Table I
Pseudo-First-Order Kinetics in the Reaction of Biphenyl Radical Anion with Biphenyl 4-Halides

| Registry no. | $C_6H_5-C_6H_4X$ X = | Temp, °C | $k \times 10^4$, $s^{-1}$ | $\Delta H$, cal $deg^{-1}$ $mol^{-1}$ |
|---|---|---|---|---|
| 324-74-3 | F | −100 | 2.58 ± 0.5 | |
| 2051-62-9 | Cl | −40 | 10.8 ± 0.9 | 15.4 ± 2.5 |
| | | −50 | 2.43 ± 0.5 | |
| 92-66-0 | Br | −40 | 14.4 ± 0.9 | 22.8 ± 3.7 |
| | | −60 | 1.44 ± 0.5 | |
| 1591-31-7 | I | −40 | 422. ± 10 | 17.8 ± 2.5 |
| | | −60 | 11.6 ± 1.0 | |
| 2920-38-9 | CN | 22 | 0.0362 ± 0.001 | |

−40° these materials were highly unstable, and below about −70° the reaction times were rather too long to measure accurately. From these measurements a very rough estimate of the activation energies may be calculated. The value obtained for 4-bromobiphenyl appears rather high, yet considering the error range, all three are somewhat similar. Nevertheless, the reaction rates of the halides Cl, Br, and I at −40° are sucessively more rapid. Since the reaction of 4-fluorobiphenyl with biphenyl$\cdot^-$ was too rapid to measure at temperatures higher than −100°, we were not able to attempt an activation energy calculation for it.[10]

We are presently investigating the corresponding naphthyl halide series, and expect to report on them in the near future.

## Experimental Section

All compounds and solvents used in this study are available from Aldrich Chemical Co. and were used as purchased (with the exception of solvents—distilled and stored over Na metal). The glass reduction apparatus in its simplest form has been described earlier.[4] The EPR instrument used is a JES-ME-1X (Jeolco) with variable temperature accessory of the Universidad de Los Andes.

A typical kinetic run may be described as follows. The sample tube (in which the K mirror and the ca. 0.3 mg of aromatic compound in 1 ml of 2:1 THF–DME solution are maintained separately) was cooled in a bath consisting of a thick syrup of isopropyl alcohol and liquid nitrogen at −135°. The sample tube was tipped and the solution allowed to contact the metal mirror for almost 1 s. On righting the tube for insertion into the cavity, the solution was agitated a bit in a bulge provided on the tube for mixing. The tube was rapidly wiped of alcohol and inserted into the precooled cavity (−135°). By this time, however, the tube itself was usually ca. −100° (the lowest temperature available for measurement). As soon as an appropriate temperature was reached, the diminution of the nine-line biphenyl signal produced was followed in sweeps of approximately 2.0 min.

The initial intensities of all halides were ±10%, and were followed for ca. 10 min at −40° and ca. 50 min at −60° (six to ten points taken). At least three runs were made on each sample and the slopes of each run were within the error range of any single run. The results presented in Table I are the average results of the three runs.

Inasmuch as the error involved in the calculation of the activation energy puts all three halides (Cl, Br, and I) within the same range, we must consider these values as only approximate.

**Registry No.**—Biphenyl radical anion, 34509-93-8.

## References and Notes

(1) A. R. Buick, T. J. Kemp, G. T. Neal, and T. J. Stone, *J. Chem. Soc. A*, 666 (1969).

(2) L. W. Bush, *Diss. Abstr. B*, **28**, 2366 (1967).

(3) J. O. Aldana, T. C. Wallace, and D. H. Eargle, Jr., *Acta Cient. Venez.*, **24**, 74 (1973).

(4) D. H. Eargle, Jr., *J. Org. Chem.*, **32**, 2227 (1967).

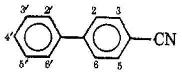
(5) "The biphenyl syndrome: anything that can form biphenyl, will". S. I. Weissman, 1960.

(6) J. K. Kim and J. F. Bunnett, *J. Am. Chem. Soc.*, **92**, 7463 (1970); J. F. Bunnett and X. Creary, *J. Org. Chem.*, **39**, 3173 (1974), and references cited therein.

(7) J. F. Bunnett and B. F. Gloor, *J. Org. Chem.*, **39**, 382 (1974).

(8) Actually pseudo-first-order, inasmuch as the aryl halide is in large excess in the bimolecular reaction of step 4.

(9) Splitting constants obtained from a McLachlan calculation and experimental values: $a^{N}_{CN} = 5.8$, $a_{3,5} = 2.8$, $a_{2,6} = 0.7$, $a_{2',4',6'} = 0.5$, $a_{3',5'} = 0.2$ G.



(10) Predicting the order of reactivity in various radical reactions of aryl halides has been a rather fruitless task: PhCN > PhI > PhBr (for $e_{aq}$) (ref 1); ArI < ArBr or ArCl (for $KNH_2$, $NH_3$) (ref 6). We too find the practice speculative, and prefer to offer for our system only the observations concerning the CN group and the order of reactivity of the halides at −40° as ArF ≫ ArI > ArBr > ArCl.

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# Synthesis of Cyanohydrins from Cyanides. Transition Metal Peroxide Reactions

E. Vedejs* and J. E. Telschow

*Department of Chemistry,*
*University of Wisconsin,*
*Madison, Wisconsin 53706*

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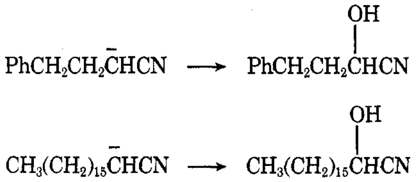
We have previously described the hydroxylation of enolates by the readily available molybdenum peroxide $MoO_5 \cdot Py \cdot HMPA$ (MoOPH).[1,2] In this paper, we report the analogous conversion of certain cyanide-stabilized anions to cyanohydrins.

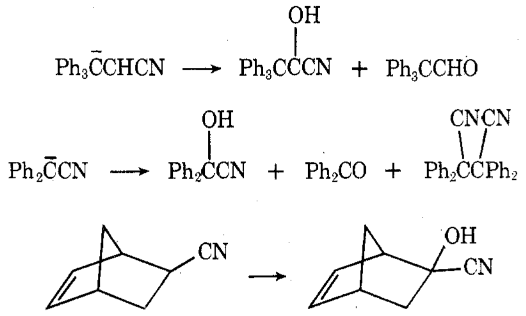
Addition of a solution of 4-phenylbutyronitrile in dry THF to lithium diisopropylamide followed by reaction with MoOPH at −23° gives hydrocinnammaldehyde cyanohydrin in 57% yield (65%, considering recovered starting material) after aqueous work-up. Similarly, 5-cyanonorbornene is hydroxylated in 35–40% yield. Although the yield for this oxidation is poor, the procedure is simple and it becomes possible to convert the acrylonitrile–cyclopentadiene Diels–Alder adduct into an easily hydrolyzed derivative of the ketene–cyclopentadiene adduct.[3] The stereochemistry of the norbornenone cyanohydrin has not been determined, but the MoOPH product is identical with the cyanohydrin obtained by treating norbornenone with acetone cyanohydrin-KCN according to NMR evidence.

Under the usual conditions, stearonitrile affords the cyanohydrin in 55–60% yield and 3,3,3-triphenylpropanonitrile yields 55% cyanohydrin and 10% triphenylacetaldehyde (68 and 12.5%, respectively, considering unreacted starting material). The reaction of diphenylacetonitrile anion with MoOPH gives a mixture of comparable amounts of cyanohydrin and benzophenone in 71% yield (81% based on recovered nitrile) together with 11% of tetraphenylsuccinonitrile, apparently formed by dimerization of diphenylcyanomethyl radicals. Since radical coupling products are not formed in detectable amounts from other MoOPH hydroxylations, we prefer to rationalize cyanohydrin formation via carbanion attack at the peroxide O–O bond of the molybdenum reagent and not by an electron transfer mechanism.



$$PhCH_2CH_2\overset{-}{C}HCN \longrightarrow PhCH_2CH_2\overset{\overset{OH}{|}}{C}HCN$$

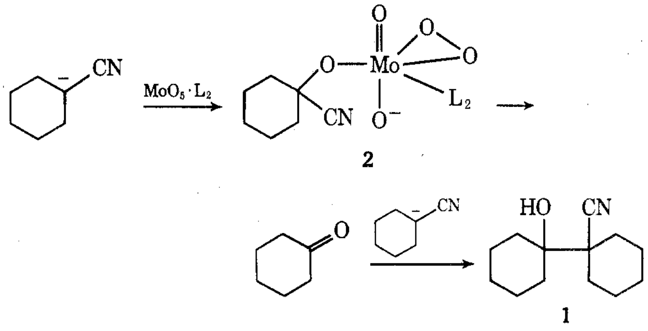
$$CH_3(CH_2)_{15}\overset{-}{C}HCN \longrightarrow CH_3(CH_2)_{15}\overset{\overset{OH}{|}}{C}HCN$$



$$Ph_3\bar{C}CHCN \longrightarrow Ph_3CC(OH)CN + Ph_3CCHO$$

$$Ph_2\bar{C}CN \longrightarrow Ph_2C(OH)CN + Ph_2CO + Ph_2C(CN)C(CN)Ph_2$$

Somewhat different results are obtained upon attempted hydroxylation of cyclohexyl cyanide. The major product from MoOPH oxidation is 1 (35%), identical with material prepared from cyclohexanone and cyclohexyl cyanide anion. Small amounts of the cyclohexanone cyanohydrin and cyclohexanone are also obtained (10–20% combined yield). Apparently an oxidation intermediate such as 2 is formed which fragments to cyclohexanone at a rate comparable to the rate of oxidation. Unreacted cyclohexyl cyanide anion then attacks the ketone in preference to the sparingly soluble MoOPH.



In general, moderate to good yields of cyanohydrins are expected from cyanides provided that the oxidation intermediates resist spontaneous fragmentation to the carbonyl compound. This condition is satisfied for typical aliphatic aldehyde cyanohydrins, but the behavior of ketone cyanohydrin precursors is unpredictable. A recent report describes a method for converting α-disubstituted cyanides into ketone cyanohydrins by oxygenation of $R_2\bar{C}CN$ to $R_2C(CN)OOH$, followed by reduction with stannous chloride.[4] This technique fails with α-monosubstituted cyanides $RCH_2CN$ which are the preferred substrates for direct hydroxylation with MoOPH. Thus, anion oxygenation and MoOPH hydroxylation are complementary techniques which allow synthesis of ketone or aldehyde cyanohydrins, respectively.

## Experimental Section

**Oxodiperoxymolybdenum(hexamethylphosphoric triamide)(pyridine) (MoOPH).** Oxodiperoxymolybdenum(hexamethylphosphoric triamide)[2,5] (18 g, 51.9 mmol) was dissolved in dry THF (40 ml) and pyridine (4.11 g, 51.9 mmol) was added with stirring. The product crystallized during addition. After filtering, washing thoroughly with ether, and vacuum drying over $P_2O_5$, yellow crystals (19.1 g, 85%) were obtained, identical with material prepared directly from $MoO_5 \cdot HMPA \cdot H_2O$ and pyridine.[2] The literature procedure[2] for preparation of MoOPH is less satisfactory because traces of hydrate may be present in the product.

**Lithium Diisopropylamide (LDA).** Purified (BaO distilled) diisopropylamine (2.18 ml, 15.6 mmol) was cooled to −80° and n-BuLi (8.0 ml, 13.1 mmol) in hexane was added dropwise under nitrogen. Dry THF was slowly added to a total volume of 16 ml and the mixture was brought to room temperature (nitrogen atmosphere throughout). The normality of the resulting LDA solution was calculated as being ca. 0.82 N. The LDA was prepared and stored under $N_2$ in a flask having no outlet other than a three-way stopcock. Aliquots were removed by syringe through the stopcock under nitrogen flow without disturbing the small amount of precipitate on the botton of the flask. With the stopcock closed, the LDA solution could be stored for several weeks at room temperature without apparent deterioration, and with no increase in the amount of precipitate.

**Hydroxylation of 4-Phenylbutyronitrile.** A solution of 4-phenylbutyronitrile (1.01 g, 6.95 mmol) in 15 ml of dry THF was added dropwise to LDA (8.6 mmol of 0.82 N solution in THF–hexane) at −78° under nitrogen. After 15 min at −78°, powdered MoOPH (3.90 g, 9.0 mmol) was added to the anion solution. The resulting mixture was stirred at −78° for 10 min and then at −23° for 40 min before being quenched with aqueous sodium bisulfite (25 ml). The mixture was stirred vigorously (ca. 5 min) at room temperature to extract molybdenum salts from the organic phase. The products were extracted with ether, and the ether layer was washed successively with 5% HCl, water, and brine, dried, evaporated, and separated by preparative layer chromatography over silica gel, using 1% methanol–$CH_2Cl_2$ to give recovered starting material (0.12 g, $R_f$ 0.5–0.6) and dihydrocinnammaldehyde cyanohydrin (0.64 g, $R_f$ 0.2–0.35).

Other cyanide hydroxylations were performed using an identical procedure, with appropriate modifications in the chromatographic separation technique.

**Attempted Hydroxylation of Cyclohexyl Cyanide.** A solution of 223 mg (2.04 mmol) of cyclohexanecarbonitrile in 4 ml of dry THF was added dropwise to 2.4 ml of 1.0 M LDA in THF–hexane at −78° under nitrogen. After 15 min at −78°, 1.130 g (2.6 mmol) of MoOPH was added to the vigorously stirred anion solution. The resulting red-brown mixture was maintained at −78° for 5 min and then allowed to warm to −23° for 10 min (light green solution). After addition of aqueous sodium bisulfite to the reaction mixture, the product was extracted with ether. The organic phase was washed successively with 5% HCl, water, and brine, dried, and evaporated to give a thick yellow oil.

The crude product, after addition of a few drops of pentane, deposited 72 mg (35%) of white crystals which were found to be identical with material obtained by quenching the anion of cyclohexanecarbonitrile with excess cyclohexanone at −70°. The hydroxynitriles produced by these two methods had mp and mmp 116–118° (from ether) and the same $R_f$ by TLC (silica gel, 50% ether–hexane or methylene chloride containing a trace of methanol): m/e calcd for $C_{13}H_{21}NO$, 207.16220; found, 207.16231.

TLC analysis (same conditions as above) of the remaining oil showed starting material, cyclohexanone, and cyclohexanone cyanohydrin by comparison with authentic samples. Cyclohexanone was assayed by GLC on 5 ft × 0.25 in. SE-30–Chromosorb P at 120° (injection port at 220°), 10–20% yield. The cyclohexanone peak tailed somewhat, apparently due to on-column decomposition of cyclohexanone cyanohydrin. Authentic cyclohexanone cyanohydrin behaved similarly under these conditions.

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**Registry No.**—1, 57527-71-6; MoOPH, 23319-63-3; oxodiperoxymolybdenum(hexamethylphosphoric triamide), 25377-12-2; LDA, 4111-54-0; 4-phenylbutyronitrile anion, 57527-72-7; dihydrocinnamaldehyde cyanohydrin, 53279-92-8; cyclohexyl cyanide anion, 57527-73-8.

## References and Notes

(1) E. Vedejs, *J. Am. Chem. Soc.*, **96**, 5944 (1974).

(2) H. Mimoun, L. Seree de Roch, and L. Sajus, *Bull. Soc. Chim. Fr.*, 1481 (1969).

(3) For alternative approaches, see E. J. Corey, T. Ravindranathan, and S. Terashima, *J. Am. Chem. Soc.*, **93**, 4326 (1971); D. A. Evans, W. L. Scott, and L. K. Truesdale, *Tetrahedron Lett.*, 121 (1972); S. Ranganathan, D. Ranganathan, and A. K. Mehrotra, *J. Am. Chem. Soc.*, **96**, 5261 (1974).

(4) S. J. Selikson and D. S. Watt, *J. Org. Chem.*, **40**, 267 (1975).

(5) The literature procedure[2] for preparation of $MoO_5 \cdot HMPA$ involves reaction of 30% $H_2O_2$ with $MoO_3$ at 40° to form $MoO_5 \cdot HMPA \cdot H_2O$ followed by vacuum drying. We have experienced no difficulties with the latter step, but it is important to control the reaction temperature and time in the first step. Reaction of $MoO_3$ and 30% $H_2O_2$ is mildly exothermic at first, depending on the rate of stirring and the scale. The heating bath should not be applied until the exotherm subsides. The reaction temperature must not exceed 40° and the reaction time should be kept to 3.5–4 h to avoid formation of amorphous, insoluble, and difficult to filter side products.