Table I
The Oxidative Decyanation of Secondary Nitriles 2 to Ketones 3

R	R'	Isolated yield of ketone 3, %
CH_3	$CH_2(CH_2)_3CH_3$	67
CH_3	c-C_6H_{11}	78
CH_3	CH_2Ph	82
CH_2Ph	CH_2Ph	90
CH_2Ph	$CH_2(CH_2)_2CH_3$	83
CH_2Ph	c-C_5H_9	70
	$-(CH_2)_5-$	64[a]
Ph	CH_3	86
Ph	CH_2CH_3	69
Ph	$CH(CH_3)_2$	81
Ph	c-C_6H_{11}	74
p-FPh	CH_3	92
p-ClPh	CH_3	79
α-Np	CH_3	80
p-PhPh	CH_3	82
Ph	Ph	92

[a] Isolated as the 2,4-dinitrophenylhydrazone derivative.

dehydes[10] 3 (R' = H). However, secondary carboxylic esters underwent α-hydroxylation in good yield.[11]

The following is a typical experimental procedure. To a solution of 1.1 mmol of lithium diisopropylamide in 3.0 ml of THF at −78° under a nitrogen atmosphere was added 145 mg (1.0 mmol) of 2 (R = CH_2Ph; R' = CH_3) in 1.0 ml of THF. Dry oxygen gas was bubbled (250 ml/min) into the lithionitrile solution for 30 min at −78°. The reaction was quenched with 2 ml of 1 *M* stannous chloride in 2 *M* hydrochloric acid and allowed to stir for 30 min at 0°. Following an ether–water work-up procedure which involved washing with 1 *M* sodium hydroxide, the product was chromatographed on Merck silica gel F254 to afford 110 mg (82%) of phenylpropanone which was identical with an authentic sample.[12]

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(6) Previous reports on the oxidation of nitriles were limited to aryl substituted acetonitriles, failed to isolate the intermediate α-hydroperoxynitriles, and noted the formation of dimeric products: (a) M. S. Kharasch and G. Sosnovsky, *Tetrahedron*, **3**, 97 (1958); (b) H. G. Aurich, *Tetrahedron Lett.*, 657 (1964); (c) S. S. Kulp, *Org. Prep. Proced.*, **2**, 137 (1970). In our hands, these procedures failed to convert dialkylacetonitriles to ketones.
(7) α-Hydroperoxynitriles **6a** have also been prepared from azobisnitriles $R_2C(CN)N{=}NC(CN)R_2$: (a) M. Talat-Erben and N. Onol, *Can. J. Chem.*, **38**, 1154 (1960); (b) L. Dulog and W. Vogt, *Tetrahedron Lett.*, 5169 (1966).
(8) Other reducing agents [HI, $NaBH_4$, $P(OCH_3)_3$, Zn–HOAc] were effective but less convenient than stannous chloride which was reported to effect the quantitative reduction of alkyl hydroperoxides to alcohols: D. Barnard and K. R. Hargraves, *Anal. Chim. Acta*, **5**, 476 (1951).
(9) All compounds had ir, nmr, and mass spectral data in accord with assigned structures. The acetate derivatives **6b**, isolated in a majority of instances, gave satisfactory elemental analyses.
(10) For example, phenylacetonitrile and 3-phenylpropionitrile afforded benzaldehyde and phenylacetaldehyde in 43% and 8% yield, respectively. The formation of carboxylic acids in the oxidation step of the sequence accounted for the low yields of aldehydes.
(11) For example, methyl cyclohexanecarboxylate afforded the α-hydroxy derivative in 69% yield. Similar α-hydroxylations of carboxylic esters have recently been reported: (a) E. Vedejs, *J. Amer. Chem. Soc.*, **96**, 5944 (1974); (b) P. E. Pfeffer and L. S. Silbert, U.S. Patent 3,652,612 (March 28, 1972) [*Chem. Abstr.*, **76**, 139938z (1972)].

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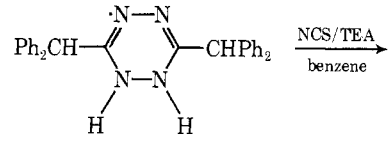
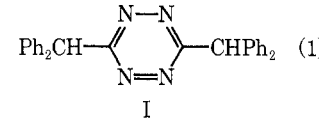
A Mild and Efficient Oxidizing Agent for Dihydroxybenzenes

Summary: A mild, efficient oxidizing reagent, *N*-chlorosuccinimide–triethylamine complex, is reported for the conversion of *o*-quinones from catechols and diphenyldiazomethane from benzophenone hydrazone and oxidative coupling of anthrone to bianthrone.

Sir: In the course of the preparation of the tetrazine I (*e.g.*, reaction 1), we discovered a marked activation effect of triethylamine (TEA) on the oxidation reactions of *N*-chlorosuccinimide (NCS).





(1)

I

Preliminary experiments indicate that the TEA–NCS reagent is a mild oxidizing agent for the conversion of catechols to *o*-quinones, hydroquinones to *p*-quinones, benzophenone hydrazone to diphenyldiazomethane, and *p*-toluenesulfonylhydrazide to *p*-toluenesulfonyl chloride and the coupling of anthrone to bianthrone. While the scope and limitations of this reagent are still under investigation, we report here on the oxidation of some dihydroxybenzenes.

There exists a number of methods for the oxidation of hydroquinones and catechols to quinones. Chromic and nitric acids,[1-3] ferric chloride,[4,5] silver oxide,[6] silver carbonate/Celite,[7] manganese dioxide,[8] sodium dichromate,[9] sodium chlorate/vanadium pentoxide,[10] thallium triacetate,[11] iodic acid,[12] cerric ammonium nitrate,[13] and *o*-chloranil[14] have been used for this transformation. Pfitzner–Moffatt[15] type oxidations have also been employed recently by Martin, *et al.*,[16] to convert hydroquinone to quinone.

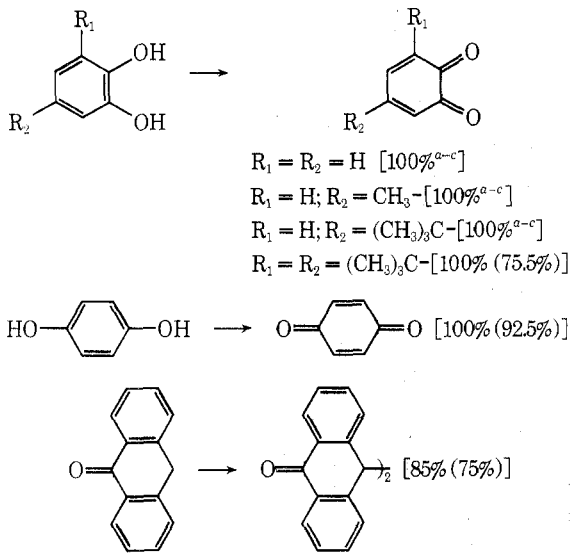
Scheme I is indicative of the efficacy of the TEA–NCS reagent.

The reaction is rapid (~10 min), quantitative (*via* nmr and ir), and takes place under mild conditions (−25 to 0°). In the case of catechol oxidations, only the red form of the *o*-quinone was observed.

The following control experiments are indicative of the specific effect of TEA: (1) the hydroxy benzenes did not react with NCS in the absence of TEA, and (2) contrary to recent reports on other aliphatic hydroxyl oxidations,[16,17] the hydroxy benzenes *did not* react with NCS in the *presence* of dimethyl sulfide (DMS) and the *absence* of TEA.

To our knowledge, TEA–NCS has not been used in the past as an oxidizing reagent. However, pyridine was used in the moderate yield NCS oxidation of alcohols to ketones.[18]

Scheme I



[a] Percentage obtained by nmr and ir analysis. [b] Isolated yields are in parenthesis, identical with authentic sample, one spot on tlc, no depression in mixture melting point. [c] Sterically unhindered *o*-quinones are unstable in concentrated solution, undergoing both polymerization and Diels–Alder dimerization. The degradation (at 35°) could be followed by nmr and a black polymer was rapidly formed in concentrated solution. However, dilute solutions of the beautiful red material could be kept for several days with no extensive degradation at 5–10°. It is best to use these unhindered *o*-quinones relatively soon after synthesis.

Corey and Kim[17] have noted that, in the NCS–DMS oxidations, TEA was the base of choice that gave the best yields.

A typical experimental procedure is given below.

To a stirred and cooled (−25°) solution of 400 mg (3 mmol) of *N*-chlorosuccinimide in 15 ml of methylene chloride was added 445 mg (2 mmol) of 3,5-di-*tert*-butylcatechol. After a 10-min interval, 0.3 ml of TEA was added dropwise. Stirring at −25° was continued for 10 min. The mixture was filtered and the filtrate evaporated. The dark red residue was dissolved in hot hexane, filtered, evaporated down to a few milliliters (until crystallization was apparent), and allowed to cool. The crystalline product (333 mg, 75.5%) thus obtained was identical in all respects with authentic *o*-quinone (Aldrich Chemical Co.).

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(19) J. P. Marino and A. Schwartz [*Chem. Commun.*, 812 (1974)] have reported a similar oxidation using NCS–DMS–TEA to form *o*-quinones and *p*-quinones in high yields. Interestingly these authors comment on the necessity for TEA but did not comment on its activating and accelerating effect. They also confirmed our control experiments. In the initial part of this work we performed the reaction with and without DMS present and found that there was no significant difference in yield or product distribution between the two reactions except in the coupling of anthrone, where a slightly purer product was obtained. Thus we feel that, when DMS is present, it may participate in the reaction but in many reactions it may not be necessary.

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γ-Alkylation of 2-Butynoic Acid. A Route to Controlled Prenol Homologation

Summary: The novel γ-alkylation of 2-butynoic acid allows a facile synthesis of *Z* trisubstituted olefins, and of *Z* isoprenoid systems in particular.

Sir: The elaboration of polyisoprenoid compounds has recently been the focus of numerous studies owing to the crucial role of polyisoprenoids in many biological systems. Insect juvenile hormones[1] and insect sex attractants[2] are isoprenoid in nature. The long-chain polyprenols exemplified by bactiprenol and dolichol participate in polysaccharide and glycoprotein synthesis in both prokaryotic and eukaryotic systems.[3]

The synthesis of *E* polyisoprenoid systems has been well established, and new preparations are still being described.[4] There are, however, very few preparations of *Z* trisubstituted olefins.[2,5,6] Recently Casey and Marten[5] reported a technique for isoprenoid synthesis involving γ-alkylation of methyl acetoacetate[5a] and stereospecific olefin synthesis using enol acetates and lithium dimethyl cuprate.[5b] We wish to report an alternative route to (*Z*)-isoprenols permitting a greater degree of stereoselectivity in the olefin synthesis. The technique involves the novel γ-alkylation of 2-butynoic acid (**1**) with 1-bromo-3-methyl-2-butene (**2**), esterification of the resulting 7-methyloct-6-en-2-ynoic acid (**3**), and treatment of this methyl ester (**4**) with lithium dimethyl cuprate[7] to give the desired methyl (*Z*)-3,7-dimethylocta-2,6-dienoate (**8**). This ester is reduced to nerol [(*Z*)-3,7-dimethylocta-2,6-dien-1-ol, **9**] with AlH_3.[8]

Alkylation of α,β-unsaturated esters and aldehydes always leads exclusively or preponderantly to α substituanion of methyl 2-butynoate primarily in the α position, giving the allene, methyl 2,3-butadienoate, as the major product. Katzenellenbogen and Crumrine[10] were able to partially γ-alkylate the copper(I) dienolate of ethyl (*E*)-3-methyl-2-hexenoate with allyl bromide, but use of 3,3-disubstituted allyl bromides gave only α-alkylation.

The development of α-alkylation of carboxylic acids *via* their dianions[11] suggested to us that the negatively charged dianion of 2-butynoic acid might be delocalized in such a way that the alkylation process would favor γ-alkylation.

We found that treatment of 2-butynoic acid (**1**) with slightly more than a 2 molar ratio of lithium 2,2,6,6-tetramethylpiperidide[12] yields a dianion (**1a**) which, when alkylated with 1-bromo-3-methyl-2-butene (**2**), yields a mix-