Oxidation of Organic Compounds with Cerium(IV). XVI. Relative Rates of Formation of Allyl, Benzyl, and *tert*-Butyl Radicals by Oxidative Cleavage of Alcohols[1]

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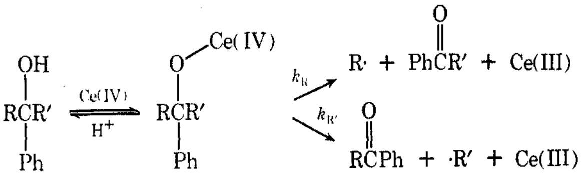
Three tertiary alcohols, allylbenzylphenylmethanol, allyl-*tert*-butylphenylmethanol, and benzyl-*tert*-butylphenylmethanol, were synthesized from the appropriate ketone and Grignard reagent and oxidized in 75% aqueous acetonitrile at 80° by ceric ammonium nitrate. All three alcohols underwent oxidation cleavage to produce ketones and, from the yields of these ketones, it is calculated that the relative rates of formation of the allyl : benzyl : *tert*-butyl radicals by oxidative cleavage are 1 : 4.4 : 19.9–62.9.

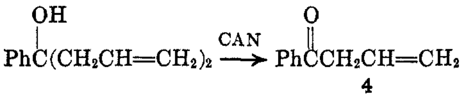
As part of our study of the effect of structure on relative rates of oxidative cleavage of alcohols by cerium(IV), a reaction shown to be a one-electron process,[2] we wished to determine the relative rates of formation of allyl, benzyl, and *tert*-butyl radicals. These are very stable radicals, and previous results have shown that benzyl[2] and *tert*-butyl[3] radicals are cleaved very rapidly from the appropriate alcohols. We chose to measure these rates by oxidizing the appropriate tertiary alcohols and measuring the relative yields of the two possible ketones for several reasons. The relative rates of formation of radicals which are cleaved very rapidly cannot be measured accurately by determining the ratios of benzaldehyde to ketone from the oxidation of the appropriate secondary alcohols (alkylphenylmethanols), since the yields of ketones are very low.[3] Also, for radicals of varying sizes the extent of complex formation for the various alkylphenylmethanols would differ considerably[4] and this variation would have to be taken into account in order to determine relative rates of formation of these radicals. With the tertiary alcohols, only one complex is formed, which then undergoes oxidative cleavage in one of two ways. The phenyl group was chosen as one of the three groups of the tertiary alcohols, since phenyl ketones are resistant to oxidation.



Results

Three tertiary alcohols, allylbenzylphenylmethanol (**1**), allyl-*tert*-butylphenylmethanol (**2**), and benzyl-*tert*-butylphenylmethanol (**3**), were synthesized from the appropriate ketone and Grignard reagent and oxidized in 75% aqueous acetonitrile at 80° by ceric ammonium nitrate (CAN). The ketones produced were identified by glpc peak enhancement with authentic samples and by the nmr spectra of the product mixtures.

All of the ketones were well behaved except allyl phenyl ketone (**4**), which gave an ill-defined glpc peak. The material responsible for this peak was collected and had nmr and ir spectra consistent with a mixture of *cis*- and *trans*-1-propenyl phenyl ketones [nmr ($\mathrm{CCl_4}$) δ 8.0–7.7 (m, 2), 7.5–7.2 (m, 3), 7.0–6.4 (m, 2), and 1.97 (d, $J = 5$ Hz, 3); ir strong bands at 1667 and 1622 cm^{-1}]. Apparently isomerization of **4** to these conjugated ketones occurred during the glpc analysis. An authentic sample of **4** was obtained by the CAN oxidation of diallylphenylmethanol. This reaction is an excellent example of the synthetic utility of the oxidative cleavage reaction, since the only reported synthesis of this base-sensitive ketone is the hydration of 1-phenylbut-3-en-1-yne[5] and synthesis of it by other methods would be difficult.



$$\mathrm{Ph}\overset{\mathrm{OH}}{\mathrm{C}}(\mathrm{CH_2CH{=}CH_2})_2 \xrightarrow{\mathrm{CAN}} \mathrm{Ph}\overset{\mathrm{O}}{\overset{\|}{\mathrm{C}}}\mathrm{CH_2CH{=}CH_2}$$

4

From **1** and **2** $>$95% of the starting alcohol was accounted for but only 85–90% of the starting material was accounted for from **3**. The oxidations of **1** and **2** were very rapid but that of **3** was much slower. It is quite likely that oxidation of some of the benzyl phenyl ketone (**5**) to benzil, a known reaction,[2b] accounts for the missing material. Oxidation of a mixture of **5** and *tert*-butyl phenyl ketone (**6**) with CAN under the reaction conditions showed that **5** is consumed more rapidly than **6**, an expected result since **6** has no α-hydrogen atoms.

In Table I are presented relative yields of the various ketones obtained from oxidation of **1**, **2**, and **3**.[6] From the yields of ketones from **1** and **2**, it is seen that formation of the benzyl radical occurs 4.4 times faster and formation of the *tert*-butyl radical occurs 19.9 times faster than formation of the allyl radical. From these values, the calculated ratio of formation of *tert*-butyl to benzyl radicals is 4.5; however, the directly measured ratio (from **3**) is 8.7. Moreover, if it is

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(1) (a) Part XV: W. S. Trahanovsky, J. R. Gilmore, and P. C. Heaton, *J. Org. Chem.*, **38**, 760 (1973). (b) This work was partially supported by Grant No. GP-18031 from the National Science Foundation. We are grateful for this support. (c) Based on work by D. B. M. in partial fulfillment of the requirements for the M.S. degree at Iowa State University. (d) Alfred P. Sloan Research Fellow, 1970–1972.

(2) (a) P. M. Nave and W. S. Trahanovsky, *J. Amer. Chem. Soc.*, **90**, 4755 (1968); (b) *ibid.*, **93**, 4536 (1971); (c) W. S. Trahanovsky in "Methods in Free-Radical Chemistry," Vol. 4, E. S. Huyser, Ed., 1973, and references cited therein.

(3) W. S. Trahanovsky and J. Cramer, *J. Org. Chem.*, **36**, 1890 (1971).

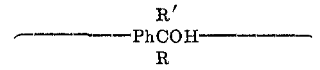
(4) L. B. Young and W. S. Trahanovsky, *J. Amer. Chem. Soc.*, **91**, 5060 (1969).

(5) I. A. Favorskaya, E. M. Auvinen, Y. P. Artsybasheva, and S. M. Kashcheeva, *Zh. Org. Khim.*, **4**, 368 (1968); *Chem. Abstr.*, **68**, 104633d (1968).

(6) In addition to the products listed in Table I, from **1** small amounts of benzyl alcohol and benzaldehyde were detected by their nmr signals and glpc peak enhancement with authentic samples, and there was ir and nmr evidence for benzyl nitrate. From **3**, small amounts of benzaldehyde and benzyl nitrate were detected by glpc analysis.

TABLE I

RELATIVE YIELDS OF PRODUCTS FROM THE CERIC AMMONIUM NITRATE OXIDATION OF VARIOUS TERTIARY METHANOLS[a]



$$\overset{R'}{\underset{R}{\mathrm{PhCOH}}}$$

Alcohol	R	R′	$PhCOCH_2Ph$	$PhCOCH_2CH{=}CH_2$	$PhCOC(CH_3)_3$
1	Allyl	Benzyl	(1)	4.4 ± 0.4[b]	
2	Allyl	*tert*-Butyl		19.9 ± 2.5[b]	(1)
3	Benzyl	*tert*-Butyl	8.7 ± 0.8[c]		(1)

[a] In 75% aqueous acetonitrile at 80°, $^1/_2$[CAN] = [starting alcohol] = 0.0625 *M*. [b] Based on four runs; analyzed by nmr. [c] Based on three runs; analyzed by glpc.

assumed that all of the 15% material balance loss from **3** is due to the oxidation of **4**, then the *tert*-butyl to benzyl radical formation becomes 14.3. Thus, the relative rates of formation of the allyl:benzyl:*tert*-butyl radicals are 1:4.4:19.9–62.9.

Discussion

Bond-dissociation energies indicate that the *tert*-butyl radical is *ca.* 6 kcal/mol less stable than either the allyl or benzyl radicals[7] and thus predict that the *tert*-butyl radical should be less rapidly cleaved from appropriate alcohols than the allyl or benzyl radicals. Although the observed order of formation is not that expected from bond-dissociation energies, other radical reactions have shown the same behavior,[8,11] which has been explained by polar,[9,12] steric,[9,12,13] and conformational effects.[9]

Previous studies have shown that a fair amount of positive charge develops on the radical which is being formed in the transition state of a cerium(IV) oxidation cleavage of an alcohol.[2] There is evidence that the *tert*-butyl cation is significantly more stable than the allyl and benzyl cations[14] and thus a polar effect could account for the more rapid rate of formation of the *tert*-butyl group. The relief of steric strain could also account for the more rapid rate of formation of the *tert*-butyl radical,[12,13] but recent results[15] have shown that relief of steric strain in a radical reaction need not be important. It is also possible that the formation of the allyl and benzyl radicals is abnormally slow owing to conformational effects which restrict the vinyl and phenyl groups from stabilizing the incipient radical to the greatest possible extent. Currently, we are studying systems which we hope will enable us to determine the relative importance of these various effects.

The relative rate of formation of the *tert*-butyl radical indicated by the products of **3** is greater than that obtained from the study of **1** and **2**. The slower rate of oxidation of **3** is no doubt a result of severe steric crowding of the hydroxy group. This increased crowding could further enhance the cleavage of the *tert*-butyl group from **3** for steric reasons or retard the rate of cleavage of the benzyl group from **3** by restricting its conformations.

Experimental Section

Methods and Materials.—Most equipment and materials have been previously described.[1a] A 6 ft × 0.25 in. SE-52 on Fluorpak 80 column was used for glpc analysis. Elemental analyses were performed by Chemalytics, Inc., Tempe, Ariz.

Allylbenzylphenylmethanol (1).—To 2.48 g (102 mmol) of magnesium turnings in 170 ml of ether which was being stirred was added 5.8 g (76 mmol) of distilled allyl chloride (Matheson Coleman and Bell). Some heating was necessary to initiate the formation of the Grignard reagent. To this reagent was slowly added *ca.* 50% of 10.0 g (51 mmol) of benzyl phenyl ketone (Aldrich) in 40 ml of ether. Addition was discontinued when the yellow color which formed at the point of addition no longer faded. The mixture was allowed to stir overnight and was hydrolyzed with 250 ml of 20% ammonium chloride (NH_4Cl) solution. The ether solution was washed with saturated sodium chloride solution, dried ($MgSO_4$), and concentrated to give 6.4 g of a yellow oil which was converted to a colorless oil by chromatographing twice on silica gel columns using a 50:50 pentane–petroleum ether (bp 60–70°) mixture and benzene as eluents: nmr (CCl_4) δ 7.4–6.8 (m, 10), 6.0–4.8 (m, 3), 3.05 (s, 2), 2.9–1.8 (m, 2), and 1.9 (s, 1). *Anal.* Calcd for $C_{17}H_{18}O$: C, 85.67; H, 7.61. Found: C, 85.36; H, 7.51.

Allyl-*tert*-butylphenylmethanol (2).—To the Grignard reagent prepared from 1.85 g (76 mmol) of magnesium turnings and 5.27 g (69 mmol) of distilled allyl chloride in 200 ml of ether was added 7.50 g (46.3 mmol) of pivalophenone[16] (which had been purified by column chromatography) in 50 ml of ether. The mixture was stirred for 6 hr and then hydrolyzed with 125 ml of 20% NH_4Cl solution. After work-up and chromatography on a silica gel column using a 50:50 benzene–petroleum ether mixture as the eluent, a colorless oil (23% yield) was obtained: nmr ($CDCl_3$) δ 7.5–7.1 (m, 5), 5.4–4.8 (m, 3), 3.3–2.3 (m, 2), 1.95 (s, 1), and 0.92 (s, 9). *Anal.* Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.53; H, 9.84.

Benzyl-*tert*-butylphenylmethanol (3).—To the Grignard reagent prepared from 3.5 g (144 mmol) of magnesium turnings and 11.3 g (90 mmol) of distilled benzyl chloride (Baker) was added 7.5 g (46.3 mmol) of pivalophenone in 20 ml of ether. The mixture was stirred for 3 hr and then hydrolyzed with 300 ml of 20% NH_4Cl solution. After work-up and chromatography on a silica gel column using benzene as the eluent a white, crystalline solid (64% yield) was obtained: mp 50.0–51.5° (lit.[17] mp 50–51°); nmr (CCl_4) δ 7.5–6.8 (m, 10), 3.25 (AB quartet, *J* = 13 Hz, 2), 1.40 (s, 1), and 1.00 (s, 9).

Allyl Phenyl Ketone (4).—Diallylphenylmethanol was prepared by the addition of 125 mmol of methyl benzoate to the

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[7] (a) S. W. Benson, *J. Chem. Educ.*, **42**, 502 (1965); (b) J. A. Kerr, *Chem. Rev.*, **66**, 465 (1966); (c) D. M. Golden and S. W. Benson, *ibid.*, **69**, 125 (1969); (d) S. W. Benson, D. M. Golden, and N. A. Gac, *J. Amer. Chem. Soc.*, **91**, 2136 (1969); (e) J. E. Taylor, D. A. Hutchings, and K. J. Frech, *ibid.*, **91**, 2215 (1969); (f) M. P. Halstead, R. S. Konar, D. A. Leathard, R. M. Marshall, and J. H. Purnell, *Proc. Roy. Soc., Ser. A*, **310**, 525 (1969); (g) W. Tsang, *Int. J. Chem. Kinet.*, **1**, 245 (1969); (h) *ibid.*, **2**, 311 (1970); (i) A. B. Trenwith, *Trans. Faraday Soc.*, **66**, 2805 (1970).

[8] Initially it was reported that *tert*-butyl radicals are formed much more rapidly in the β-scission of *tert*-alkoxy radicals than are benzyl radicals,[9] but later work[10] has shown that these results must be reexamined since competing chlorine atom chain reactions have been shown to complicate the results from the decomposition of *tert*-alkyl hypochlorites, especially when benzyl radicals are involved.

[9] C. Walling and A. Padwa, *J. Amer. Chem. Soc.*, **85**, 1593 (1963).

[10] C. Walling and J. A. McGuinness, *ibid.*, **91**, 2053 (1969).

[11] W. A. Pryor, D. L. Fuller, and J. P. Stanley, *ibid.*, **94**, 1632 (1972), and references cited therein.

[12] C. Rüchardt, *Angew. Chem., Int. Ed. Engl.*, **9**, 830 (1970).

[13] R. F. Bridger and G. A. Russell, *J. Amer. Chem. Soc.*, **85**, 3754 (1963).

[14] (a) J. L. Franklin, J. G. Dillard, H. M. Rosenstock, J. T. Herron, K. Draxl, and F. H. Field, "Ionization Potentials, Appearance Potentials, and Heats of Formation of Gaseous Positive Ions," National Bureau of Standards Reference Data Series, No. 26, 1969, and references cited therein; (b) F. P. Lossing and G. P. Semeluk, *Can. J. Chem.*, **48**, 955 (1970).

[15] G. J. Abruscato and T. T. Tidwell, *J. Amer. Chem. Soc.*, **94**, 673 (1972).

[16] J. H. Ford, C. D. Thompson, and C. S. Marvel, *ibid.*, **57**, 2621 (1935).

[17] Ramart-Lucas, *Ann. Chim. Phys.*, [8] **30**, 363 (1913).

Grignard reagent obtained from 250 mmol of allyl chloride. The crude product was purified by chromatography on a silica gel column using benzene as the eluent: nmr ($CDCl_3$) δ 7.4–7.0 (m, 5), 5.9–4.7 (m, 6), 2.50 (m, 4), and 2.14 (s, 1). To 2.96 g (15.8 mmol) of this alcohol in 25 ml of acetonitrile was added 18.95 g (34.6 mmol) of CAN in 20 ml of acetonitrile and 5 ml of water at 80°. After 10 min the initially formed deep red color faded to a light yellow. The mixture was cooled and 50 ml of water and 50 ml of ether were added. The ether layer was separated, washed with saturated NaCl solution, dried ($MgSO_4$), and concentrated. Distillation gave 3.7 mmol (23% yield) of a yellowish oil: bp 59–63° (0.04 mm) [lit.[5] bp 100–102° (0.5 mm)]; nmr ($CDCl_3$) δ 8.1–7.8 (m, 2), 7.6–7.2 (m, 5), 6.4–6.9 (m, 3), and 3.60 (m, 2).

Oxidation Procedure.—Typically, 0.625 mmol of the alcohol, 7.50 mmol of acetonitrile, and 1.25 ml of water were added to a flask equipped with a condenser and magnetic stirring bar. A quantity of 1.25 ml of 1.00 *M* CAN was added, the flask was immersed in an oil bath at 80°, and the solution was stirred. In the case of **1** and **2** an initial dark red color formed which faded to a light yellow after 4 min. In the case of **3** the initial color was bright yellow and it faded to a light yellow after 30 min. After the reaction was complete, the flask was cooled in a water bath and 8 ml of water and 8 ml of ether were added to it. The ethereal solution was washed three times with 8-ml portions of water, dried ($MgSO_4$), and concentrated. The products from **1** were determined by nmr analysis by integration of the signals for the methylene protons of **4** (δ 3.55, m), the benzylic protons of **5** (δ 4.15, s), and the benzylic protons of **1** (δ 3.05, s). In several runs, the total recovery was determined by the use of octadecane or *p*-di-*tert*-butylbenzene as standards. The products from **2** were determined by nmr analysis by integration of the signals for the methyl protons of **2** (δ 0.90, s), the methyl protons of **6** (δ 1.22, s), and the methylene protons of **4** (δ 3.55, m). In several cases, the total recovery was determined by the use of mesitylene as a standard. The products from **3** were determined by glpc analysis using benzophenone as a standard and correcting for thermal conductivity and extraction differences as previously described.[2b]

Stability of Benzyl Phenyl Ketone (5) and Pivalophenone (6) to the Oxidation Conditions.—To 0.193 g (1.00 mmol) of **5** and 0.163 g (1.00 mmol) of **6** in 24 ml of acetonitrile and 7.4 ml of water at 80° was added 0.60 ml of a 1.00 *M* CAN solution. After 30 min at 80°, the mixture was cooled and 0.1822 g of standard (benzophenone) was added. Ether and water (20 ml of each) were added and after extraction the ether layer was separated, washed three times with water, dried ($MgSO_4$), and concentrated. Analysis by glpc (correcting for extraction and thermal conductivity differences) showed 97% recovery of **4** and quantitative recovery of **5**.

Registry No.—**1**, 38400-73-6; **2**, 38400-74-7; **3**, 38400-75-8; **4**, 6249-80-5; **5**, 451-40-1; **6**, 938-16-9; allyl chloride, 107-05-1; benzyl chloride, 100-44-7; diallylphenylmethanol, 38400-77-0; cerium, 7440-45-1.

The Reaction of Oxo-Osmium(VI)–Pyridine Complexes with Thymine Glycols

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We have synthesized *trans*-thymine glycol, *trans*-thymidine glycol, and *trans*-1,3-dimethylthymine glycol by isomerization of the corresponding cis glycols. Both the cis and trans glycols react in aqueous buffer solutions, pH 7–10, with the Os(VI) species, $Os_2O_6py_4$ (formulated by Criegee as OsO_3py_2) to give the corresponding bis(pyridine) *cis*-osmate (VI) esters. The 3-chloropyridine and 3-picoline osmate(VI) esters were also made. Kinetic studies show that the reactions are first order in Os(VI) and in substrate, and inverse first order in pyridine. The rate of reaction increases with increasing pH, but the apparent order in hydroxyl ions is less then one. Labeling experiments with ^{18}O show that ester formation takes place without cleavage of the C–O bond. We also report some observations on the equilibria of the Os(VI) species which suggest a pH-dependent monomer–dimer interconversion and concurrent ligand dissociation.

The radiolysis of nucleic acids, particularly their pyrimidine components, has received a good deal of attention. The recent elegant work of Téoule and Cadet[1] has provided a clearer picture of the course of events for thymine. Twenty-three products of the radiolysis of thymine have been identified. Under typical conditions 25% of the final products are the *cis*- and *trans*-thymine glycols (5,6-dihydroxy-5,6-dihydrothymine). Criegee and his coworkers have shown that the compound then thought to be OsO_3(pyridine)$_2$, among other Os(VI) species, reacts with glycols to form bis(pyridine) osmate(VI) esters.[2] We have shown that these bis(pyridine) esters, in contrast to the uncomplexed esters, are of sufficient hydrolytic stability to allow their easy manipulation in aqueous systems.[3,4] In continuation of our goals of developing selective reactions for the characterization of nucleic acids, we have undertaken this study, which may aid the recognition by electron-microscopic techniques[5,6,7a] of those thymine residues in a DNA molecule damaged by radiolysis. Oxo-osmium species have also been used recently in X-ray diffraction analyses of transfer RNA.[7b]

Results and Discussion

Structure and Equilibria.—Criegee and coworkers[2] formulated the product of the reaction of osmium tetroxide and pyridine in the presence of ethanol as OsO_3py_2. Griffith and Rossetti[8a] have recently presented good spectroscopic evidence which suggests that this compound in the solid state is actually the dimer, $Os_2O_6py_4$, with trans O=Os=O osmyl groups

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[1] J. Cadet and R. Téoule, *Biochim. Biophys. Acta*, **238**, 8 (1971); R. Téoule and J. Cadet, *Chem. Commun.*, 1269 (1971).

[2] R. Criegee, B. Marchand, and H. E. Wannowius, *Justus Liebigs Ann. Chem.*, **550**, 99 (1942).

[3] L. R. Subbaraman, J. Subbaraman, and E. J. Behrman, *Bioinorg. Chem.*, **1**, 35 (1971).

[4] L. R. Subbaraman, J. Subbaraman, and E. J. Behrman, *Inorg. Chem.*, **11**, 2621 (1972).

[5] M. Beer and E. N. Moudrianakis, *Proc. Natl. Acad. Sci. U. S.*, **48**, 409 (1962).

[6] A. V. Crewe, J. Wall, and J. Langmore, *Science*, **168**, 1338 (1970).

[7] (a) R. M. Henkelman and F. P. Ottensmeyer, *Proc. Natl. Acad. Sci. U. S.*, **68**, 3000 (1971); R. F. Whiting and F. P. Ottensmeyer, *J. Mol. Biol.*, **67**, 173 (1972). (b) R. W. Schevitz, M. A. Navia, D. A. Bantz, G. Cornick, J. J. Rosa, M. D. H. Rosa, and P. B. Sigler, *Science*, **177**, 429 (1972); S. H. Kim, G. Quigley, F. L. Suddath, A. McPherson, D. Sneden, J. J. Kim, J. Weinzierl, P. Blattmann, and A. Rich, *Proc. Natl. Acad. Sci. U. S.*, **69**, 3746 (1972); *Science*, **179**, 285 (1973).

[8] (a) W. P. Griffith and R. Rossetti, *J. Chem. Soc., Dalton Trans.*, 1449 (1972). (b) Griffith reports privately that the 640-cm^{-1} band was indeed observed in the ir and that its omission in ref 8a is an error.