared in 52–70% yields from 1-ethoxycyclohexene (**4b**) as above, at 105 °C (0.25 torr) produced in 90% yield ester **11**: IR (neat) C=O 1740 (s), C=C 1630 (m) cm^{-1}; ^1H NMR δ 1.32 (t, 3, J = 7 Hz, Me), 1.6–2.7 (m, 8, methylenes), 4.29 (q, 2, J = 7 Hz, OCH_2), 6.93 (s, 1, olefinic H). Anal. ($C_{11}H_{14}O_3$) C, H.

The conversion of ester **5a** into α-furoate **11** could be accomplished by pyrolysis over glass powder at 180 °C for 1 h (49% yield), flash distillation over solid zinc chloride or dipotassium phosphate at 200 °C (24% and 43%, respectively), and treatment in ether with sodium methoxide at 25 °C, zinc chloride at 0 °C, or boron trifluoride etherate at −180 °C (17%, 25%, and 71%, respectively).

Ethyl 2,9-Dioxabicyclo[4.3.0]non-7-ene-8-carboxylate (7). A solution of 500 mg of ethyl diazopyruvate (**1**) in 6 mL of dihydropyran (**6**) was added dropwise over a 4.5-h period to a refluxing suspension of 100 mg of copper bronze in 2 mL of dihydropyran under nitrogen and the heating continued for 20 min. The mixture was filtered through Celite and the filtrate evaporated under vacuum. Distillation of the residue at 90 °C (0.05 torr), chromatography of the oily distillate (400 mg) on basic alumina (activity IV), and elution with 6:1 hexane–benzene yielded 390 mg (57%) of colorless, liquid ester **7**: IR (neat) C=O 1740 (s), C=C 1625 (m) cm^{-1}; ^1H NMR δ 1.29 (t, 3, J = 7 Hz, Me), 1.6–1.8 (m, 4, methylenes), 2.98 (m, 1, allyl H), 3.75 (m, 2, nuclear OCH_2), 4.23 (q, 2, J = 7 Hz, OCH_2), 5.77 (d, 1, J = 8 Hz, OCHO), 5.92 (d, 1, J = 3 Hz, olefinic H); mass spectrum, m/e 198 (M^+, 49), 125 (43), 97 (base). Exact mass: m/e 198.0895; calcd for $C_{10}H_{14}O_4$: 198.0888.

Ethyl 3,4-Benzo-2,6-dioxabicyclo[3.3.0]oct-7-ene-7-carboxylate (9). A solution of 1.00 g of ethyl diazopyruvate (**1**) in 10 mL of freshly distilled benzofuran (**8**) was added dropwise over a 5-h period to a stirring suspension of 110 mg of copper bronze in 2 mL of benzofuran at 110 °C under nitrogen. Filtration of the hot mixture through Celite and distillation of the filtrate led to the recovery of 9.2 mL of benzofuran (**8**) (bp 84–85 °C (25 torr)). Chromatography of the distillation residue on neutral alumina (activity III) and elution with 9:1 hexane–benzene gave 328 mg (27%) of solid, whose crystallization from methylene chloride–hexane yielded crystalline ester **9**: mp 102–102.5 °C; IR (KBr) C=O 1735 (s) cm^{-1}; ^1H NMR δ 1.22 (t, 3, J = 7 Hz, Me), 4.17 (q, 2, J = 7 Hz, OCH_2), 5.88 (dd, 1, J = 3, 8 Hz, allyl OCH), 6.11 (d, 1, J = 3 Hz, olefinic H), 6.11 (d, 1, J = 3 Hz, olefinic H), 6.11 (d, 1, J = 8 Hz, benzyl OCH), 6.7–7.4 (m, 4, aromatic Hs). Anal. ($C_{13}H_{12}O_4$) C, H.

4,5-Diethyl-2-furoic Acid (12d). A solution of 500 mg of ethyl diazopyruvate (**1**) and 5 mL of freshly distilled 3-hexyne in 6 mL of dry benzene was added dropwise over a 4-h period to a refluxing suspension of 100 mg of copper bronze and 2 mL of 3-hexyne in 24 mL of benzene under nitrogen and the heating continued for 30 min. The hot mixture was filtered through Celite and the filtrate evaporated under vacuum. Distillation of the residue at 75 °C (0.35 torr) afforded 339 mg (51%) of liquid ester **12a**: IR (neat) C=O 1710 (s), C=C 1605 (w) cm^{-1}; ^1H NMR δ 1.14, 1.23 (t, 3 each, J = 7 Hz, Me_2), 1.33 (t, 3, J = 7 Hz, Me of OEt), 2.37 (q, 2, J = 7 Hz, 4-CH_2), 2.64 (q, 2, J = 7 Hz, 5-CH_2), 4.28 (q, 2, J = 7 Hz, OCH_2), 6.99 (s, 1, olefinic H). A solution of 420 mg of the latter in 5 mL of 10% methanolic potassium hydroxide was refluxed for 1 h and then cooled and brought to pH 7 with 0.1 N hydrochloric acid. The resultant suspension was extracted with chloroform and the extract washed with water, dried ($MgSO_4$), and evaporated. Crystallization of the solid residue, 351 mg, from hexane–chloroform and sublimation at 80 °C (1.5 torr) gave 311 mg (82%) of crystalline acid **12d**: mp 92.5–93 °C; IR (KBr) C=O 1690 (s), C=C 1605 (w) cm^{-1}. Anal. ($C_9H_{12}O_3$) C, H.

2,3-Diethylfuran (12e). A mixture of 120 mg of acid **12d**, 5 mg of copper powder, and 5 mg of glass powder was heated at 260 °C (90 torr) for 45 min in a microdistillation apparatus attached to a dry ice–acetone trap. This experiment led to 71 mg (85%) of liquid furan **12e**: ^1H NMR δ 1.13, 1.19 (t, 3 each, J = 7 Hz, Me_2), 2.35 (q, 2, J = 7 Hz, 3-CH_2), 2.58 (q, 2, J = 7 Hz, 2-CH_2), 6.15 (d, 1, J = 2 Hz, CH), 7.17 (d, 1, J = 2 Hz, OCH); mass spectrum, m/e 124 (M^+, 37), 109 (base), 95 (7). Exact mass: m/e 124.0876; calcd for $C_8H_{12}O$: 128.0888.

Furoic Esters 12b and 12c. Duplication of the procedure for the preparation of ester **12a** (vide supra) with 1-hexyne and distillation of the crude product at 100 °C (0.4 torr) led to a 24% yield of an ester mixture, consisting (by GC analysis) of 60% of ester **12b** and 19% of ester **12c**. Preparative GC separation gave liquid ethyl 4-*n*-butyl-2-furoate (**12b**): IR (neat) C=O 1730 (s) cm^{-1}; ^1H NMR δ 0.92 (t, 3, J = 7 Hz, Me), 1.2–1.5 (m, 4, methylenes), 1.27 (t, 3, J = 7 Hz, Me of OEt), 2.43 (t, 2, J = 7 Hz, benzyl CH_2), 4.19 (q, 2, J = 7 Hz, OCH_2), 7.04 (s, 1, olefinic H), 7.33 (d, 1, J = 1 Hz, OCH); mass spectrum, m/e 196 (M^+, 36), 153 (base), 125 (53). Anal. ($C_{11}H_{16}O_3$) C, H.

The minor product was liquid ethyl 5-*n*-butyl-2-furoate (**12c**): IR (neat) C=O 1730 (s) cm^{-1}; ^1H NMR δ 0.92 (t, 3, J = 7 Hz, Me), 1.2–1.5 (m, 4, methylenes), 1.35 (t, 3, J = 7 Hz, Me of OEt), 2.68 (t, 2, J = 7 Hz, benzyl CH_2), 4.34 (q, 2, J = 7 Hz, OCH_2), 6.10 (dt, 1, J = 1, 4 Hz, H-4), 7.06 (d, 1, J = 4 Hz, H-3); mass spectrum, m/e 196 (M^+, 10), 154 (base), 153 (16), 125 (16). Anal. ($C_{11}H_{16}O_3$) C, H.

2-Isopropyl-4,5,6,7-tetrahydrobenzofuran (13b). An ethereal solution of methyllithium (10 mL of 1.9 N) was added to a solution of 657 mg of ester **11** in 15 mL of anhydrous ether and cooled in a dry ice–acetone bath under nitrogen at such a rate as to keep the temperature below −60 °C. The mixture then was stirred at −20 °C for 2 h, and the reaction was terminated by the addition of 3 mL of methanol and 1 mL of brine. The organic layer was washed with water, dried ($MgSO_4$), and evaporated, to yield 499 mg of a liquid mixture of alcohol **13a** [IR (neat) OH 3350 (br m), C=C 1605 (m) cm^{-1}; ^1H NMR δ 1.5–1.8 (m, 4, methylenes), 1.48, 1.50 (s, 3 each, Me_2), 2.1–2.5 (m, 4, benzyl methylenes), 5.90 (s, 1, olefinic H)] and up to 45% dehydration product. A solution of 487 mg of this mixture and 111 mg of sodium acetate in 2 mL of acetic anhydride was refluxed for 0.5 h and then diluted with 25 mL of hexane, washed with water, 3% aqueous sodium carbonate, and water again, dried ($MgSO_4$), and evaporated. Rapid passage of an ether solution of the residue, 410 mg, through 7 g of basic alumina (activity IV) yielded 395 mg of colorless, liquid olefin **14**: IR (neat) C=C 1610 (m), 1650 (w) cm^{-1}; ^1H NMR δ 1.6–1.9 (m, 4, methylenes), 1.96 (s, 3, Me), 2.3–2.7 (m, 4, benzyl methylenes), 4.85 5.43 (d, 1 each, J = 2 Hz, olefinic CH_2), 6.11 (s, 1, furan H).

A solution of 200 mg of this unstable oil, 900 mg of *p*-toluenesulfonyl hydrazine, and one pellet of potassium hydroxide in 6 mL of diglyme was heated at 150 °C under nitrogen for 40 min. The mixture was diluted with hexane, washed with water, 10% sodium bicarbonate solution, and water again, dried ($MgSO_4$), and evaporated. Chromatography with neutral alumina (5 g, activity III) and elution with pentane yielded 160 mg of colorless, liquid furan **13b**: IR (neat) C=C 1650 (w) cm^{-1}; ^1H NMR δ 1.18 (d, 6, J = 7 Hz, Me_2), 1.6–1.8 (m, 4, methylenes), 2.2–2.6 (m, 4, benzyl methylenes), 2.85 (quint, 1, J = 7 Hz, CH), 5.71 (s, 1, furan H); mass spectrum, m/e 164 (M^+, 49), 163 (10), 149 (base), 121 (40). Exact mass: m/e 164.1198; calcd for $C_{11}H_{16}O$: 164.1201.

***trans*-2-Methyl-3-(β-oxo-γ-hydroxylsopentyl)tetrahydropyran (15).** A mixture of methylmagnesium iodide, prepared from 1.20 g of magnesium turnings and 7.10 g of methyl iodide in 100 mL of benzene, and 800 mg of ester **7** in 25 mL of anhydrous ether was heated at 60 °C for 20 h and then poured into water. The organic layer was washed with saturated brine solution, dried (Na_2SO_4), and evaporated. Chromatography of the residue on neutral alumina (activity III) and elution with 1:1 benzene–chloroform yielded 495 mg (62%) of colorless, liquid ketol **15**: IR (neat) OH 3500 (m), C=O 1705 (s) cm^{-1}; ^1H NMR δ 1.08 (d, 3, J = 6 Hz, Me), 1.26 (s, 6, *i*-Pr Me_2), 1.4–1.9 (m, 5, methylenes), 2.30 (dd, 1, J = 8, 16 Hz, $COCH_2$ H), 2.48 (dd, 1, J = 6, 16 Hz, $COCH_2$ H), 3.06 (dq, 1, J = 6, 8 Hz, OCH), 3.25 (dt, 1, J = 3, 11 Hz, OCH_2 H), 3.83 (d m, 1, J = 11 Hz, OCH_2 H). Anal. ($C_{11}H_{20}O_3$) C, H.

Fétizon Oxidations of β-Oxycyclopropylcarbinols. A benzene solution of the alcohol was added to a stirring suspension of silver carbonate–Celite (3–10-mol excess of oxidizing agent) in benzene, from which water had been removed azeotropically, and the mixture was refluxed for as long as TLC monitoring of the reaction progress indicated the presence of starting alcohol (normally 1–3 h). The hot mixture was filtered through a low-porosity filter paper, and the solid was washed exhaustively with benzene. Evaporation of the combined filtrate and washings yielded the dihydrofuran.

2-*n*-Butoxy-2,3-dihydrofuran (17) (liquid, 91%): bp 59 °C (10 torr); IR (neat) 1615 (m) cm^{-1}; ^1H NMR δ 0.91 (t, 3, J = 7 Hz, Me), 1.3–1.6 (m, 4, methylenes), 2.4–2.8 (m, 2, allyl Hs), 3.4–3.8 (m, 2, OCH_2), 4.92 (d, 1, J = 2 Hz, olefinic H), 5.48 (dd, 1, J = 3, 8 Hz, OCHO), 6.25 (d, 1, J = 2 Hz, olefinic OCH). Exact mass: m/e 142.0994; calcd for $C_8H_{14}O_2$: 142.0999.

7a-Ethoxy-3a,4,5,6,7,7a-hexahydrobenzofuran (19) (liquid, 97%): IR (neat) C=C 1618 (m) cm^{-1}; ^1H NMR δ 1.14 (t, 3, J = 7 Hz, Me),

1.0–2.1 (m, 8, methylenes), 2.62 (m, 1, allyl H), 3.53 (q, 2, J = 7 Hz, OCH_2), 4.93 (d, 1, J = 2 Hz, olefinic H), 6.26 (m, 1, olefinic OCH). Anal. ($C_{10}H_{16}O_2$) C, H.

2,9-Dioxabicyclo[4.3.0]non-7-ene (21) (liquid, 86%): IR (neat) 1620 (m) cm^{-1}; ^1H NMR δ 1.4–2.4 (m, 4, methylenes), 2.81 (m, 1, allyl H), 3.6–3.9 (m, 2, OCH_2), 4.86 (d, 1, J = 2 Hz, olefinic H), 5.61 (d, 1, J = 8 Hz, OCHO), 6.36 (d, 1, J = 2 Hz, olefinic OCH). Anal. ($C_7H_{10}O_2$) C, H.

3,4-Benzo-2,6-dioxabicyclo[3.3.0]oct-7-ene (23) (unstable, air- and acid-sensitive liquid, 17%): ^1H NMR δ 5.14 (t, 1, J = 2 Hz, olefinic H), 5.80 (dd, 1, J = 2, 8 Hz, allyl H), 5.87 (d, 1, J = 8 Hz, benzyl H), 6.45 (d, 1, J = 2 Hz, olefinic OCH), 6.70, 7.27 (d, 1 each, J = 8 Hz, aromatic Hs next to bridgeheads), 6.76, 7.12 (t, 1 each, J = 8 Hz, other aromatic Hs). Exact mass: m/e 160.0526; calcd for $C_{10}H_8O_2$: 160.0524.

A solution of 7.00 g of ethyl diazoacetate in 15 mL of methylcyclohexane was added dropwise over a 5-h period to a stirring suspension of 1.2 g of copper bronze and 6.00 g of phenyl vinyl ether in 10 mL of methylcyclohexane at 95 °C under nitrogen and the heating continued for 2 h. The mixture was filtered and the filtrate evaporated under vacuum, leaving 6.00 g (62%) of a mixture of esters **27a** and **28a**, bp 94 °C (0.15 torr). Chromatography of 1.50 g of the mixture on neutral alumina (activity III) and elution with 8:1 hexane–benzene yielded consecutively 450 mg of **28a** and 870 mg of **27a**.

Ethyl *cis*-2-Phenoxycyclopropanecarboxylate (28a): IR (neat) C=O 1730 (s) cm^{-1}; ^1H NMR δ 0.98 (t, 3, J = 7 Hz, Me), 1.2–2.1 (m, 3, CH_2, CH), 3.77 (q, 1, J = 6 Hz, OCH), 3.92 (q, 2, J = 7 Hz, OCH_2), 6.3–7.3 (m, 5, aromatic Hs).

Ethyl *trans*-2-Phenoxycyclopropanecarboxylate (27a): IR (neat) C=O 1730 (s) cm^{-1}; ^1H NMR δ 1.24 (t, 3, J = 7 Hz, Me), 1.3–1.7 (m, 2, CH_2), 1.90 (m, 1, CH), 4.00 (m, 1, OCH), 4.12 (q, 2, J = 7 Hz, OCH_2), 6.8–7.3 (m, 5, aromatic Hs).

A solution of 370 mg of ester **27a** in 5 mL of anhydrous ether was added dropwise to a stirring suspension of 100 mg of lithium aluminum hydride in 25 mL of ether and the mixture refluxed for 5 h. Ethyl acetate and then aqueous methanol were added, and the mixture was extracted with ether. Evaporation of the extract left 290 mg (98%) of colorless alcohol **27b**: ^1H NMR δ 0.57 (m, 1, CH), 0.95, 1.41 (m, 1 each, CH_2), 3.27 (m, 2, OCH_2), 3.50 (m, 1, OCH), 6.8–7.3 (m, 5, aromatic Hs).

Fētizon oxidation of the latter for 6 h gave 260 mg of oil (containing ca. 10% of starting alcohol), whose chromatography on 25 g of basic alumina (activity III) and elution with hexane yielded 5 mg (5%) of colorless, liquid 2-phenoxy-2,3-dihydrofuran (**29a**): IR (neat) C=C 1610 (m) cm^{-1}; ^1H NMR δ 2.5–3.1 (m, 2, CH_2), 5.03 (q, 1, J = 2 Hz, olefinic H), 6.06 (dd, 1, J = 2, 7 Hz, OCHO), 6.33 (q, 1, J = 2 Hz, olefinic OCH), 6.9–7.3 (m, 5, aromatic Hs). Exact mass: m/e 162.0682; calcd for $C_{10}H_{10}O_2$: 162.0681. Anal. ($C_{10}H_{10}O_2$) C, H.

Elution with benzene afforded 209 mg (72%) of unstable, liquid *trans*-2-phenoxycyclopropanecarboxaldehyde (**27c**): IR (neat) C=O 1705 (s), C=C 1600 (m) cm^{-1}; ^1H NMR δ 1.4–2.1 (m, 3, CH_2, CH), 3.91 (m, 1, OCH), 6.8–7.1 (m, 5, aromatic Hs), 9.56 (d, 1, aldehyde H). Exact mass: m/e 162.0689; calcd for $C_{10}H_{10}O_2$: 162.0681.

A solution of 4.00 g of ethyl diazoacetate and 8.00 g of (*E*)-β-phenoxystyrene in 20 mL of methylcyclohexane was added dropwise over a 5-h period to a stirring suspension of 1.0 g of copper bronze in 5 mL of methylcyclohexane at 95 °C under nitrogen and the heating continued 1.5 h. The mixture was filtered through Celite and the filtrate evaporated under vacuum. A mixture of the residue and 5 mL of methanol in 25 mL of 10% aqueous potassium hydroxide solution was refluxed for 4 h and then extracted with ether (for recovery of unreacted enol ether). After being brought to pH 6 by the addition of 5% hydrochloric acid, the aqueous solution was extracted with ether. The extract was dried (Na_2SO_4) and added to a solution of diazomethane (from 7.00 g of *N*-nitrosomethylurea) in 200 mL of ether. After 15 min, acetic acid was added and the mixture evaporated. Distillation of the residue (4.2 g) led to 4.00 g (39%) of a mixture of esters **27d** and **28b** (bp 153–154 °C (0.1 torr)) whose chromatographic separation on alumina yielded ester **28b** [IR (neat) C=O 1725 (s), C=C 1600 (m) cm^{-1}; ^1H NMR δ 2.45 (dd, 1, J = 6. 7 Hz, COCH), 3.08 (dd, 1, J = 4, 6 Hz, CH), 3.58 (s, 3, Me), 4.12 (dd, 1, J = 4, 9 Hz, OCH), 6.8–7.5 (m, 10, aromatic Hs); mass spectrum, m/e 268 (M^+, 5), 237 (3), 290 (12)] and **27d** [IR (neat) C=O 1725 (s), C=C 1600 (m) cm^{-1}; ^1H NMR δ 2.46 (dd, 1, J = 3, 11 Hz, COCH), 3.04 (dd, 1, J = 5, 11 Hz, CH), 3.47 (s, 3, Me), 4.70 (dd, 1, J = 3, 5 Hz, OCH), 6.8–7.5 (m, 10, aromatic Hs). Anal. ($C_{17}H_{16}O_3$) C, H].

A solution of 1.00 g of ester **27d** in 10 mL of anhydrous ether was added dropwise to a stirring suspension of 350 mg of lithium aluminum hydride in 30 mL of ether and the mixture refluxed for 5 h. The usual work up (vide supra) gave 880 mg (98%) of solid, whose crystallization from methanol yielded crystalline alcohol **27e**: mp 113–113.5 °C; IR (KBr) OH 3200 (s), C=C 1600 (m) cm^{-1}; ^1H NMR δ 1.85 (ddt, 1, J = 3, 8, 11 Hz, CH), 2.58 (dd, 1, J = 3, 11 Hz, PhCH), 3.59 (m, 2, OCH_2), 4.10 (t, 1, J = 3 Hz, OCH), 6.9–7.3 (m, 10, aromatic Hs); mass spectrum, m/e 240 (M^+, 2), 210 (31), 116 (base). Anal. ($C_{16}H_{16}O_2$) C, H.

Fētizon oxidation of 720 mg of alcohol **27e** for 3 h led to the recovery of 49% of starting alcohol (which on two more oxidations raised the aldehyde yield to 80%) and on chromatography on 15 g of basic alumina (activity III) and elution with 1:1 hexane–benzene to 348 mg (48%) of colorless, liquid aldehyde **27f**: IR (neat) C=O 1700 (s), C=C 1600 (m) cm^{-1}; ^1H NMR δ 2.48 (dt, 1, J = 3, 10 Hz, COCH), 3.24 (dd, 1, J = 5, 10 Hz, CH), 4.68 (dd, 1, J = 3, 5 Hz, OCH), 6.8–7.2 (m; 10, aromatic Hs), 9.19 (d, 1, J = 3 Hz, aldehyde H). Anal. ($C_{16}H_{14}O_2$) C, H.

Isomerizations of β-Oxycyclopropanecarboxaldehydes. A solution of 810 mg of alcohol **22a** in 15 mL of dry methylene chloride was added slowly over a 5-min period to a stirring suspension of chromium trioxide–pyridine complex (from 2.00 g of chromium trioxide and 4.74 g of anhydrous pyridine) in 15 mL of methylene chloride at 0 °C, and the stirring was continued for 40 min. Methanol (4 mL) was added and the mixture poured into water. The organic layer was washed with 10% potassium hydroxide solution, 5% cupric sulfate solution, and water, dried ($MgSO_4$), and evaporated. Chromatography of the residue (790 mg) on 10 g of basic alumina (activity IV) and elution with 4:1 benzene–hexane led to the recovery of 92 mg of starting alcohol. Prior elution with 1:1 hexane–benzene yielded 715 mg (88%) of liquid, air-sensitive aldehyde **22b**: IR (neat) C=O 1695 (s), C=C 1625 (w), 1600 (w) cm^{-1}; ^1H NMR δ 1.52 (ddd, 1, J = 1, 2, 3 Hz, COCH), 3.36 (dd, 1, J = 3, 6 Hz, CH), 4.99 (dd, 1, J = 1, 6 Hz, OCH), 6.76, 7.29 (d, 1 each, J = 8 Hz, aromatic Hs next to bridgeheads), 6.82, 7.03 (t, 1, J = 8 Hz, other aromatic Hs), 9.85 (d, 1, J = 2 Hz, aldehyde H); mass spectrum, m/e 160 (M^+, 14), 131 (35), 83 (82), 52 (base). Exact mass: m/e 160.0525; calcd for $C_{10}H_8O_2$: 160.0524.

A mixture of 600 mg of aldehyde **22b** and 50 mg of silver tetrafluoroborate in 10 mL of dry tetrahydrofuran was refluxed under nitrogen for 2 h. Saturated sodium chloride solution (1 mL) was added and the mixture filtered. The filtrate was extracted with ether and the extract washed with water, dried (Na_2SO_4), and evaporated. Chromatography of the residual oil, 551 mg, on 8 g of basic alumina (activity III) and elution with pentane yielded 83 mg (14%) of tricycle **23** (spectrally identical with above sample) and 123 mg (21%) of highly air- and acid-sensitive, rapidly deteriorating, liquid 3,4-dibenzo-2,8-dioxabicyclo[3.3.0]oct-6-ene (**24**): ^1H NMR δ (CCl_4) 4.38 (dd, 1, J = 2, 8 Hz, CH), 5.03 (d, 1, J = 2 Hz, olefinic H), 6.27 (br s, 1, olefinic OCH), 6.48 (d, 1, J = 8 Hz, OCHO), 6.7–7.0 (m, 4, aromatic Hs); mass spectrum, m/e 160 (M^+, 66), 131 (base). Exact mass: 160.0525; calcd for $C_{10}H_8O_2$: 160.0524.

A solution of 521 mg of alcohol **25a** in 10 mL of methylene chloride was added slowly over a 4-min period to a stirring suspension of chromium trioxide–pyridine complex (from 1.92 g of chromium trioxide and 3.03 g of anhydrous pyridine) in 10 mL of methylene chloride at 0 °C and the stirring continued for 2 h. Methanol (1 mL) was added and the mixture poured into water. Work up as above, chromatography of the crude, oily product (501 mg) on 8 g of basic alumina (activity III), and elution with hexane yielded 30 mg (6%) of unstable liquid tricycle **24** (vide supra). Elution with 9:1 hexane–benzene afforded 374 mg (72%) of isomer **23** (vide supra).

A mixture of 195 mg of aldehyde **27c** and 70 mg of silver tetrafluoroborate in 15 mL of dry benzene was refluxed under nitrogen for 3 h. Saturated sodium chloride solution (1 mL) was added and the mixture filtered. The filtrate was washed with water, dried ($MgSO_4$), and evaporated. Chromatography of the residue on 10 g of neutral alumina (activity III) and elution with 4:1 hexane–benzene yielded 54 mg (25%) of dihydrofuran **29a**.

A mixture of 126 mg of aldehyde **27f** and 116 mg of silver tetrafluoroborate in 5 mL of anhydrous tetrahydrofuran was refluxed under nitrogen for 7 h. Saturated sodium chloride solution (2 mL) was added and the mixture filtered. The filtrate was extracted with ether and the extract dried ($MgSO_4$) and evaporated. Chromatography of the residue on 10 g of basic alumina (activity III) and elution with 1:1 hexane–benzene led to the recovery of starting aldehyde, whose two further treatments with the silver salt raised the product yield to 41%. Earlier elution with hexane led to 43 mg of a mixture of starting material and product, whose rechromatography on basic alumina (activity II) and elution with pentane afforded 30 mg (24%) of colorless, liquid *trans*-2-phenoxy-3-phenyl-2,3-dihydrofuran (**29b**): ^1H NMR δ 4.14 (q, 1, J = 3 Hz, CH), 5.25 (t, 1, J = 3 Hz, olefinic H), 5.79 (d, 1, J = 3 Hz, OCHO), 6.54 (d, 1, J = 3 Hz, olefinic OCH). Anal. ($C_{16}H_{14}O_2$) C, H.

1-Diazo-3,3-dimethoxy-2-butanone (31b). A mixture of 27.7 g of 3,3-dimethoxy-2-butanone (**31a**) and 18.5 g of freshly distilled ethyl formate was added dropwise over a 2-h period to a stirring suspension of 13.5 g of freshly prepared sodium methoxide in 300 mL of anhydrous

ether at 0 °C under nitrogen, and the stirring was continued at room temperature for 16 h. The resultant pink precipitate was filtered, washed thoroughly with cold, dry methanol, and dried under vacuum to yield 36.1 g of the sodium salt of 4,4-dimethoxy-1-hydroxy-1-penten-3-one. A solution of 21.7 g of *p*-toluenesulfonyl azide in 20 mL of methanol was added dropwise to a solution of 20.0 g of the salt in 250 mL of methanol at 5 °C, and the mixture was stirred at room temperature for 3 h. After removal of half of the solvent, the mixture was poured into benzene and water. The organic layer was washed with 5% sodium hydroxide solution and water, dried ($MgSO_4$), and evaporated. Distillation of the residue at low temperature and high vacuum yielded 9.10 g (52%) of liquid diazo ketone **31b**: bp 45–47 °C (0.15 torr); IR (neat) C=N_2 2115 (s), C=O 1645 (s) cm^{-1}; ^1H NMR δ 1.41 (s, 3, Me), 3.23 (s, 6, 2 OMe), 5.81 (s, 1, N_2CH). Anal. ($C_6H_{10}O_3N_2$) C, H, N.

1-Diazo-3-methoxy-3-buten-2-one (32b). A mixture of 10.00 g of 3,3-dimethoxy-2-butanone (**31a**) and 20 mg of *p*-toluenesulfonic acid was heated at 150 °C for 0.5 h. By application of a moderate vacuum, a yellow liquid was distilled away from the reaction mixture at 105–115 °C (140 torr) over a 1.5-h period. Fractional distillation of the liquid led to the recovery of 6.60 g of starting ketone (bp 76–79 °C (90 torr)) and in an earlier fraction 2.35 g (31%) of 88% pure 3-methoxy-3-buten-2-one (**32a**) (unstable at room temperature, preservable at 0 °C for a few weeks): IR (neat) C=O 1700 (s), C=C 1610 (s) cm^{-1}; ^1H NMR δ (CCl_4) 2.28 (s, 3, Me), 3.61 (s, 3, OMe), 4.41, 5.08 (d, 1, J = 3 Hz, CH_2); mass spectrum, m/e 100 (M^+, 86), 70 (33), 57 (52), 43 (base). Exact mass: m/e 100.0521; calcd for $C_5H_8O_2$: 100.0523.

A condensation of 3.00 g of ketone **32a** with 2.22 g of ethyl formate as in the above preparation of **31b** yielded 3.50 g of dry sodium salt. A solution of 9.85 g of *p*-toluenesulfonyl azide in 10 mL of absolute methanol was added slowly to a solution of 7.50 g of the salt in 80 mL of methanol at 0 °C and the mixture stirred at room temperature for 6 h. After evaporation of the solvent at 25 °C to one-third of the volume, the mixture was poured into water and extracted with benzene. The extract was dried ($MgSO_4$) and evaporated. Chromatography of the viscous residue on 30 g of Florisil and elution with benzene gave 1.5 g of a mixture of product and starting azide. Rechromatography on 25 g of Florisil and elution with hexane yielded 410 mg of azide and 860 mg (11%) of yellow, liquid diazo ketone **32b**: IR (neat) C=N_2 2110 (s), C=O 1610 (s) cm^{-1}; ^1H NMR δ (CCl_4) 3.52 (s, 3, Me), 4.18, 5.05 (d, 1 each, J = 3 Hz, CH_2), 5.61 (s, 1, N_2CH). The material underwent decomposition within hours at 25 °C and within days at 0 °C.

A solution of 22.0 g of methyl pyruvate, 30.0 g of trimethyl orthoformate, and 0.1 mL of concentrated sulfuric acid in 60 mL of absolute methanol was refluxed for 5 h, whereupon 40 mL of solvent was removed by distillation. The remaining solution, cooled to 10 °C, was poured into a solution of 600 mg of potassium hydroxide in 300 mL of water, and the mixture was extracted continuously with ether over 12 h. The extract was dried ($MgSO_4$) and evaporated. Distillation of the residual oil furnished 31.0 g (97%) of methyl α,α-dimethoxypropionate [bp 65–66 °C (8 torr); IR (neat) C=O 1745 (s) cm^{-1}; ^1H NMR δ 1.48 (s, 3, Me), 3.25 (s, 6, 2 OMe), 3.77 (s, 3, ester OMe)]. A mixture of 10.0 g of the latter and 200 mg of *p*-toluenesulfonic acid was heated at 140 °C under conditions of the removal of methanol by distillation. Two fractional distillations of the residue yielded 6.60 g of methyl α-methoxyacrylate [bp 151–154 °C; IR (neat) C=O 1735 (s), C=C 1622 (s) cm^{-1}; ^1H NMR δ 3.63 (s, 3, Me), 3.78 (s, 3, ester OMe), 4.58, 5.28 (d, 1 each, J = 3 Hz, CH_2)]. A solution of 11.25 g of the latter, 6.60 g of potassium hydroxide, and 10 mL of water in 100 mL of methanol was refluxed for 6 h. Removal of the solvent by distillation and vacuum drying of the residual solid gave 13.5 g of salt, to whose suspension in 200 mL of anhydrous ether at 0 °C under nitrogen there was added slowly 30 g of freshly distilled thionyl chloride. The mixture was refluxed for 3 h and evaporated under moderate vacuum. Fractional distillation (75–80 °C (60 torr)) of the residue gave 9.90 g (84%) of unstable, liquid α-methoxyacryl chloride: IR (neat) C=O 1760 (s), C=C 1610 (s) cm^{-1}; ^1H NMR δ 3.70 (s, 3, Me), 4.87, 5.60 (d, 1 each, J = 3 Hz, CH_2). A solution of 20.0 g of the latter in 50 mL of anhydrous ether was added dropwise to a stirring solution of 0.45 mol of diazomethane in 500 mL of dry ether at 0 °C. The mixture was stirred at room temperature for 2 h, cooled to 0 °C, and washed with 5% sodium bicarbonate solution and water. Drying ($MgSO_4$) of the organic solution and evaporation led to 14.0 g of desired product (85% purity), whose chromatography on Florisil (vide supra) gave diazo ketone **32b**.

1-Acetoxy-1-methyl-2-(α,α-dimethoxypropionyl)cyclopropane (33). A bright yellow solution of 1.50 g of diazo ketone **31b** and 1.50 g of benzophenone in 10 mL isopropenyl acetate in a Pyrex tube was irradiated with a Hannovia 250-W high-pressure mercury lamp for 18 h. Removal of the excess starting acetate by distillation left a residual oil, whose two fractional distillations yielded recovered benzophenone and 1.10 g (46%) of liquid keto ester **33** (ca. 1:1 stereoisomer mixture): bp 64 °C (0.025 torr); IR (neat) C=O 1750 (s), 1715 (s) cm^{-1}; ^1H NMR δ 1.26, 1.35 (s, 1.5 each, Me), 1.41, 1.53 (s, 1.5 each, cyclopropyl Me), 1.86, 1.93 (s, 1.5 each, COMe), 2.0–3.0 (m, 3, CH_2, CH), 3.15 (s, 3, OMe), 3.18, 3.21 (s, 1.5 each, OMe); mass spectrum, m/e 230 (M^+, 1), 89 (90), 43 (base). Anal. ($C_{11}H_{18}O_5$) C, H.

A solution of 1.55 g of diazo ketone **31b** in 7 mL of isopropenyl acetate was added dropwise over a 2.5-h period to a stirring suspension of 100 mg of copper bronze in 1 mL of isopropenyl acetate at 85 °C under nitrogen, and the stirring was continued for another 0.5 h. Filtration of the mixture through Celite and removal of excess enol acetate by distillation of the filtrate left a residual oil, whose several fractional distillations yielded 719 mg (57%) of liquid, highly unstable (decomposing at 0 °C within a few hours) keto ether **34** [bp 31–34 °C (0.02 torr); IR (neat) C=O 1725 (s), C=C 1615 (s) cm^{-1}; ^1H NMR δ 3.35 (s, 3, OMe), 3.66 (s, 3, olefinic OMe), 4.30 (s, 2, CH_2), 4.36, 5.15 (d, 1 each, J = 2 Hz, olefinic Hs] and 267 mg (19%) of keto ester **33** (spectrally identical with the above sample).

1-*n*-Butoxy-2-(α,α-dimethoxypropionyl)cyclopropane (35) and 2-*n*-Butoxy-5-(α,α-dimetboxyethyl)-2,3-dihydrofuran (36). A solution of 1.50 g of diazo ketone **31b** in 5 mL of *n*-butyl vinyl ether was added dropwise over a 3-h period to a stirring suspension of 100 mg of copper bronze in 1 mL of the ether at 90 °C under nitrogen and the stirring continued for an additional 20-min period. Filtration of the mixture and removal of excess enol ether from the filtrate by distillation left a residual oil, whose distillation gave 1.50 g (69%) of colorless, liquid keto ether 35: bp 65–66 °C (0.05 torr); IR (neat) C=O 1705 (s) cm^{-1}; ^1H NMR δ 0.93 (t, 3, J = 7 Hz, Bu Me), 1.0–2.7 (m, 7, COCH, methylenes), 1.33 (s, 3, Me), 3.27 (s, 6, 2 OMe), 3.5–4.2 (m, 3, OCH, OCH_2). Anal. ($C_{12}H_{22}O_4$) C, H.

Distillation of 100 mg of the product through a vertical, 2-ft quartz column (packed with glass helices and kept at 250 °C (0.2 torr)) and collection of the vapors in a dry ice–acetone trap led to the recovery of 99 mg of a pale yellow oil, whose distillation yielded 89 mg (89%) of colorless, liquid dihydrofuran **36**: bp 66–67 °C (0.02 torr); IR (neat) C=C 1665 (m) cm^{-1}; ^1H NMR δ 0.93 (t, 3, J = 7 Hz, Bu Me), 1.33 (s, 3, Me), 1.0–1.6 (m, 4, methylenes), 2.4–2.7 (m, 2, allyl Hs), 3.06 (s, 6, 2 OMe), 4.85 (d, 1, J = 3 Hz, olefinic H), 5.33 (dd, 1, J = 3, 6 Hz, OCHO); mass spectrum, m/e 230 (M^+, 3), 215 (2), 199 (15), 157 (3), 89 (base). Exact mass: m/e 199.1347; calcd for $C_{11}H_{19}O_3$: 199.1333.

The transformation of cyclopropylketone **35** into dihydrofuran **36** occurred also on being kept at room temperature for 72 h (29% yield), although not below 5 °C, and on being heated over copper bronze in *n*-butyl vinyl ether solution (60%).

γ-Oxo-δ,δ-dimethoxycaproaldehyde (37a) and 2,2,6,6-Tetramethoxy-3-hexanone (37b). Chromatography of 1.00 g of ketone **35** on 25 g of silica gel and elution with benzene yielded sequentially 410 mg (41%) of dihydrofuran **36**, 135 mg of unidentified material, and 360 mg (48%) of liquid aldehyde **37a** [IR (neat) CHO 2830 (m), C=O 1730 (s) cm^{-1}; ^1H NMR δ 1.28 (s, 3, Me), 2.5–2.8 (m, 4, methylenes), 3.13 (s, 6, 2 OMe), 9.90 (t, 1, J = 1 Hz, CHO)]. A mixture of the latter, 0.5 g of methanol-washed Amberlite IR-120-H, 1 mL of methanol, and 3 mL of trimethyl orthoformate was stirred at room temperature for 18 h. Filtration and evaporation of the filtrate gave 370 mg of a residue, whose chromatography on Florisil and elution with benzene afforded 369 mg (81%) of colorless, liquid ketone **37b**: IR (neat) C=O 1725 (s) cm^{-1}; ^1H NMR δ (CCl_4) 1.25 (s, 3, Me), 1.73 (m, 2, J = 6, 7 Hz, CH_2), 2.49 (t, 2, J = 7 Hz, $COCH_2$), 3.13 (s, 6, C-2 methoxyls), 3.18 (s, 6, C-6 methoxyls), 4.21 (t, 1, J = 6 Hz, OCHO); mass spectrum, m/e 219 (M^+ − 1, 2), 189 (2), 89 (base), 75 (20). Exact mass (M^+ − 1): m/e 219.1225; calcd for $C_{10}H_{19}O_5$: 219.1231.

Veratrole (38). A solution of 1.00 g of ketone **35** in 10 mL of absolute methanol was poured into 25 mL of absolute methanol saturated with hydrogen chloride gas at 0 °C, and the mixture was stirred at this temperature for 1 h. It then was poured slowly into 100 mL of ice-cold 10% methanolic potassium hydroxide solution, and the alkaline solution was mixed with 500 mL of water. The mixture was extracted exhaustively with methylene chloride and the extract washed with water, dried (Na_2SO_4), and evaporated. Chromatography of the residue (890 mg) on Florisil and elution with 1:1 hexane–benzene provided 365 mg (61%) of veratrole (**38**), identical in all respects with an authentic sample. Elution with 5:1 benzene–hexane furnished 370 mg (39%) of ketone **37b** (vide supra).

When a solution of 500 mg of ketone **35** in 20 mL of absolute methanol saturated with hydrogen chloride gas was refluxed for 10 min and the mixture worked up as above, there was isolated 270 mg (90%) of veratrole (**38**).

Methyl α-Oxostearate (40e). A solution of 1.00 g of α-hydroxystearic acid (**40c**) (mp 88–89 °C) and diazomethane (from 2.00 g of *N*-methyl-*N*-nitrosourea) in 15 mL of ether was kept at room temperature for 15 min and thereafter nitrogen bubbled through the solution for the

removal of the excess diazomethane. Evaporation and crystallization of the residue from ether yielded 1.03 g of methyl α-hydroxystearate (**40d**); mp 62–64 °C. To a solution of the latter in 15 mL of glacial acetic acid, kept below 35 °C, was added dropwise over a 2-h period a solution of 300 mg of chromium trioxide in 2 mL of water and 5 mL of acetic acid. After being stirred at room temperature for 48 h, the mixture was treated with methanol for the destruction of the excess oxidizing agent and poured into 100 mL of water. The mixture was extracted with ether and the extract washed with water and evaporated. Water (10 mL) was added to the residue and the mixture shaken and filtered. The precipitate was washed with water, dried under vacuum, and crystallized from ether, yielding 840 mg (83%) of large, colorless plates of ester **40e**: mp 53–53.5 °C; IR (Nujol) C=O 1760 (s), 1723 (s) cm^{-1}; mass spectrum, *m/e* 312 (M^+, 16), 253 (base). Anal. ($C_{19}H_{36}O_3$) C, H.

Methyl α,α-Dimethoxystearate (40f). A solution of 10.5 g of ester **40e**, 0.1 mL of concentrated sulfuric acid, and 30 mL of trimethyl orthoformate in 30 mL of methanol was refluxed for 5 h and then poured into an ice-cold aqueous solution of 1 g of potassium hydroxide. The mixture was extracted with ether and the extract washed with water, dried ($MgSO_4$), and evaporated. Crystallization of the residual oil from methanol yielded 11.8 g (99%) of colorless, powdery ester **40f**: mp 33.5–34 °C; IR (Nujol) C=O 1755 (s) cm^{-1}; ^1H NMR δ 0.87 (t, 3, *J* = 7 Hz, Me), 1.27 (s, 30, 15 CH_2), 3.22 (s, 6, 2 ketal OMe), 3.75 (s, 3, OMe); mass spectrum, *m/e* 358 (M^+, 1), 299 (base). Anal. ($C_{21}H_{42}O_4$) C, H.

3,3-Dimethoxy-2-nonadecanone (41a). A solution (1.48 N) of 29.6 mmol of methyllithium in 20.0 mL of hexane was added dropwise over a 0.5-h period by syringe to a solution of 5.00 g (14.0 mmol) of ester **40f** in 50 mL of dry tetrahydrofuran at below 10 °C under nitrogen, and the mixture was stirred at room temperature for 1 h. It then was poured into a mixture of 100 g of ice and 20 mL of 3 N hydrochloric acid in 150 mL of water and extracted exhaustively with ether. The extract was washed with saturated brine solution, dried ($MgSO_4$), and evaporated to yield 4.35 g (91%) of liquid ketone **41a** (2,4-dinitrophenylhydrazone, mp 143–146 °C): IR (neat) C=O 1725 (s) cm^{-1}; ^1H NMR δ 0.86 (t, 3, *J* = 7 Hz, Me), 1.27 (s, 30, 15 CH_2), 2.15 (s, 3, COMe), 3.15 (s, 6, 2 OMe); mass spectrum, *m/e* 342 (M^+, 1), 311 (4), 299 (base), 43 (26). Exact mass (M^+ – OMe): *m/e* 311.2952; calcd for $C_{20}H_{39}O_2$: 311.2949.

1-Diazo-3,3-dimethoxy-2-nonadecanone (41b). A solution of 9.00 g of ketone **41a** and 2.40 g of freshly distilled ethyl formate in 50 mL of anhydrous ether was added dropwise over a 1-h period to a stirring suspension of 1.51 g of freshly prepared sodium methoxide in 50 mL of dry ether at 5 °C under nitrogen and the mixture then stirred at room temperature for 20 h. It was cooled to 5 °C and the solid filtered. Washing of the precipitate with cold ether and drying it under vacuum afforded 9.50 g of the sodium salt of formylated starting ketone (**41**, Y = CHO^-,Na^+). A solution of 4.73 g of *p*-toluenesulfonyl azide in 20 mL of methanol was added to a solution of 9.00 g of the salt in 70 mL of tetrahydrofuran and 200 mL of methanol at 0 °C and the mixture stirred at 5 °C for 2 h. Then a second, identical batch of azide solution was added and the mixture stirred at room temperature for 12 h. Solvent evaporation at room temperature to one-third of the original volume and filtration of the remaining mixture yielded 5.9 g of a solid; mp 62–64 °C. The filtrate was poured into 100 mL of water and extracted with benzene. The extract was washed with saturated brine solution, dried ($MgSO_4$), and evaporated. Two crystallizations of the residue and the earlier solid from methanol gave 6.50 g (67%) of colorless needles of diazo ketone **41b**: mp 66–66.5 °C; IR (Nujol) C=N_2 2120 (s), C=O 1625 (s) cm^{-1}; ^1H NMR δ 0.88 (t, 3, *J* = 7 Hz, Me), 1.26 (br s, 30, 15 CH_2), 3.18 (s, 6, 2 OMe), 5.71 (s, 1, N_2CH). Anal. ($C_{21}H_{40}O_3N_2$) C, H.

Hydrourushiol Monomethyl Ether (39b). A solution of 1.00 g of diazo ketone **41b** in 15 mL of *n*-butyl vinyl ether was added dropwise over a 1.5-h period to a stirring suspension of 120 mg of copper bronze in 2 mL of the enol ether at 120 °C under nitrogen and the stirring continued for 20 min. The mixture was filtered and the filtrate exposed to low-temperature vacuum distillation for the removal of the excess enol ether. The residual oil (1.15 g) was composed (TLC analysis) of mostly two components—2-*n*-butoxy-1-(α,α-dimethoxystearyl)cyclopropane (**42**) (over 90%) [IR (neat) C=O 1700 (s) cm^{-1}; ^1H NMR δ 0.88 (t, 3, *J* = 7 Hz, Me), 1.0–1.9 (m, 32, 16 CH_2), 2.4–2.7 (m, 1, COCH), 3.21 (s, 6, 2 OMe), 3.3–3.6 (m, 1, OCH)] and 2-*n*-butoxy-5-(α,α-dimethoxyheptadecyl)-2,3-dihydrofuran (**43**) (under 9%) [IR (neat) C=C 1660 (m) cm^{-1}; ^1H NMR δ 0.90 (t, 6, *J* = 7 Hz, Me_2), 1.25 (s, 30, 15 CH_2), 2.4–2.7 (m, 2, allyl Hs), 3.10, 3.13 (s, 3 each, methoxyls), 4.98 (t, 1, *J* = 3 Hz, olefinic H), 5.41 (dd, 1, *J* = 3, 6 Hz, OCHO)]—whose instability on adsorbants prevented their chromatographic separation. A solution of the oily mixture in 30 mL of dry methanol was refluxed for 10 min while hydrogen chloride gas was bubbled continuously through the solution. It then was basified by being poured into a mixture of 100 g of ice and 25 g of potassium hydroxide in 200 mL of water and extracted immediately with ether. The extract was washed with water, dried ($MgSO_4$), and evaporated. Chromatography of the residual oil (1.14 g) on silica gel and elution with benzene afforded a pale yellow oil, whose crystallization from methanol gave 321 mg (35%) of a colorless solid, mp 42–43 °C. Thick-layer chromatography of the latter on silica yielded colorless, hair-like needles of 6-methoxy-2-pentadecylphenol (**39b**): mp 43–43.5 °C; IR (Nujol) OH 3580 (w), 3475 (m), 3400 (m), C=C 1615 (m), 1590 (m) cm^{-1}; ^1H NMR δ 0.80 (t, 3, *J* = 7 Hz, Me), 1.23 (s, 26, 13 CH_2), 2.54 (t, 2, *J* = 8 Hz, benzyl Hs), 3.76 (s, 3, OMe), 6.57 (s, 3, aromatic Hs); mass spectrum, *m/e* 334 (M^+, 100), 138 (20), 137 (35). Anal. ($C_{22}H_{38}O_2$) C, H.

Registry No. 1, 14214-10-9; **2**, 61558-26-7; **3**, 61558-27-8; **4a**, 931-57-7; **4b**, 1122-84-5; **5a**, 84521-58-4; **5b**, 84521-59-5; **6**, 110-87-2; **7**, 84521-60-8; **8**, 271-89-6; **9**, 84521-61-9; **11**, 30568-64-0; **12a**, 84521-62-0; **12b**, 84521-63-1; **12c**, 84521-64-2; **12d**, 84521-65-3; **12e**, 84521-66-4; **13a**, 84521-67-5; **13b**, 84521-68-6; **14**, 84521-69-7; **15**, 84521-70-0; **16** (isomer 1), 84521-71-1; **16** (isomer 2), 84521-72-2; **17**, 84521-73-3; **18** (isomer 1), 84581-12-4; **18** (isomer 2), 84581-13-5; **19**, 84521-74-4; **20** (isomer 1), 51197-04-7; **20** (isomer 2), 51144-35-5; **21**, 84521-75-5; **22a**, 63703-28-6; **22b**, 84521-76-6; **23**, 84521-77-7; **24**, 84521-78-8; **25a**, 63730-26-7; **26a**, 766-94-9; **26b**, 66694-17-5; **27a**, 2120-92-5; **27b**, 2055-69-8; **27c**, 84521-79-9; **27d**, 84521-80-2; **27e**, 84521-81-3; **27f**, 84521-82-4; **28a**, 2120-91-4; **28b**, 84581-14-6; **29a**, 84521-83-5; **29b**, 84521-84-6; **31** (Y = CHO^-,Na^+), 84521-85-7; **31a**, 21983-72-2; **31b**, 84521-86-8; **32** (Y = CHO^-,Na^+), 84521-87-9; **32a**, 51933-10-9; **32b**, 84521-88-0; **33** (isomer 1), 84521-89-1; **33** (isomer 2), 84521-90-4; **34**, 84521-91-5; **35**, 84521-92-6; **36**, 84521-93-7; **37a**, 84521-94-8; **37b**, 84521-95-9; **38**, 91-16-7; **39b**, 16825-58-4; **40c**, 629-22-1; **40d**, 2420-35-1; **40e**, 2380-18-9; **40f**, 77022-34-5; **41** (Y = CHO^-,Na^+), 84521-96-0; **41a**, 77022-35-6; **41a** 2,4-dinitrophenylhydrazone, 84521-97-1; **41b**, 77022-36-7; **42**, 77022-37-8; **43**, 77022-38-9; cyclohexene, 110-83-8; 3-hexyne, 928-49-4; 1-hexyne, 693-02-7; ethyl diazoacetate, 623-73-4; methyl pyruvate, 600-22-6; trimethyl orthoformate, 149-73-5; methyl α,α-dimethoxypropionate, 10076-48-9; methyl α-methoxyacrylate, 7001-18-5; potassium α-methoxyacrylate, 83402-41-9; α-methoxyacryl chloride, 84537-07-5; isopropenyl acetate, 108-22-5; *n*-butyl vinyl ether, 111-34-2.