Oxoiminium Ions for N-Demethylation: 1-Oxo-2,2,6,6-tetramethylpiperidinium Chloride

Duncan H. Hunter,* Julie S. Racok, Allan W. Rey, and Yolanda Zea Ponce

Department of Chemistry, University of Western Ontario, London, Ontario, Canada N6A 5B7

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In an attempt to assess the synthetic utility of oxoiminium ions as oxidizing agents and to delineate their reaction mechanisms, we reacted 1-oxo-2,2,6,6-tetramethylpiperidinium chloride (1) with several *N,N*-dialkylanilines. With *N,N*-dimethylaniline the only basic product was *N*-methylaniline while *N*-methylformanilide was the only neutral product. The relative amounts of base and neutral product proved to be sensitive to the amount of water present in the reaction medium. With *N*-alkyl-*N*-methylanilines, the basic products were *N*-alkylanilines from exclusive loss of the *N*-methyl group. The neutral products were the *N*-alkylformanilides. The alkyl groups studied were ethyl, *n*-butyl, isopropyl, and benzyl. With *N*-*tert*-butyl-*N*-methylaniline, there was no observed reaction, and *N,N*-diethylaniline was found to be significantly less reactive than *N,N*-dimethylaniline. This study has shown that 1 is selective in N-demethylation of anilines in the presence of other alkyl groups either on the same nitrogen or on separate nitrogens. These results have been interpreted in terms of important steric interactions resulting from formation of an adduct en route to an intermediate iminium ion.

Oxoiminium salts are an interesting but relatively unexplored class of oxidizing agents in which only a few examples[1-3] have been isolated and characterized. Of these, the 1-oxo-2,2,6,6-tetramethylpiperidinium ion (1) is the first to be reported[3] and is the most studied. The chloride salt of 1 is readily prepared from the corresponding nitroxy radical TEMPO by reaction[4,5] with gaseous chlorine in carbon tetrachloride. The bright orange powder obtained from this reaction can be used without further purification and is stable at room temperature for extended periods. It is slowly bleached by light. We have found that 1 reacts with many typical solvents at room temperature, but for most reactions methylene chloride has proven to be a satisfactory solvent.

Although oxoiminium ions appear to be very reactive, they also show selectivity in their reactions. Thus, for example, 1 reacts with alcohols,[3,6-9] amines,[3,5,10] phosphines,[5] phenols,[5] and ketones[5,11] but not with sulfides, ethers, aldehydes, nor olefins.

The reaction of amines has attracted our attention. While both aliphatic and aromatic amines have been observed to undergo rapid reaction even at low temperatures, we have directed our efforts to understanding the reactions of anilines. We have already reported[5] that *N,N*-dimethylaniline (2) undergoes facile conversion to *N*-methylaniline (3) without apparent production of aniline itself. Since demethylation or dealkylation of amines might be of interest, we decided to look in more detail at this type of reaction. We report the results of treatment of some N,N-disubstituted anilines with 1.

Scheme I

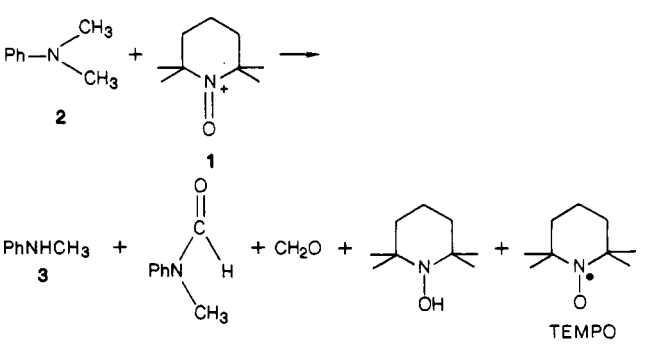

Table I. Effect of the Ratio of Oxoiminium Ion/Substrate on the Reactions of *N,N*-Dimethylaniline (2) at 0 °C and at −80 °C

			% amines		
temp, °C	ratio[a]	% formanilide[b]	total	2	3
0	1.2	30	65	41	24
0	2	10	78	3	75
0	2	13	87	11	76
−80	1		*c*	41	59
−80	1.2		*c*	48	52
−80	2		*c*	0	100

[a] Millimoles of 1/millimoles of 2. [b] *N*-Methylformanilide. [c] Total amines were isolated in about 50% yield by weight.

Results and Discussion

In this study, 1-oxo-2,2,6,6-tetramethylpiperidinium chloride (1) was used exclusively as the oxidizing agent. Its preparation and characterization are described in the Experimental Section, and some of its properties are described above. Workup of reactions of 1 with the various anilines involved separation of crude reaction mixtures into bases and neutrals. Yields were based upon the weights of these materials, which were analyzed for purity and constitution by GC, TLC, and NMR. The hydroxylamine, 1-hydroxy-2,2,6,6-tetramethylpiperidine, was a common side product which interfered with NMR analysis of the bases due to its spontaneous but slow air oxidation to TEMPO. These analyses were facilitated by intentional conversion of the basic hydroxylamine to the neutral TEMPO followed by its removal by extraction.

***N,N*-Dimethylaniline (2).** Most of the attempts to find optimum reaction conditions were run by using 2 as

(1) Osiecki, J. H.; Ullman, E. F. *J. Am. Chem. Soc.* **1968**, *90*, 1078. Boocock, D. G. B.; Ullman, E. F. *J. Am. Chem. Soc.* **1968**, *90*, 6873.
(2) Heinzer, F.; Soukup, M.; Eschenmoser, A. *Helv. Chim. Acta* **1978**, *61*, 2851.
(3) Golubev, V. A.; Rozantsev, E. G.; Neiman, M. B. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1965**, 1898.
(4) Golubev, V. A.; Zhdanov, R. I.; Rozantsev, E. G. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1970**, 186.
(5) Hunter, D. H.; Barton, D. H. R.; Motherwell, W. J. *Tetrahedron Lett.* **1984**, *25*, 603.
(6) Golubev, V. A.; Borislavskii, V. N.; Aleksandrov, A. L. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1977**, 1874.
(7) Semmelhack, M. F.; Chou, C. S.; Cortes, D. A. *J. Am. Chem. Soc.* **1983**, *105*, 4492.
(8) Semmelhack, M. F.; Schmid, C. R.; Cortes, D. A.; Chou, C. S. *J. Am. Chem. Soc.* **1984**, *106*, 3374.
(9) Miyazawa, T.; Endo, T.; Shiihashi, S.; Okawara, M. *J. Org. Chem.* **1985**, *50*, 1332.
(10) Semmelhack, M. F.; Schmid, C. R. *J. Am. Chem. Soc.* **1983**, *105*, 6732.
(11) Golubev, V. A.; Zhdanov, R. I.; Protsishin, I. T.; Rozantsev, E. G. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1970**, 2043. Golubev, V. A.; Zhdanov, R. I.; Protsishin, I. T.; Rozantsev, E. G. *Dokl. Phys. Chem. (Engl. Transl.)* **1970**, *195*, 952. Golubev, V. A.; Miklyush, R. V. *J. Org. Chem. USSR (Engl. Transl.)* **1972**, *8*, 1376.

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Table II. Selectivity in the Dealkylation of *N*-Alkyl-*N*-methylanilines

substrate[b]	% formanilide	% amines[a] total	substrate	3	NRA[c]	NRA/3
4	17[d]	65	0	0	65	≥65
4	30[d]	73	0	0–2	71	35
BMA	17[e]	83	13	0–2	71	35
iPMA	5[f]	92	10	0–1	89	89
BzMA	0	70	0	0	70	≥70

[a] Mole % based on starting aniline. [b] BMA = *N*-butyl-*N*-methylaniline, iPMA = *N*-isopropyl-*N*-methylaniline, BzMA = *N*-benzyl-*N*-methylaniline. [c] NRA = *N*-alkylaniline. [d] *N*-Ethylformanilide. [e] *N*-Butylformanilide. [f] *N*-Isopropylformanilide.

substrate. As illustrated in Scheme I, the products obtained from its reaction with 1 in methylene chloride were identified to be 3, *N*-methylformanilide, formaldehyde as its 2,4-dinitrophenylhydrazone (2,4-DNP), 1-hydroxy-2,2,6,6-tetramethylpiperidine, TEMPO, and the starting material, 2. The relative amounts of these materials proved to be sensitive to the ratio 1/2 and to the amount of water present. Table I presents the results of reactions at 0 and −80 °C in which the ratio 1/2 was changed from 1 to 1.2 to 2. At both temperatures, loss of substrate was essentially complete when 1 was used in onefold excess. Although not included, larger ratios of 1/2 had little effect on the product distribution, and consequently, subsequent reactions were run by using twofold 1. An indication of the reproducibility of our results is shown in lines 2 and 3 of Table I. In all of these reactions, *N*-methylformanilide was produced as the major side product.

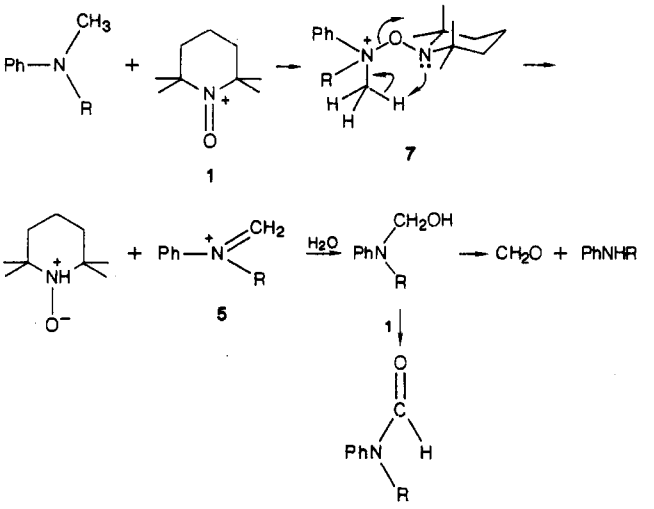
On the basis of the observed products, the reaction sequence shown in Scheme II is postulated, which involves formation of an iminium ion intermediate 5. If water is present in the reaction medium, rapid conversion to the amino alcohol should occur. Because 1 is present, this primary alcohol should oxidize to the formanilide. Unlike alcohols, aldehydes are not readily oxidized[7,9] by 1, and thus the formanilide should be resistant to further reaction. If water is not present, then the reaction should stop at the iminium ion stage. Addition of water during workup should result in hydrolysis of the iminium ion to formaldehyde and 3.

Support for aspects of this scheme comes from other observations. In a duplicate reaction to experiment 6 of Table I, the formaldehyde produced was trapped and weighed as its 2,4-dinitrophenylhydrazone. It corresponded in molar amount to the 3 that had been produced (see Experimental Section for details). Thus the methyl group lost from 2 is converted to formaldehyde. A control reaction using 3 as substrate produced aniline itself. However, aniline is not observed with 2 as substrate. Thus it appears that 3 does not arise until the reaction is quenched with water and the iminium salt 5 is hydrolyzed.

The amount of water present in the reaction medium of a duplicate reaction prior to addition of 1 was measured by Karl-Fischer titration. This adventitious water corresponded in approximate molar amount to the *N*-methylformanilide that was produced. To provide further evidence on the role of water, we ran a series of reactions with varying amounts of water with both 2 and *N*-ethyl-*N*-methylaniline (4) as substrates. When attempts were made to keep the water content low (≤5 mol %), anilines were formed in preference to formanilides. In contrast, the addition of a large excess of water resulted in formation of formanilide exclusive of anilines.

The synthetic utility of this reaction would be improved if the products could be directed to either formanilides or anilines. However, even the most careful drying of solvent and substrate led inevitably to formation of some formanilide. Inclusion of water in excess did not lead to good

Scheme II



yields of formanilide. It is worth mentioning that hydrolysis of the formanilides could result in good combined yields of anilines. We have not pursued this possibility.

***N*-Alkyl-*N*-methylanilines.** One feature of both mechanistic and synthetic interest in the reaction of 1 with anilines was its selectivity. There are two aspects to this selectivity. Does the reagent show a selectivity between alkyl groups on the same nitrogen, and does it show a selectivity between differently substituted nitrogens? The results gathered in Table II are intended to provide answers to the first question. Five *N*-alkyl-*N*-methylanilines were reacted with twofold 1. The alkyl groups chosen were ethyl, *n*-butyl, isopropyl, *tert*-butyl, and benzyl. In the case of *tert*-butyl, no reaction was observed, but for the others which reacted, in no case was more than 2% of 3 produced. Instead, the *N*-alkylaniline was the greatly predominant amine product. The *N*-alkylformanilides were isolated and identified as the only component of the neutral fractions. Thus, if these reactions proceed through an iminium ion as proposed, it is the methyl group exclusively that loses a hydride to form the iminium double bond.

The selectivity shown by 1 suggests that steric interactions play an important role, and thus we have postulated an adduct 7 as an intermediate. This intermediate is analogous to that proposed recently for the oxidation of alcohols.[12] Formation of such an intermediate would account for the selection of methyl over other alkyl groups once 7 is produced, but it would also account for the reluctance of some substrates to react at all. Thus, *N*-*tert*-butyl-*N*-methylaniline did not react and *N*,*N*-diethylaniline (6) was slow to react.

Competition experiments were run in which 1 mmol of 6 competed with 1 mmol of 2 for the 1 that was present. With either 1 mmol or 2 mmol of 1, there was a decided

(12) Semmelhack, M. F.; Schmid, C. R.; Cortes, D. A. *Tetrahedron Lett.* **1986**, *27*, 1119.

preference for reaction of **2** over **6** as judged by the disappearance of **2** and the appearance of **3**. For example, with 2 mmol of **1** the recovered amines contained only 3% of **2** but 75% of **6**. Thus **1** is showing a strong preference for reaction with an *N*-methyl group over an *N*-ethyl group although in this case they are on different anilino nitrogens.

The oxoiminium ion **1** reacts rapidly but selectively with *N*-methyl groups of anilines to produce both the demethylated product and the formanilide, whose relative amounts depend upon the water present. The selectivity for *N*-methyl groups occurs when methyl and alkyl groups are on the same nitrogen or on different nitrogens. It is known that **1** will react rapidly with amines as well as anilines, but the products of these reactions have not been characterized and nothing has been reported on the selectivity of these reactions.

Experimental Section

Instruments. Melting points reported are uncorrected. Gas chromatographic separations and analyses were accomplished with a 6-ft stainless steel column packed with 10% Carbowax 20M on Chromosorb P. HPLC chromatographic analyses were run on a Varian MCH-N-Cap-5 reverse-phase column with acetonitrile–water mixtures as eluant. Water analyses by the Karl–Fischer method were run on a Photovolt Aquatest-IV automatic titrator. Proton NMR spectra ($CDCl_3$) were recorded on a Varian T-60, EM-360, XL-100, or XL-200 spectrometer. Mass spectra were run on a Varian MAT 311A spectrometer.

Reagents. With the exceptions of *N*-methyl-*N*-*tert*-butylaniline and *N*-isopropyl-*N*-methylaniline,[13] the anilines were purchased commercially and distilled before use. These anilines all showed just one spot on TLC and one peak on GC and had proton NMR spectra consistent with their structures. The 2,2,6,6-tetramethylpiperidine was purchased commercially and used without further purification. The 2,2,6,6-tetramethylpiperidinyloxy, TEMPO, was purchased commercially or was prepared by oxidation of 2,2,6,6-tetramethylpiperidine.[14]

2,2,6,6-Tetramethyl-1-oxopiperidinium Chloride (1). Into a solution of TEMPO (15.6 g, 0.1 mol) in 200 mL of carbon tetrachloride at room temperature was bubbled chlorine gas until no further precipitate formed. The insoluble pumpkin-colored solid was filtered and washed several times with fresh carbon tetrachloride. This material was transferred to a round-bottom flask and dried under vacuum overnight by using a vacuum pump, to yield 17 g (90%) of **1** of mp 116–117 °C dec (lit.[4,5] mp 118–119 °C). This product was analyzed for chloride by the Mohr procedure and found to have 0.985 chlorines/molecule.

The product was used without further purification. This material would slowly bleach when exposed to direct sunlight and was somewhat hygroscopic.

Preparation of *N*-*tert*-Butylaniline. To 250 mL of a 1.5 M solution of methyllithium (0.38 mol) in ether at −80 °C was added *N*-phenylacetone imine[15] (17 g, 0.13 mol) in 100 mL of ether dropwise over about 10 min. After a further 15 min, the reaction mixture was poured onto about 20 g of ice in 150 mL of water. The reaction mixture was then extracted with ether, and the ether layer was washed with water, dried, and evaporated to yield 17 g of material, which was analyzed by GC to be a mixture of *N*-phenylacetone imine (65%), aniline (24%), and *N*-*tert*-butylaniline (11%).

The desired amine was isolated first by distillation collecting the material of bp 90–100 °C at 16 mm, which now contained about 35% of *N*-*tert*-butylaniline. Column chromatography on neutral alumina with ether–hexanes as eluant yielded 2 g of material, which gave one peak on GC and one spot on TLC. After redistillation (bp 103–104 °C (21 mm) (lit.[16] bp 97 °C (19 mm))), 1.8 g of material was obtained whose mass spectrum had a molecular ion of *m/e* 149.120; calcd for $C_{10}H_{15}N$, 149.120.

The NMR spectrum showed a singlet (9 H) at 1.3 ppm, a singlet (1 H) at 3.3 ppm, and an aromatic multiplet (5 H) in the 6.8–7.3-ppm range.

Preparation of *N*-*tert*-Butyl-*N*-methylaniline.[17] To a stirred solution of *tert*-butylaniline (770 mg, 5.2 mmol) and formaldehyde (2.2 mL of a 37% solution, 30 mmol) in 20 mL of acetonitrile was added sodium cyanoborohydride (550 mg, 8.8 mmol). After being stirred for 1 h with occasional addition of acetic acid to maintain a pH of about 9, the reaction mixture was taken to dryness on a rotary evaporator. The residue was transferred to a separatory funnel with 2 M sodium hydroxide, which was extracted with ether. The ether extracts were combined and extracted with 1 M hydrochloric acid. The acid layer was made basic with sodium hydroxide and extracted with ether a few times. These combined ether extracts were washed with water and dried, and then the ether was evaporated to yield 604 mg (72%) of a product, which showed one spot on TLC and had a proton NMR spectrum consistent with *N*-methyl-*N*-*tert*-butylaniline.

Distillation of this product (bp 94 °C (19 mm)) resulted in an overall yield of 58% of a material whose mass spectrum gave a molecular ion of *m/e* 163.136; calcd for $C_{11}H_{17}N$, 163.136.

Typical Oxidation Procedure Using 1. Although a number of reactions were run at different temperatures, with different ratios of reagents and modified workup conditions, the following description of the reaction involving **2** is typical of the procedure used for the majority of the reactions in this study.

***N*,*N*-Dimethylaniline.** A 2-mmol sample (382 mg) of dried **1** was placed in a sidearm on a three-necked flask, and then 1 mmol of **2** (128 mg) and 10 mL of dried methylene chloride (≤40 μg of water/mL) were introduced into the flask, which was then cooled in a dry ice–acetone bath. The **1** in the sidearm was added in four portions over about 15 min to the well-stirred reaction mixture. After being stirred for an additional 30 min, the reaction mixture was allowed to warm to room temperature. The reaction was quenched by pouring into an excess of water, which was then acidified with about 10 mL of dilute hydrochloric acid and extracted three times with methylene chloride.

The combined methylene chloride layers were washed with water, dried, and evaporated to yield 240 mg of material, which showed two spots by TLC (1:1 ether–hexanes on alumina) and two peaks by GC. These two components were identified as TEMPO (≈70%) and *N*-methylformanilide (≈30%) by collection of the peaks from the GC. The TEMPO was identical with an authentic sample and did not result in a depressed mixed melting point. The isolated *N*-methylformanilide had an NMR spectrum and IR spectrum consistent with its structure and gave a molecular ion of *m/e* 135.068; calcd for C_8H_9NO, *m/e* 135.068.

The acidic aqueous layer was made basic with excess sodium hydroxide and then extracted with methylene chloride. After a water wash and drying, the solvent was evaporated to yield 375 mg of material, which was analyzed by both TLC and GC. By comparison with the chromatographic properties of an authentic sample, this material was found to contain a large percentage of 1-hydroxy-2,2,6,6-tetramethylpiperidine. This compound slowly air oxidized to TEMPO, which interfered with analysis by NMR.

Consequently this mixture of bases was dissolved in ether and stirred overnight with about 700 mg (3 mmol) of silver oxide. After filtration, the ether was extracted with excess dilute hydrochloric acid, washed with water, and dried. After solvent evaporation, the residue was sublimed (70 °C at 20 mm) to yield 240 mg of TEMPO.

The aqueous layer was made basic and then extracted with ether. The ether layer was washed with water, dried, and evaporated to yield 70 mg of material, which was analyzed by TLC, GC, and NMR to be 90% **3** and 10% **2**.

A control reaction involving **2**, **3**, and 1-hydroxy-2,2,6,6-tetramethylpiperidine showed that the ratio and amounts of the two anilines remained unchanged after treatment with silver oxide.

Isolation and Identification of Formaldehyde as Its 2,4-Dinitrophenylhydrazone. **2** (109 mg, 0.90 mmol) and **1** (351

(13) Gribble, G. W.; Lord, P. D.; Skotnicki, J.; Dietz, S. E.; Eaton, J. T.; Johnson, J. J. *J. Am. Chem. Soc.* **1974**, *96*, 7812.
(14) Rauckman, E. J.; Rosen, G. M.; Abou-Donia, M. B. *Synth. Commun.* **1975**, *5*, 409.
(15) Eaton, D. R.; Tong, J. P. K. *Inorg. Chem.* **1980**, *19*, 740.
(16) Paul, D. F.; Haberfield, P. *J. Org. Chem.* **1976**, *41*, 3170.
(17) Borch, R. F.; Hassid, A. I. *J. Org. Chem.* **1972**, *37*, 1673.

mg, 1.8 mmol) were reacted and then poured into 0.3 M hydrochloric acid by following the procedure described above. After this aqueous layer was washed twice with methylene chloride, it was transferred to a round-bottom flask bearing a glass tube leading into a solution of 2,4-dinitrophenylhydrazine (182 mg, 0.92 mmol) in 10 mL of methanol and concentrated hydrochloric acid (10 drops). Some of the aqueous solution was transferred to the 2,4-dinitrophenylhydrazine solution by distillation, leading to the formation of a yellow precipitate. Filtration yielded 77 mg (41%) of the 2,4-dinitrophenylhydrazone of formaldehyde of mp 165–167 °C.

Two control reactions were run. In one control, the usual procedure was followed but 1 was omitted and no 2,4-DNP was formed. In the other control, the reaction product was simulated by a mixture of TEMPO, 1-hydroxy-2,2,6,6-tetramethylpiperidine, 3, and formaldehyde in methylene chloride. Extraction with dilute hydrochloric acid and distillation led to production of the anticipated amount of the 2,4-DNP of formaldehyde.

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Registry No. 1, 26864-01-7; 2, 121-69-7; 3, 100-61-8; 6, 91-66-7; TEMPO, 2564-83-2; BMA, 3416-49-7; B_2MA, 614-30-2; $PhNH_2$, 62-53-3; $PhN(CH_2CH_3)CH_3$, 613-97-8; $H_3CC(=NPh)CH_3$, 1124-52-3; $PhNHC(CH_3)_3$, 937-33-7; $PhN(CH_3)C(CH_3)_3$, 70974-88-8; $PhN(CH_3)CH(CH_3)_3$, 10545-45-6; $PhNHCH_2Ph$, 103-32-2; $PhNHCH(CH_3)_2$, 768-52-5; $PhNH(CH_2)_3CH_3$, 1126-78-9; $PhNHCH_2CH_3$, 103-69-5; $PhN(CH_2CH_3)CHO$, 5461-49-4; $PhN((CH_2)_3CH_3)CHO$, 35082-00-9; $PhN(CH(CH_3)_2)CHO$, 52008-97-6; $H_3CN(Ph)CHO$, 93-61-8; 1-hydroxy-2,2,6,6-tetramethylpiperidine, 7031-93-8.

Oxidations of Vitamin E (α-Tocopherol) and Its Model Compound 2,2,5,7,8-Pentamethyl-6-hydroxychroman. A New Dimer

Cacang Suarna, Donald C. Craig, Keith J. Cross, and Peter T. Southwell-Keely*

School of Chemistry, University of New South Wales, P.O. Box 1, Kensington, N.S.W. 2033, Australia

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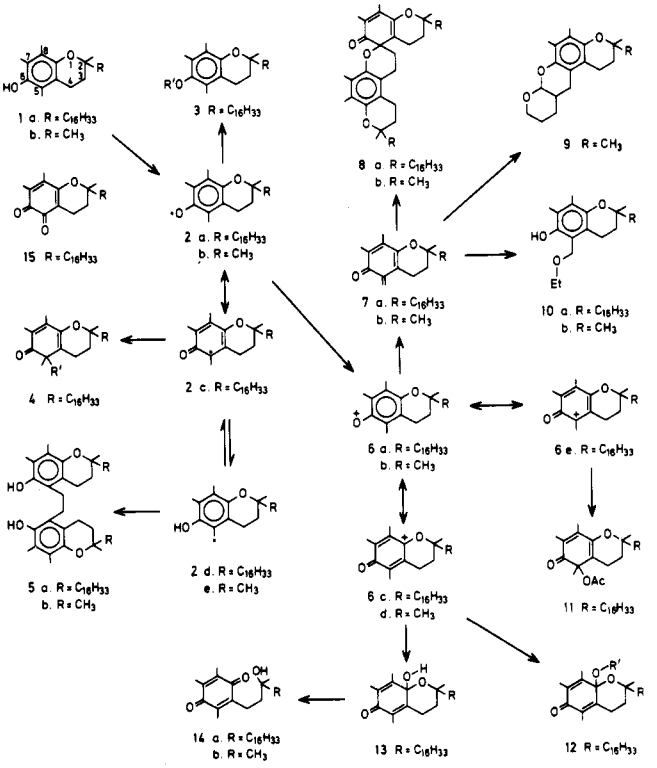
Oxidation of α-tocopherol (**1a**) with *tert*-butyl hydroperoxide in reagent-grade chloroform gave a new dimeric product which appeared to be both aromatic and quinonoid. Repetition of the reaction with the tocopherol model compound 2,2,5,7,8-pentamethyl-6-hydroxychroman (**1b**) gave the corresponding dimer in high yield (30%). This product was shown by two-dimensional, long-range proton–carbon correlation NMR spectra and subsequently by X-ray diffraction to be 2,3-dihydro-3,3,5,6,9,10,11a(*R*)-heptamethyl-7a(*S*)-(3-hydroxy-3-methylbutyl)-1*H*-pyrano[2,3-*a*]xanthene-8(7a*H*),11(11a*H*)-dione (**16b**). It appeared to be formed by Diels–Alder addition of the intermediate quinone methide **7b** to 2-(3-hydroxy-3-methylbutyl)-3,5,6-trimethylbenzo-1,4-quinone (**14b**), a known product of oxidation.

Since the major role of α-tocopherol (**1a**) appears to be that of a cellular antioxidant,[1] much interest has been shown in the products of its reactions, and those of its model compound 2,2,5,7,8-pentamethyl-6-hydroxychroman (**1b**), with many organic and inorganic oxidants.[2,3]

Oxidation of **1a** and **1b** is believed to occur in two single-electron steps leading firstly to the tocopheroxyl (**2a**) and chromanoxyl (**2b**) radicals, respectively (Scheme I).[4-6] **2a** and **2b** are capable of reacting with alkyl radicals to form derivatives at both the 6-phenoxyl (**3**) and also the 5-position (**4**)[7] and also of dimerization to produce stable dihydroxy dimers (**5a**, **5b**).[8]

Loss of a second electron from the initial radicals leads to the phenoxylium (**6a**, **6b**) and subsequently quinone methide (**7a**, **7b**) species both of which are unstable and react further. **6a** and **6b** have not been isolated but such species are known to exist[9,10] and their presence in oxidations of **1a** is inferred from products which include the 8a-hydroxy- (**13**), 8a-alkoxy- (**12**), 8a-acetoxy-, and 5-acetoxy-5-methyltocopherones (**11**)[11-13] and the 1,4-

Scheme I



(1) Burton, G. W.; Ingold, K. U. *Acc. Chem. Res.* **1986**, *19*, 194–201.
(2) Parkhurst, R. M.; Skinner, W. A. In *Heterocyclic Compounds*; Ellis, G. P., Lockhart, I. M., Eds.; John Wiley and Sons: New York, 1981; pp 59–137.
(3) Sumarno, M.; Atkinson, E.; Suarna, C.; Saunders, J. K.; Cole, E. R.; Southwell-Keely, P. T. *Biochim. Biophys. Acta* **1987**, *920*, 247–250.
(4) Matsuo, M.; Matsumoto, S.; Ozawa, T. *Org. Magn. Reson.* **1983**, *21*, 261–264.
(5) Doba, T.; Burton, G. W.; Ingold, K. U. *J. Am. Chem. Soc.* **1983**, *105*, 6505–6506.
(6) Burton, G. W.; Doba, T.; Gabe, E.; Hughes, L.; Lee, F. L.; Prasad, L.; Ingold, K. U. *J. Am. Chem. Soc.* **1985**, *107*, 7053–7065.
(7) Urano, S.; Yamanoi, S.; Hattori, Y.; Matsuo, M. *Lipids* **1977**, *12*, 105–108.
(8) Skinner, W. A.; Alaupovic, P. *J. Org. Chem.* **1963**, *28*, 2854–2857.
(9) Meerwein, H. *Angew. Chem.* **1955**, *67*, 374–380.
(10) Dimroth, K.; Umbach, W.; Thomas, H. *Chem. Ber.* **1967**, *100*, 132–141.

0022-3263/88/1953-1281$01.50/0