The Peracid Oxidation of Tetramethylallene[1]

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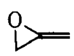
Abstract: The peracetic acid oxidation of tetramethylallene leads to a mixture of products containing acetone, 2-acetoxy-2,4-dimethyl-3-pentanone (**3**), 2-acetoxy-4-hydroxy-2,4-dimethyl-3-pentanone (**4**), 2,2,4,4-tetramethyl-3-oxetanone (**5**), 2,2,4-trimethyl-3-oxa-4-hydroxypentanoic acid lactone (**6**), and 4-hydroxy-2,4-dimethylpent-1-en-3-one (**7**). These products are accounted for by a scheme which postulates the formation of allene oxide (**8**) and dioxaspiropentane (**9**) species as unisolated reactive intermediates. Trapping experiments with propionoic acid and methanol are used to support this proposal.

This paper details our initial work concerning the peracid oxidation of the allene functional group.[2] The primary motivation behind this study is the characterization of the elusive allene oxide (methyleneoxirane) functionality represented by structure **1**. Allene oxides have been considered on occasion in the literature in connection with their potential intermediacy in the Favorskii and related reactions.[3] In this regard it is of interest to examine the possibility of valence tautomerism of system **1** and the alternate molecular array of a cyclopropanone (**2**). Ambiguities associated with the bond, strain, and resonance energies of these small-ring heterocycles makes it difficult to devise a meaningful estimate of the relative stabilities of **1** and **2**. Nonetheless, it is quite apparent from recent elegant work leading to the isolation and characterization of cyclopropanone and its derivatives[4] that interconversion resulting in the accumulation of observable amounts of the corresponding allene oxide does not obtain under the conditions that have been examined to date.[5] Thus, if facile valence tautomerism occurs, equilibrium must ordinarily lie far on the side of the cyclopropanone.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Our approach to the synthesis of compounds of type **1** has been the straightforward one of double-bond epoxidation. Surprisingly little work has been recorded on the peracid oxidation of allenes. As part of his classical epoxidation studies, Boeseken very early examined the reaction of 1,1-dimethylallene with peracetic acid and demonstrated the presence of 3-acetoxy-3-methyl-2-butanone in the product.[6,7] Russian workers have since performed similar oxidations on several substituted allenes and isolated a number of products apparently resulting from dioxidation.[8] However, the evidence supporting the unusual structures proposed by these workers is at best uncompelling.

The oxidation system utilized acetic acid-free solutions of peracetic acid which were prepared by adding commercial 40% peracetic acid to a cold, stirred slurry of powdered sodium carbonate in methylene chloride.[9] The resulting filtered solution was used in the presence of additional sodium carbonate as a scavenger for the acetic acid liberated in the reaction. An experiment performed by adding tetramethylallene to 3 equiv of peracid was utilized for product studies. The products were isolated by preparative glpc and identified on the basis of their characteristic spectroscopic properties which are detailed in the Experimental Section. In most instances these assignments were confirmed by actual comparison with authentic samples. The major product was 2-acetoxy-2,4-dimethyl-3-pentanone (**3**) in analogy with the earlier work.[6,7] However, a comparable amount of 2-acetoxy-4-hydroxy-2,4-dimethyl-3-pentanone (**4**) and minor but significant quantities of acetone, 2,2,4,4-tetramethyl-3-oxetanone (**5**), the corresponding lactone **6**, and 4-hydroxy-2,4-dimethylpent-1-en-3-one (**7**) were also found. The relative proportions of these materials was subject to change with variation in the experimental parameters, but in a typical example the following was observed: 52% **3**, 39% **4**, 3% **5**, 2% **6**, and 4% **7**. Acetoxy ketone **3** was prepared by lead tetraacetate oxidation[10] of diisopropyl ketone; hydroxy acetoxy ketone **4** was secured by semiacetylation of dihydroxy diisopropyl ketone; and a bromination–dehydrobromination sequence led to conjugated ketone **7** from hydroxy diisopropyl ketone.

The stability of each of the products to the reaction conditions was investigated next. As expected oxetanone **5** underwent smooth Baeyer–Villiger reaction to yield lactone **6**. On the other hand, both **3** and **4**

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[1] Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation (GP-3891) for partial support of this work.

[2] A preliminary report has appeared: J. K. Crandall and W. H. Machleder, *Tetrahedron Lett.*, 6037 (1966).

[3] A. W. Fort, *J. Amer. Chem. Soc.*, **84**, 2620, 2625, 4979 (1962); H. O. House and W. F. Gilmore, *ibid.*, 83, 3980 (1961); H. O. House and H. W. Thompson, *J. Org. Chem.*, 28, 164 (1963); H. O. House and G. A. Frank, *ibid.*, 30, 2948 (1965); H. O. House and F. A. Richey, *ibid.*, **32**, 2151 (1967); R. C. Cookson and M. J. Nye, *J. Chem. Soc.*, 2009 (1965); R. C. Cookson, B. Halton, I. D. R. Stevens, and C. T. Watts, *J. Chem. Soc., C*, 928 (1967); R. C. Cookson, M. J. Nye, and G. Sabrahmanyam, *ibid.*, 473 (1967). See also, A. S. Kende, *Org. Reactions*, **11**, 261 (1960).

[4] N. J. Turro, W. B. Hammond, and P. A. Leermakers, *J. Amer. Chem. Soc.*, 87, 2774 (1965); W. B. Hammond and N. J. Turro, *ibid.*, 88, 2880 (1966); N. J. Turro and W. B. Hammond, *ibid.*, **88**, 3672 (1966); J. F. Pazos and F. D. Greene, *ibid.*, **89**, 1030 (1967).

[5] Structural studies also support this conclusion: J. M. Pochan, J. E. Baldwin, and W. H. Flygare, *ibid.*, **90**, 1072 (1968).

[6] J. Boeseken, *Rec. Trav. Chim. Pays-Bas*, **54**, 657 (1935).

[7] Similar results have been found for epoxidation of a number of allenes by L. Skattebøl and S. Solomon. We thank Dr. Skattebøl for informing us of these unpublished results and for several stimulating discussions on the subject.

[8] V. I. Pansevich-Kolyada and Z. B. Idelchik, *J. Gen. Chem. USSR*, **24**, 1601 (1954).

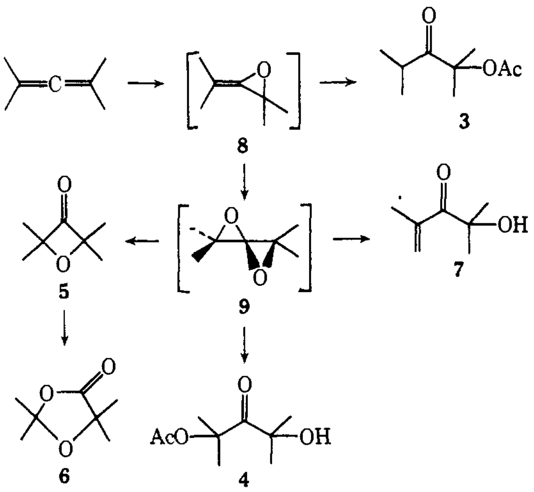
[9] M. Korach, D. R. Nielsen, and W. H. Rideout, *J. Amer. Chem. Soc.*, 82, 4328 (1960).

[10] H. B. Henbest, D. N. Jones, and G. P. Slater, *J. Chem. Soc.*, 4472 (1961).

were surprisingly resistant to further oxidation. Unsaturated ketone **7** was completely destroyed by peracid with acetone the only observed product. Presumably the remaining fragment was methacrylic acid which was lost as its sodium salt. Finally, the stability of the oxetanone to acetic acid in methylene chloride ruled out the possibility that this material was the precursor of **4** or **7**.

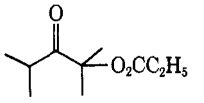
Chart I illustrates the scheme proposed to accomodate these results. The initial step in this sequence is the epoxidation of tetramethylallene to give allene oxide **8**. This reactive intermediate apparently does not accumulate in the reaction mixture but is rapidly partitioned between reaction with acetic acid to yield **3** and with peracetic acid to produce the dioxaspiropentane **9** as a second unisolated intermediate.[11] This latter species serves admirably as a rational source of higher oxidation products. Thus, molecular rearrangement of **9** to the oxetanone is readily visualized as either a thermal or, more likely, an acid-induced process. Further Baeyer–Villiger oxidation yields lactone **6** as was demonstrated experimentally above. Finally, protonation and isomerization of spiro dioxide **9** by one of several available pathways leads logically to unsaturated ketone **7** and acetoxy hydroxy ketone **4**.[11] The postulation of an allene oxide intermediate, therefore, quite nicely accounts for the observed oxidation products of tetramethylallene, particularly the more highly oxidized materials.

Chart I



Although the sequence in Chart I is a particularly appealing one, others can be advanced and additional evidence supporting the true intermediacy of the unisolated species **8** and **9** was sought. If these entities are in fact generated and have a finite lifetime in solution, then it should be possible to divert them from their usual transformations by the inclusion of reagents which can compete with acetic acid for the oxide intermediates. On the contrary, direct conversion to the isolated products without the benefit of intermediate stopping points would not be expected to be affected appreciably by foreign reagents. Distinction between these possibilities was provided by an oxidation experiment in which propionic acid was included in a peracetic acid solution that was added dropwise to the allene. Under these conditions the usual array of products was supplemented by the propionate esters **10** and **11**. These materials are the propionate analogs of acetates **3** and **4**, and most logically derive from competitive reaction of the postulated oxide intermediates with acetic and propionic acids. Furthermore, the relative amounts of acetates to propionates for both pairs **3** and **10** and **4** and **11** were in approximately the same ratio as the available carboxylic acids. Thus the data are fully compatible with the existence of both **8** and **9** as real intermediates which are independent of their mode of formation.

Supplementary, but less clean-cut, information was secured with methanol as the added nucleophile. In this instance the product mixture included 2-hydroxy-4-methoxy-2,4-dimethyl-3-pentanone (**12**) in addition to the materials characterized earlier. This suggests trapping of spiro dioxide **9**, but the expected methanol adduct of allene oxide **8**, namely 2-methoxy-2,4-dimethyl-3-pentanone (**13**), was not found. A second experiment consisted of adding peracid very slowly to a large excess of allene and methanol. Higher oxidation products were not observed under these conditions, but acetoxy ketone **3** was the only important product. Also produced were acetone and 4-methoxy-2,4-dimethyl-2-pentene (**14**). The latter compound was a result of simple acid-catalyzed addition of methanol to the allene. The absence of methoxy ketone **13** might be attributed to a substantial selectivity of the allene oxide (but not the spiro dioxide) in favor of reaction with acetic acid over methanol. Alternatively compound **13** may actually be formed in these reactions but not accumulate owing to further reaction with peracid. Consistent with this explanation is the demonstration that authentic **13** is destroyed by peracid.



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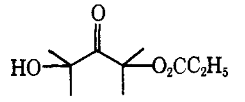

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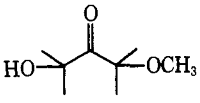

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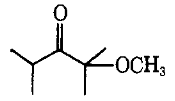

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Particularly expedient syntheses of acetate **3** and propionate **10** were achieved by irradiation of tetramethylcyclobutane-1,3-dione (**15**) in the presence of acetic or propionic acid. Reaction almost certainly proceeds by addition of carboxylic acid to the intermediate photolysis product, tetramethylcyclopropanone (**16**).[4] The question of possible allene oxide to cyclopropanone valence isomerism is raised by this experiment. Acetoxy ketone **3** is readily rationalized as a direct product of acetic acid addition to allene oxide **8**, but the available data do not distinguish between this process and a pathway proceeding from the allene oxide to **3** *via* preliminary conversion to cyclopropanone **16**. This ambiguity and the more general problem of valence isomerism must wait more discerning experimentation for resolution and further discussion is accordingly deferred.

During the course of our work evidence accrued that singlet oxygen is generated upon base decomposition

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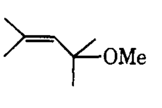
[11] An analog of **9** has recently been isolated from peracid oxidation of an allene: J. K. Crandall, W. H. Machleder, and M. J. Thomas, *J. Amer. Chem. Soc.*, 90, 7346 (1968). The chemistry of the isolated spiro dioxide closely parallels that proposed for **9**.



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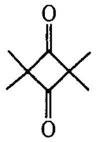

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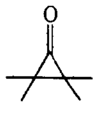

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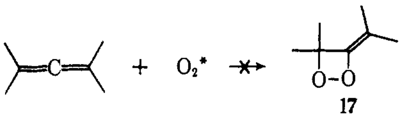
of peracids.[12] In view of the reaction conditions utilized in the oxidation reactions above, it appeared necessary to consider the possible involvement of this oxidant in these reactions.[13] For example, cycloaddition of singlet oxygen to the allene could lead to the heterocycle **17**, which is a conceivable precursor of some of the products (*e.g.*, **5** and **7**) which were rationalized above as coming from spiro dioxide **9**.[11] However, when tetramethylallene was treated with singlet oxygen generated by the hydrogen peroxide–sodium hypochlorite procedure,[13] it was found to be inert.



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In the course of attempting to isolate the allene oxide intermediate, qualitative information on the peracid oxidation was accumulated for a range of experimental conditions. Infrared and nmr examination of product mixtures gave no indication for either of the postulated oxide intermediates, but rather the data were consistently interpretable in terms of a summation of the individual *isolated* components. Methylene chloride was far superior to other solvents studied as a reaction medium. Changes in temperature from −78 to 0° did not appreciably change product mixtures under a given set of reaction conditions. However, at room temperature with addition of peracid to an excess of allene, little of the higher oxidation products were formed. In other experiments generally conducted at 0°, an increase in **4**, **5**, and **6** was evident when the allene was added to the peracid and when the ratio of peracid to allene was increased. The ratio of oxetanone **5** to lactone **6** varied with amount of peracid and reaction time as expected and the amount of unsaturated ketone **7** was also quite variable undoubtedly owing to its further reaction with peracid. In one experiment, *m*-chloroperbenzoic acid was substituted as the oxidizing agent. A thorough product study was not performed, but materials possessing spectral properties appropriate for the *m*-chlorobenzoate analogs of **3** and **4** were obtained. All of this information is consistent with the proposed mechanistic rationale. Our allene epoxidation studies are continuing with the hope of isolating an authentic example of an allene oxide, examining the question of valence isomerism, and confirming the reactivity patterns postulated in the present work.

Experimental Section

General. All nmr spectra were recorded on a Varian A-60 spectrometer. Carbon tetrachloride was used as solvent; chemical shifts are reported as τ values. Infrared spectra were obtained as liquid films with a Perkin-Elmer Infracord Model 137 spectrophotometer unless indicated otherwise. Gas chromatography (glpc) was performed on Aerograph A600 (flame ionization detector) and A700 (preparative) instruments. The analytical columns were 5 ft × $^1/_8$ in. of 15% Carbowax 20M on 60–80 Chromosorb W and 5 ft × $^1/_8$ in. of 10% SE-30 on 80–100 Chromosorb W; preparative columns were 10 or 20 ft × $^3/_8$ in. of 15% Carbowax on 60–80 Chromosorb W. Percentage composition data on product mixtures were estimated by peak areas and are uncorrected except where noted. Analyses were performed by Midwest Microlabs, Inc. Anhydrous magnesium sulfate was used as a drying agent.

Peracetic Acid Solutions. Acetic acid was removed from commercially available 40% peracetic acid by adding the peracid dropwise to a cold mixture of excess anhydrous sodium carbonate suspended in methylene chloride.[9] After the mixture was stirred for 45 min, the inorganic salts were removed by suction filtration through a layer of glass wool and anhydrous magnesium sulfate. The peracid solution, which is subsequently referred to as acetic acid free peracid, was used immediately in the oxidation reaction. Nmr analysis indicated a 95:5 mixture of peracetic and acetic acids. When peracid is mentioned below, this implies that the given amount of 40% peracetic acid was treated according to the above procedure and used as the resulting acetic acid free methylene chloride solution. The total oxidizing activity of the acetic acid free peracid was undiminished as determined by titration with ceric sulfate and sodium thiosulfate.[14]

Oxidation of Tetramethylallene. To a mixture of 89.0 g of peracetic acid and 140 g of sodium carbonate in 400 ml of methylene chloride was added slowly 15.0 g of tetramethylallene. After the mixture was stirred for 51 hr at ice-bath temperature the inorganic salts were removed by suction filtration, and the solvent was removed by spinning-band distillation to give a pale yellow oil. Glpc analysis indicated five significant components which were isolated by preparative glpc. The first component was identified as acetone. The second component was a crystalline solid, mp 45–46°, identified as tetramethyloxetanone (**5**) on the basis of a 5.49 μ carbonyl band in the infrared and a single sharp signal in the nmr at τ 8.60, as well as comparison with an authentic sample.[15] The third component was found to be 2-hydroxy-2,4-dimethylpent-1-en-3-one (**7**) by comparison with a synthetic sample. The fourth component was identified as 2-acetoxy-2,4-dimethyl-3-pentanone (**3**) by comparison with a synthetic sample, as was the fifth component, 2-acetoxy-4-hydroxy-2,4-dimethyl-3-pentanone (**4**). Lactone **6** was not isolated until a subsequent reaction. Its presence here was indicated by characteristic 5.57-μ absorption in the infrared spectrum of the crude product.

In a typical example, the peracetic acid oxidation gave the following product percentages by glpc analysis: **3**, 52%; **4**, 39%; **5**, 3%; **6**, 2%; and **7**, 4%.

2,2,4-Trimethyl-3-oxa-4-hydroxypentanoic Acid Lactone (6). A 2.6-g sample of 40% peracetic acid was added to a mixture of 0.7 g of **5**, 0.6 g of sodium carbonate, and 40 ml of methylene chloride, and the resulting mixture was stirred at room temperature for 63 hr. The inorganic salts were removed by suction filtration and the solvent was removed by distillation to give a 93% conversion of **5** to **6** as calculated by glpc. The structure was confirmed by spectral data: ir 5.57 μ; nmr equivalent sharp singlets at τ 8.48 and 8.60.

Anal. Calcd for $C_7H_{12}O_3$: C, 58.32; H, 8.39. Found: C, 58.09; H, 8.29.

2-Bromo-4-hydroxy-2,4-dimethyl-3-pentanone. To a solution of 3.7 g of 2-hydroxy-2,4-dimethyl-3-pentanone[16] in 20 ml of carbon tetrachloride at reflux temperature was added slowly 4.7 g of bromine. The reaction was almost instantaneous as evidenced by the rapid decolorization of the bromine. The solution was stirred for 1 hr and cooled, and the solvent was removed on the flash evaporator to give 5.3 g of a pale yellow oil. The crude product was purified by distillation to give 4.8 g (82%) of 2-bromo-4-hydroxy-2,4-dimethyl-3-pentanone: bp 73–74° (8 mm); ir 2.78 and 5.87 μ; nmr τ 7.08 (s, 1), 8.02 (s, 6), and 8.53 (s, 6).

4-Hydroxy-2,4-dimethylpent-1-en-3-one (7). A 25-ml portion of *sec*-collidine was added directly to 3.0 g of 2-bromo-4-hydroxy-2,4-dimethyl-3-pentanone and this mixture was refluxed for 2.5 hr. During the reaction a large quantity of solid material formed. The reaction mixture was poured into 120 ml of 2% aqueous hydrochloric acid, precooled to ice-bath temperature, and extracted with 500 ml of ether. The ether extracts were combined, washed with saturated

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[12] E. McKeown and W. A. Waters, *J. Chem. Soc., B*, 1040 (1966).

[13] C. S. Foote, S. Wexler, W. Ando, and R. Higgins, *J. Amer. Chem. Soc.*, **90**, 975 (1968).

[14] F. P. Greenspan and D. G. MacKellar, *Anal. Chem.*, 20, 1061 (1948).

[15] B. L. Murr, G. B. Hoey, and C. T. Lester, *J. Amer. Chem. Soc.*, 77, 4430 (1955).

[16] J. Colonge and J. Dubin, *Bull. Soc. Chim. Fr.*, 1180 (1960).

sodium chloride, and dried. The ether was removed on the flash evaporator, and the crude product was distilled to give 1.3 g (71%) of **7**, bp 59–60° (8 mm). A sample of **7** was further purified by glpc: ir 2.86, 3.33, 6.02, 6.12, and 10.3 μ; nmr τ 3.92, 4.23 (m, 1 each, C=CH_2), 5.86 (s, 1, OH), 8.11 (m, 3, C=CCH_3), and 8.56 (s, 6, C(CH_3)$_2$); uv (EtOH) λ_{max} 221 mμ (ϵ 7700).

Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.37; H, 9.65.

2-Acetoxy-2,4-dimethyl-3-pentanone (3). Diisopropyl ketone (1.0 g) was added to a solution of 4.3 g of lead tetraacetate and 7.4 g of boron trifluoride etherate in 70 ml of acetic acid. The reaction was stirred for several hours at room temperature under a nitrogen atmosphere. After the acetic acid was removed by distillation, the residue was carefully poured into a saturated sodium bicarbonate solution and the inorganic salts formed were removed by suction filtration. The aqueous solution was extracted with ether and the combined extracts dried. The solvent was removed by flash evaporation to give 0.77 g of crude material. A pure sample of **3**[16] was collected by preparative glpc: ir 5.76, 5.82, and 8.00 μ; nmr τ 7.10 (septet, 1, J = 7 Hz), 7.99 (s, 3), 8.57 (s, 6), and 8.98 (d, 6, J = 7 Hz).

2-Acetoxy-4-hydroxy-2,4-dimethyl-3-pentanone (4). 2,4-Dihydroxy-2,4-dimethyl-3-pentanone[17] (1.0 g) was added to 0.62 g of sodium hydride in 30 ml of anhydrous ether. After the mixture was refluxed for 1.5 hr, it was cooled in an ice bath, and an ethereal solution of 0.63 g of acetyl chloride was added slowly. The reaction mixture was stirred for 15 min at 0° and then for 3 hr at room temperature. The solvent was removed by flash evaporation to give 1.4 g of crude product. Glpc analysis indicated one product (69%) plus unreacted starting material. The crude product was purified by column chromatography on silica gel (5% ether–hexane). A sample of **4** was further purified by glpc: ir 2.9, 5.75, 5.83, and 7.9 μ; nmr τ 6.84 (s, 1, OH), 7.93 (s, 3, OAc), 8.36 (s, 6, C(CH_3)$_2$), and 8.55 (s, 6, C(CH_3)$_2$).

Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.32; H, 8.64.

Reaction of Tetramethyloxetanone (5) with Acetic Acid. A solution composed of 40 mg of **5** and 10 mg of mesitylene (used as an internal glpc standard) in 15 ml of methylene chloride was prepared and analyzed by glpc. To this solution was added 60 mg of glacial acetic acid. The solution was stirred at room temperature for 8 days. The reaction solution was washed with two portions of saturated sodium bicarbonate and dried. Glpc analysis indicated complete recovery of starting material.

Baeyer–Villiger Oxidation of 4-Hydroxy-2,4-dimethylpent-1-en-3-one (7). To a solution of 0.5 g of **7** in 20 ml of methylene chloride was added 7.2 g of sodium carbonate followed by addition of 2.2 g of 40% peracetic acid. After stirring for several hours at ice-bath temperature, the mixture warmed to room temperature and stirring was continued for 72 hr. Glpc analysis of the crude product showed complete reaction of **7**. The only new peak present was identified as acetone.

Reaction of 2-Acetoxy-2,4-dimethyl-3-pentanone (3) with Peracetic Acid. To a solution of 0.154 g of **3** and 0.043 g of mesitylene in 10 ml of methylene chloride was added 0.51 g of 40% peracetic acid and 1.7 g of sodium carbonate. The reaction mixture was stirred at room temperature for 70 hr. After the inorganic salt were removed by filtration, the crude product was analyzed by ir and glpc, which indicated complete recovery of starting material. Similar results were obtained with **4**.

Oxidation of Tetramethylallene in the Presence of Propionic Acid. To an ice-cold solution of 2.0 g of tetramethylallene in 50 ml of methylene chloride was added a solution containing 11.9 g of peracid and 9.2 g of propionic acid. After 3 hr, 32.5 g of sodium carbonate was added. The mixture gave a negative starch–iodide test after 47 hr and was worked-up in the usual fashion to give 5.6 g of crude product. In addition to the usual products (**3**, **4**, **5**, and **6**), two new materials were obtained. These were characterized as 2-propionoxy-2,4-dimethyl-3-pentanone (**10**) and 2-hydroxy-4-propionoxy-2,4-dimethyl-3-pentanone (**11**). The assignment of structure **11** is based on spectral data: ir 2.84, 5.75, and 5.82 μ; nmr τ 7.08 (s, 1, OH), 7.73 (q, 2, J = 8 Hz, COCH_2), 8.42 (s, 6, C(CH_3)$_2$), 8.63 (s, 6, C(CH_3)$_2$), and 8.90 (t, 3, J = 8 Hz, COCH$_2$CH_3).

Anal. Calcd for $C_{10}H_{18}O_4$: C, 59.39; H, 8.97. Found: C, 59.24; H, 8.93.

The ratio of major products **3**:**4**:**10**:**11** as determined by glpc was 3.4:1:6.7:1.4.

In a control experiment a mixture of **3** and **4** was stirred with propionic acid in methylene chloride solution for 2 days. Glpc analysis indicated no **10** or **11** at the end of this time.

An ice-cold methylene chloride solution of peracetic acid (3.0 g) containing 2.2 g of propionic acid and 0.6 g of benzene (nmr standard) was stirred for 45 min. Sodium carbonate was then added, and the mixture was stirred for 4 hr. Nmr analysis of the filtrate from this mixture showed that neither propionic nor perpropionic acid was present.

Oxidation of Tetramethylallene in the Presence of Methanol. Tetramethylallene (2.0 g) was slowly added to a mixture of 11.9 g of peracid, 3.3 g of methanol, and 19.3 g of sodium carbonate cooled in an ice bath. After 67 hr the reaction mixture gave a negative peracid test and was worked up in the usual fashion. The crude product (4.6 g) was separated by glpc into six components. Five were identified as **5** (2%), **6** (2%), **7** (2%), **3** (58%), and **4** (27%). The sixth product (3%) was identified as 2-methoxy-4-hydroxy-2,4-dimethyl-3-pentanone (**12**) by spectral data: ir 2.83, 3.51, and 5.81 μ; nmr τ 5.52 (s, 1, OH), 6.66 (s, 3, OCH_3), 8.63 (s, 6, C(CH_3)$_2$), and 8.69 (s, 6, C(CH_3)$_2$). Careful glpc retention time studies, on several different columns with an authentic sample,[18] indicated that 2-methoxy-2,4-dimethyl-3-pentanone (**13**) was not present to any measurable extent in the crude mixture.

A solution of 0.26 g of 40% peracetic acid in 200 ml of methylene chloride was added at a rate of 15 drops per minute to a mixture of 1.27 g of tetramethylallene, 0.6 g of sodium carbonate, and 1.3 g of methanol in 20 ml of methylene chloride cooled in an ice bath. After several hours the reaction mixture warmed to room temperature and was stirred for an additional 68 hr at which point it was treated in the usual fashion. Glpc analysis indicated three major components: acetone, **3**, and a third previously unobserved product. Careful infrared and glpc analysis indicated that the higher oxidation products **5**, **6**, **7**, or **4** were not present in significant amounts in the crude product. The new product was identified as 4-methoxy-2,4-dimethyl-2-pentene (**14**) from its characteristic spectral data: ir 3.34, 3.52, and 9.30 μ; nmr τ 4.98 (m, 1, C=CH), 6.97 (s, 3, OCH_3), 8.21 (d, 3, J = 2 Hz, C=CCH_3), 8.31 (d, 3, J = 2 Hz, C=CCH_3), and 8.79 (s, 6, C(CH_3)$_2$).

Anal. Calcd for $C_8H_{16}O$: C, 74.94; H, 12.58. Found: C, 74.82; H, 12.53.

Reaction of 2-Methoxy-2,4-dimethyl-3-pentanone (13) with Peracetic Acid. A solution of 111 mg of **13** and 46 mg of mesitylene in 6 ml of methylene chloride was prepared. To this solution was added 1.4 g of sodium carbonate and 4.4 g of 40% peracetic acid. The reaction mixture was stirred at room temperature for 48 hr. Glpc analysis indicated that 80% of **13** had undergone reaction, but no new peaks were observed on the glpc trace.

Reaction of Tetramethylallene with Methanol. A solution containing 2.0 g of tetramethylallene and 2.0 g of methanol in 10 ml of methylene chloride was stirred at room temperature for 4 days. The progress of the reaction was followed by glpc. After 21 hr a new product was observed whose retention time was identical with that of 4-methoxy-2,4-dimethyl-2-pentene (**14**). After 91 hr the infrared spectrum of the crude product showed a 5.83-μ carbonyl absorption in addition to absorption bands corresponding to tetramethylallene and **14**. All absorption in the nmr of the crude product could readily be assigned to the starting materials and **14** except for a single sharp singlet at τ 7.90. The appearance of a 5.83 μ carbonyl and a τ 7.90 singlet indicate the presence of acetone. Based on nmr integration, the relative ratio of acetone:allene:**14** was 1:2:2.4.

Photolysis of Tetramethylcyclobutane-1,3-dione in Propionic Acid. A sample of the dione (1.0 g) in 13 ml of propionic acid was photolyzed with 3000-Å light in a Rayonet photochemical reactor for 24 hr. The reaction solution was poured into 50 ml of pentane, carefully washed with saturated sodium carbonate, and dried. After the solvent was removed, 0.8 g (60%) of a crude product was obtained. A pure sample of **10** was collected by glpc: ir 5.74 and 5.81 μ; nmr τ 7.12 (septet, 1, J = 7 Hz, CH(CH$_3$)$_2$), 7.71 (q, 2, J = 7 Hz, COCH_2), 8.57 (s, 6, C(CH_3)$_2$), 8.89 (t, 3, J = 7 Hz, COCH$_2$CH_3), and 8.98 (d, 6, J = 7 Hz, CH(CH_3)$_2$).

Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.23; H, 9.77.

A similar experiment with acetic acid in dioxane as the solvent gave **3** as the only significant product.

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Reaction of Tetramethylallene with Singlet Oxygen.[13] Sodium hypochlorite (100 ml of a 4% solution) was added slowly to a vigorously stirred, ice-cold solution of 2.0 g of tetramethylallene and 6.1 g of 30% hydrogen peroxide in 150 ml of methanol. After 1.5 hr the solution was poured into 500 ml of water and extracted with pentane. The solvent was removed from the dried extracts and the crude product was shown to be recovered starting material by glpc and nmr analysis.

Photochemistry of Electron-Transport Quinones. I. Model Studies with 2-Methyl-1,4-naphthoquinone (Vitamin K_3)

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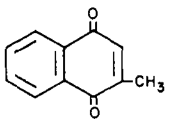
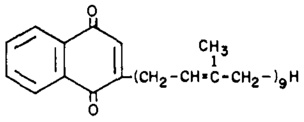
Abstract: The notion that near-ultraviolet radiation induces photochemical modification of electron-transport quinones in bacteria prompted us to study the effects of near-ultraviolet on 2-methyl-1,4-naphthoquinone (vitamin K_3), which can serve as a model for several naturally occurring quinones. Four near-ultraviolet cyclobutane photodimers of vitamin K_3 have been prepared and characterized by nmr, uv, and mass spectral analysis. Sunlight irradiation leads to the formation of the *syn* head-to-head and head-to-tail dimers, in contrast to the previously reported *anti* assignment. The *anti* dimers were prepared by near-ultraviolet irradiation of vitamin K_3 adsorbed on silica gel or dissolved in acetone. Two other photochemical products that were characterized were an oxetane dimer and an uncommon dimer of vitamin K_3 resulting from photochemical oxidation, 3,3′-bi(2-methyl-1,4-naphthoquinone).

In many recent studies concerned with the biological effects of radiation, the far-ultraviolet region of the spectrum (200–300 nm) has received preponderant attention. This was to be expected following the unraveling of deoxynucleic acid structure and the realization that this genetic material is the principal cellular target of far-ultraviolet radiation.[2] Because the irradiation of living organisms with near-ultraviolet light (300–400 nm) is considered to engender somatic rather than genetic damage, far fewer studies have been undertaken to uncover the harmful photomolecular events than has been the case with damage induced by far-ultraviolet illumination. Nevertheless, progress in this direction has been made. Brodie and coworkers[3] have studied extensively the effects of near-ultraviolet irradiation on bacteria and bacterial substructures that perform oxidative metabolism. Their work pinpoints the quinones that serve as electron carriers in electron transport as the principal uv targets and shows that photochemical modification of these quinones disrupts the oxidative and phosphorylative capacities of bacterial respiratory particles. Damage to bacterial quinones has been invoked also by Jagger[4] to explain the decreased sensitivity of *E. coli* B to far-ultraviolet radiation when the bacteria have received a prior or subsequent near-ultraviolet treatment.

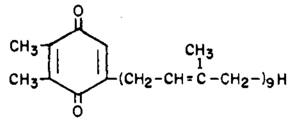
Although these studies leave little doubt that bacterial naphthoquinones and ubiquinones are the natural near-ultraviolet targets, as far as we are aware no reports have appeared on the separation and identification of quinone photoproducts arising *in situ*. Studies encompassing this objective were initiated, and in this publication we report on the near-ultraviolet modification of 2-methyl-1,4-naphthoquinone[5] (I) under several experimental conditions. This simple quinone can be considered as a model for two naturally occurring quinones: demethyl vitamin K_2 (II), which has been identified in *H. parainfluenzae*[6] and *S. faecalis*,[7] and plastoquinone[8] (III), present in plastids and serving as an intermediate in photosynthetic electron transport.[9]



I



II



III

Our studies have led to the isolation and characterization of the four possible cyclobutane photodimers of vitamin K_3 having the *syn* and *anti* head-to-head and head-to-tail configurations. The assignments of *syn* and *anti* isomers were made on the basis of infrared analysis and nmr shielding criteria while differentiation

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