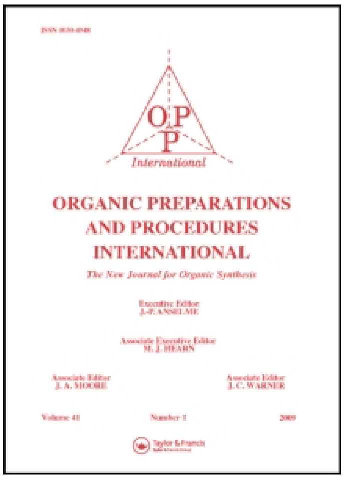


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

A CONVENIENT PREPARATION OF 1-HYDROPEROXY-(1-*p*-NITROPHENYL)ETHANOL BY THE ACID-CATALYZED OXIDATION OF *p*-NITROACETOPHENONE WITH HYDROGEN PEROXIDE

Lázaro F. R. Cafferata[a]; Juan C. Autino[a]
[a] Programa LADECOM (CONICET), Departamento de Química Facultad de Ciencias Exactas, Universidad National de La Plata, La Plata, ARGENTINA

To cite this Article Cafferata, Lázaro F. R. and Autino, Juan C.(1995) 'A CONVENIENT PREPARATION OF 1-HYDROPEROXY-(1-*p*-NITROPHENYL)ETHANOL BY THE ACID-CATALYZED OXIDATION OF *p*-NITROACETOPHENONE WITH HYDROGEN PEROXIDE', Organic Preparations and Procedures International, 27: 4, 483 — 487

To link to this Article: DOI: 10.1080/00304949509458482

URL: http://dx.doi.org/10.1080/00304949509458482

A CONVENIENT PREPARATION OF 1-HYDROPEROXY-(1-*p*-NITROPHENYL)ETHANOL BY THE ACID-CATALYZED OXIDATION OF *p*-NITROACETOPHENONE WITH HYDROGEN PEROXIDE

Submitted by (08/30/94)

Lázaro F. R. Cafferata* and Juan C. Autino

Programa LADECOM (CONICET), Departamento de Química
Facultad de Ciencias Exactas, Universidad
Nacional de La Plata, calle 47 esq. 115, (1900) La Plata, ARGENTINA

The reaction of aliphatic or alicyclic ketones in sulfuric acid-acetonitrile at low temperatures with conc. hydrogen peroxide constitutes an excellent general method for the preparation of the corresponding substituted 1,2,4,5-tetroxanes.[1] However, with aromatic ketones the major products are esters and lactones (Baeyer-Villiger oxidation).[2] Some *gem*-hydroxyhydroperoxides or aliphatic *gem*-bishydroperoxides have been isolated and characterized.[3,4] Ozonolysis in water is a good preparative method,[5] but the *gem*-hydroxyhydroperoxides obtained are generally unstable. Moreover, a stable *gem*-hydroxyhydroperoxide was produced in the benzophenone photosensitized oxidation of 2-propanol by molecular oxygen.[6] We now report the preparation of a particularly stable and chiral *gem*-hydroxyhydroperoxide.

The reaction of *p*-nitroacetophenone (**1**) with hydrogen peroxide in acetonitrile-sulfuric acid at -30-0° gave the products shown, in addition to unreacted **1**. The yields depended strongly on the temperature and the procedure followed (Table).

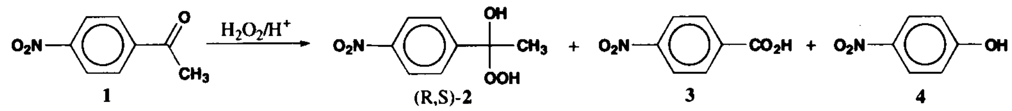
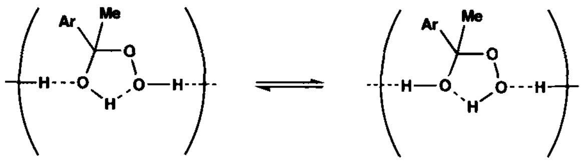


TABLE. Yields (%) of Oxidation Products of 1 with H_2O_2-H_2SO_4[a]

Procedure[b]	Temp. (°C)	1 (Recovered)	2[c]	3	4
A	0	19	45 (56)	2	88
A	-20	28	62 (87)	2	7
A	-30	46	9 (17)	3	41
B	0	33	2 (3)	1	64
B	-20	33	33 (50)	10	23
B	-30	9	69 (82)	9	6

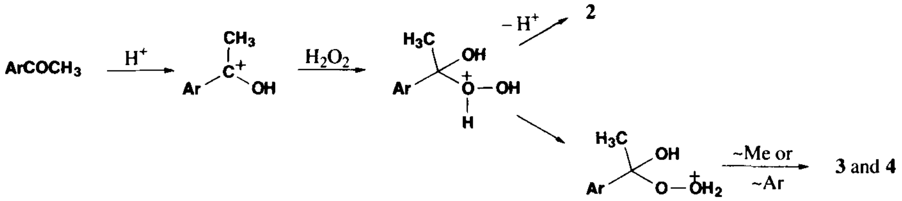
a) The yields were determined by HPLC analysis of the crude reaction mixture after removal of H_2SO_4 (254 nm detection). b) See Experimental Section. c) Based on recovered **1**, in parentheses.

Compound **2** was isolated as a white, microcrystalline substance, mp. (uncorr.) 172-173° (dec. giving off reddish vapors). It reacts[7] with KI in acetone-acetic acid medium giving iodine and its titration against standard aqueous thiosulfate led to the equivalent weight of 98 g equiv^{1} (calcd. 99.5), which shows that **2** behaves as an oxidant. The structure of **2** is suggested on the basis of the following spectral data: IR ν_{max}: 3440 (OH), 1133 (C-OO), 882 cm^{-1} (O-O); bands at 3450, 1325, 1270 and 880 cm^{-1} have been assigned to some hydroperoxides, being highly characteristic for these compounds.[8] ^{1}H NMR (acetone-d$_6$): the low field peak at 9.15 ppm (br s) assigned to the OOH group,[9] might be the result of rapid proton exchange.



^{13}C NMR: δ_c 110.52, attributable to a carbon bearing HO, HOO and C substituents. A similar value (108 ppm) for C-3 of 3-hydroxyphthalide[10] with a C-3 methyl, can be calculated using correlation charts. The UV of **2** has a band at 264 nm (log ε 4.07) which is present in many hydroperoxidic compounds.

Although **2** has geminal hydroxyl and hydroperoxyl groups, it is sufficiently stable to survive procedures employed for its isolation and purification. However, it was not possible to recrystallize the crude reaction product because **2** was sparingly soluble in the common organic solvents. Instead, sublimation, though lengthy and time consuming, was the most efficient procedure to eliminate impurities from **2** (unreacted **1** and rather volatile **3** and **4**). Compound **2** could be chromatographed on silica gel (rapid TLC), although slight decomposition to **1** was observed. It has already been suggested that the presence of electronwithdrawing groups on the carbon atom bearing a hydroperoxyl substituent enhances the thermal stability of that hydroperoxide molecule. The formation of the observed products could be rationalized as shown.



It is worth noting that *p*-nitrophenyl acetate was not detected among the products. Perhaps, the reason for the formation of the hydroxyhydroperoxide is the reluctance of the *p*-nitrophenyl to migrate. Chiral HPLC analysis led to resolution of racemic **2**.

Compound **2** as solid is safe to be handled and non-explosive on impact. It decomposes in DMSO at room temperature giving a yellowish solution. Its thermal decomposition in boiling acetone (~4 10^{-3} M, 4 hrs) gave ketone **1** in nearly quantitative yield; its decomposition in methanol (~10^{-3} M, 1 week) or in boiling water or boiling glacial acetic acid (~10^{-3} M, 4 hrs) also yields **1** as the major product (GC and HPLC). These results, which support the proposed structure, show that on solvolysis, compound **2** does not lead to aryl migration to yield the phenol **4**, as would be expected from the behavior of most hydroperoxides;[2a] this could be rationalized by the fact that in **2** the aryl group is *p*-nitrophenyl.

Work on the effect of substituents on the oxidation of analogous ketones is currently in progress in this laboratory.

EXPERIMENTAL SECTION

The TLC was carried out on Merck silica gel-60 aluminum-backed sheets with fluorescent indicator at 254 nm. The HPLC analyses of the acid-free reaction mixtures were performed at 25° with 73% v/v methanol-water, flowrate 0.2 mL/min in a LKB instrument equipped with a 20 μL loop Rheodyne injection valve, Spherisorb SuperPac RP-18 column (ODS, 2.5 μm, 4.0 x 100 mm) and UV detection at 254 nm. In these conditions the retention time of **2** was ca. 15.1 min and the other products showed optimal resolution at shorter RT. The isomeric analysis was performed by HPLC using a chiral column (4.0 x 150 mm) packed with cellulose *tris*-(3,5-dimethylphenylcarbamate), and a Chiralyser detector (IBZ Messtechnik, Hannover, Germany) in series with a UV detector at 254 nm. In this case the solution of **2** in acetone was run at 23° with *n*-hexane ethanol azeotrope (9:1 v/v} as mobile phase, and 1 mL/min flow. GC analyses were performed on a Hewlett-Packard model 5840A instrument with a fused silica capillary column {HP-SP-2100, 30 m length, 0.25 mm i.d., 150°) with FID detection. The injection temperature was 80° and the carrier gas was nitrogen at 1 mL/min flowrate. In this case, for the quantitative determinations of **1** (RT 6.28 mm) in the thermolysis of **2**, naphthalene (RT 2.24 min) was used as internal standard. The IR spectra (KBr disks) were obtained on a Model 435 Shimadzu spectrophotometer. The ^{1}H NMR and ^{13}C NMR spectra were measured at 200 and 50.2 Hz respectively in an ACE-200 Bruker spectrometer at 20° and are reported in ppm downfield TMS. The UV was recorded with a Hewlett-Packard model 5482A instrument.

Preparation of 1-Hydroperoxy-1-(p-nitrophenyl)ethanol (2). *Procedure A*.- Conc. sulfuric acid (2 mL) was added to a cold (-20°) suspension of **1** (4 g, 24 mmoles) in MeCN (5 mL) with stirring, followed by successive dropwise addition of MeCN (7 mL) and hydrogen peroxide (66% v/v, 2 mL) *(CAUTION: Use an explosion proof safety screen!)* to the agitated slurry. The solid obtained was stirred further at the indicated temperature (see Table) for 3 hrs, and the oily yellowish precipitate was centrifuged. It was thoroughly washed with water until the washes were neutral and then with several portions of methanol. The finely powdered crude solid obtained, which contained some of the unreacted **1** and the by-products, was dried at ~1 Torr and 30°, and then was purified by sublimation at 20° and 0.1 Torr for 3 hrs, cooling with liquid air. The solid **2** (2.86 g, 60%) which remained (mp. 172-173°, dec) was nearly pure by TLC and GLC (see above).

Procedure B.- Hydrogen peroxide (66% v/v, 2 mL) *(CAUTION!)*, followed by conc. sulfuric acid (2 mL) were dropwise added to 10 mL of cold MeCN (-30°). Then, a solution of **1** (24 mmoles) in MeCN (5 mL) was added to that solution over a period of 1 hr, and the reaction mixture was stirred further (2 hrs) at this temperature. The yellowish precipitate was worked up and purified as described in Procedure A, yielding 3.14 g (66%) of **2**. The TLC analysis of **2** shows R_f 0.4 with toluene-MeOH (90:10 v/v) mixture as eluent, with slight decomposition to **1**. Compound **2** is sparingly soluble in most common organic solvents such as acetonitrile, MeOH, AcOEt and even acetone (~0.19 g/100 mL at reflux, with decomposition).

It is worth mentioning that the usual chromatographic methods on silica gel or alumina columns were unsuccessful for the purification of **2** (especially in the latter adsorbent) because of substantial loss of material by decomposition. Furthermore, reasonably pure **2** (99% w/w by GC analysis of the **1** formed in its thermolysis in boiling acetone; 92% w/w by HPLC with 254 nm detection) was obtained after removal of most of the volatile impurities by careful sublimation under the above conditions.

Anal. Calcd. for $C_8H_9NO_5$: C, 48.24; H, 4.56; N, 7.03. Found: C, 48.40; H, 4.62; N, 7.43

IR (KBr): 3440 m (OH), 3110 w, 3000 w, 1600 m, 1515 s (N-O), 1490 m, 1405 m, 1340 s (N-O), 1315 w, 1263 m (C-O), 1133 m (C-OO), 1112 m, 1100 m, 1080 m, 1010 m, 978 w, 882 m (O-O), 850 s (C-N), 758 m, 700 m, 610 m.

^{1}H NMR (200 MHz, acetone-d_6): δ 1.79 (s, 3H, CH_3), 7.85, 8.27 (A_2X_2, 2H ea, Ar), 9.15 (br s, OH).

^{13}C NMR (50.2 MHz, acetone-d_6): δ_c 23.78 (CH_3), 110.52 (HO-C-OOH), 124.08 (C-3'), 128.45 (C-2'), 142.12 (C-4'), 147.09 (C-1'). UV (MeOH, c 5.10^{-5} M) λ_{max}/nm (log ε): 204 (4.10), 214 sh (3.93), 264 (4.07).

ACKNOWLEDGEMENTS.- The cooperation of Lic. M. M. Schiavoni in the early stages of this work is very much appreciated. The HPLC analysis using the chiral column and detector were performed in the Zentrum for Selektive Organische Synthese (Berlin, Germany), by Prof. Annamarie Kunath, to whom the authors wish to express their recognition. The financial support of CONICET and Universidad Nacional de La Plata (ARGENTINA) is acknowledged.

REFERENCES

1. M. Schulz and K. Kirschke, in *Organic Peroxides,* Vol. 3, CH II, D. Swern, Ed., John Wiley & Sons, NY, R. E. Krieger Publ. Co., Malabar, FL, 1972. Reprint edition 1981.
2. a) J. March, *Advanced Organic Chemistry,* 3rd. Ed., John Wiley & Sons, New York, NY, 1985; b) H. D. House, *Modern Synthetic Reactions,* 2nd. Ed., W. A. Benjamin, New York, NY, 1972.
3. K. J. McCullough, A. R. Morgan, D. C. Nonhebel and P. L, Pauson, *J. Chem. Res. (5),* **85**, 34 (1980).
4. M. S. Kharasch and G. Sosnovsky, *J. Org. Chem.,* **23**, 1322 (1958).
5. a) P. S. Bailey, *Ozonation in Organic Chemistry. Olefinic Compounds,* Academic Press, New York, NY, Vol. 1 (1978); b) K. J. McCullough and M. Nojima in *Organic Peroxides,* CH 13, W. Ando, Ed., John Wiley & Sons, Chichester, 1992.
6. G. O. Schenck and H. D. Becker, *Angew. Chem.,* **70**, 504 (1958).
7. R. M. Johnson and I. W. Siddiqui, *The Determination of Organic Peroxides,* CH 5, p. 15, Pergamon Press, Oxford, 1970.

8. V. A. Terent'ev and V. L. Antonovskii, *J. Gen. Chem. USSR*, **34**, 1525 (1964).

9. D. A. Casteel and K. E. Jung, *J. Chem. Soc., Perkin Trans. I*, 2597 (1991).

10. E. Breitmaier and A. Voelter, *"Carbon-13 NMR Spectroscopy"* CH 4, p. 232, 3rd. Ed,, Verlag Chemie, Weinheim, 1989.

11. W. V. Turner and S. Gab, *J. Org. Chem.*, **57**, 1660 (1992).

****

NEW CONDENSATION PRODUCTS OF DIAMINES WITH 3-UREIDOMETHYLENECOUMARIN

Submitted by
(02/14/94)

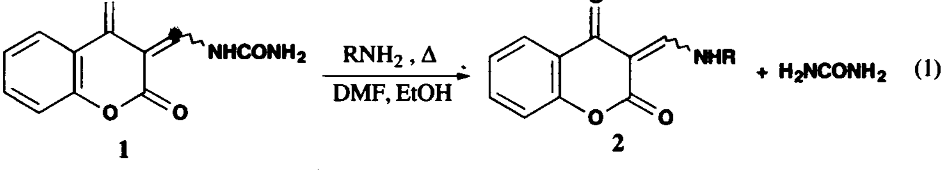
M. Hamdi

Laboratoire des Composés Organiques Hétérocycliques
Institut de Chimie, Université des Sciences et de la Technologie
B.P. 32 El-Alia, Bab Ezzouar, Alger, ALGERIA

and R. Sakellariou and V. Spéziale*

Laboratoire des Interactions Moléculaires
et Réactivité Chimique et Photochimique, CNRS URA 470
Université Paul Sabatier
118 Route de Narbonne, 31062 Toulouse Cedex, FRANCE

A recent publication described the facile synthesis of N-(methylene-4-oxocoumarinyl)-amines (**2**) by reaction of 3-ureidomethylenecoumarin (**1**) with a variety of substituted amines to afford a single product in good yield.[1]



The possibility that diamines might react further intermolecularly or intramolecularly [2] at either of the two carbonyl groups, prompted us to examine the interaction of diamines with **1**.

The reactions of equimolar amounts of **1** and **3** were carried out at reflux in DMF-ethanol for 3 hrs. With 1,2-diaminoethane and 1,2-diaminopropane (**3a** and **3b**), thin layer chromatography showed the formation of a single product in both cases. Their ^{1}H NMR spectra showed the presence of two