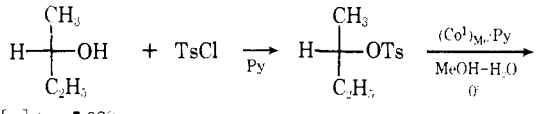
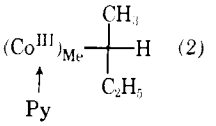
sec-butylcobaloxime[13] (**5**) was too highly colored to give a measurable rotation on several polarimeters.[14] Cleavage of the carbon–cobalt bond by either bromine or iodine at 0° in methylene chloride and isolation of the product by preparative gas chromatography gave *sec*-butyl halides of the same configuration[12] as the starting alcohol (eq 2 and 3). Cleavage by chlorine

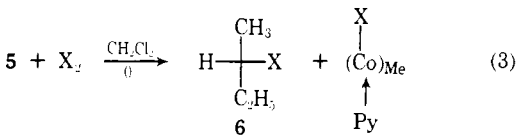


$[\alpha]^{22}D$ −5.93°



(2)

5



(3)

6a, X = Br, yield = 24%,
$[\alpha]^{22}D$ −12.56° (neat); overall retention = 85%

b, X = I, yield = 10%,
$[\alpha]^{22}D$ −13.72° (neat); overall retention = 95%

also occurs with predominant inversion but the exact stereospecificity has not been determined. Previously it has been shown that the alkylation of cobaloxime(I) occurs with inversion at carbon.[9] Therefore, the reaction sequences 2 and 3 demonstrate that the postulated electrophilic cleavages also occur with inversion of configuration at carbon.

The observed net loss in stereospecificity in reactions 2 and 3 likely occurs in part in reaction 2. Thus, when **5** is allowed to stand for several hours with an excess of cobaloxime(I), reisolated, and subjected to bromodemetalation, 2-bromobutane 70% racemized is obtained.[15] Apparently this racemization occurs by repeated SN2 displacements by cobalt(I) on carbon. The low yields in reactions 1 and 3 result, at least in part, from competing reactions of bromine with the dimethylglyoxime ligand.

The carbon–cobalt bond in alkylcobalamins and alkylcobaloximes is very hindered to front-side attack. The discovery of the facile electrophilic cleavage by bromine with inversion on carbon leads to the expectation that even bulky electrophiles might bring about such cleavages with highly hindered organometallic compounds.

Also, these results provide another example of the electrophilic inversion pathway which is favored when: (a) the organometallic compound is unable to coordinate with the incoming group; (b) the leaving metal is not an exceedingly strong Lewis acid.[8b]

Considerable current interest exists regarding the possible electrophilic cleavage of methyl B_{12} by mercuric ion in lake and river bottoms to produce "methylmercury." All cleavages of carbon–metal bonds by mercuric ions whose stereochemistry is known proceed by retention of configuration. In certain systems it has been established that mercury has an apparent small steric requirement (*e.g.*, the bromomercuri group has no conformational preference in cyclohexanes)[16] and therefore front-side attack cannot be eliminated. Schrauzer and coworkers[8] have postulated without supporting evidence that the mercuric ion cleavage of carbon–cobalt bonds occurs with inversion of configuration on carbon. No stereochemical evidence is available, and their relative rate data for cleavage of various alkyl derivatives are not in accord with the relative rate profile expected for an SE2 inversion process.[8b]

Acknowledgment. Support of this research by the National Institutes of Health under Grant No. GM 15373 and a Postdoctoral Fellowship to D. H. B. is gratefully acknowledged.

(13) Elemental analyses and infrared and nmr spectra are all in accord with the proposed structure of this compound.

(14) No rotation was observed on solutions sufficiently dilute to allow passage of light on Zeiss (photoelectric) or Bendix-143A (Faraday effect) polarimeters or by ORD or CD measurements on a Cary-60 instrument. However, "ghost" rotations were observed on the Zeiss instrument, under conditions where the samples were essentially opaque to light.

(15) Unpublished results with V. Madan.

(16) F. R. Jensen and L. H. Gale, *J. Amer. Chem. Soc.*, **81**, 6337 (1959).

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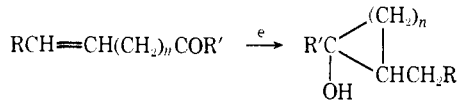
Electroorganic Chemistry. VIII. Intramolecular Cycloaddition of Nonconjugate Olefinic Ketones to Form Cyclic Tertiary Alcohols

Sir:

Attempts to synthesize cyclic tertiary alcohols (**1**) by the intramolecular reactions of organometallic reagents formed from halo ketones are generally unsuccessful due to the extreme difficulty of the generation of such organometallics.[1] In the present study, we wish to describe a novel electrochemical method of synthesis of **1** through the intramolecular cyclization of nonconjugated olefinic ketones, initiated by the electron transfer from an electrode to the carbonyl group. The stereochemistry of the alcohols **1** obtained by the



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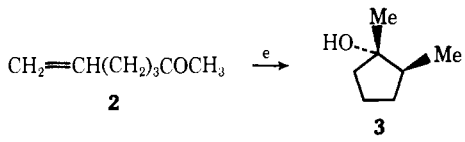
electrochemical method differs from that of those prepared by treatment of cyclic ketones with the Grignard reagent. The electroreduction of 6-hepten-2-one (**2**) (0.03 mol) in the mixed solvent of dioxane (50 ml) and methanol (10 ml) containing tetraethylammonium *p*-toluenesulfonate (20 g) as the supporting electrolyte was carried out at the cathode potential of −2.7 V *vs.* sce (0.2 A) using carbon rod electrodes. The cathodic and anodic chambers were separated by a ceramic cylinder. After about 3 F/mol of electricity was passed, 1,2-dimethylcyclopentanol (**3**) was obtained in 66% yield.

3 was identified by comparison of its ir and nmr spectra and its gas chromatographic behavior with those of the independently prepared sample.[2] The exclusive

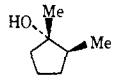
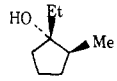
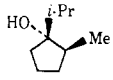
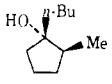
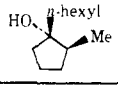
(1) E. J. Corey and I. Kuwajima, *J. Amer. Chem. Soc.*, **92**, 395 (1970).



2 3

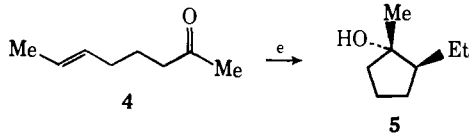
formation of *cis*-**3** in the electrode reaction is interesting since the corresponding alcohol given by the reaction of 2-methylpentanone with RMgI mainly consisted of the trans isomer. Furthermore, this remarkable control of stereochemistry was observed without exception in the electroreduction of a series of olefinic ketones under similar conditions (Table I).[3]

Table I. Reduction of $CH_2{=}CH(CH_2)_3COR$

R	Product	Yield, %
Me		66
Et		47
i-Pr		45
n-Bu		35
n-Hexyl		40

All of the products shown in Table I and mentioned hereafter were identified by spectroscopic (ir, nmr), gas chromatographic, and elemental analyses. The yields were determined by gas chromatography using acetophenone as the internal standard, and the isolated yields were about 80–85% of the gas chromatographic yields.

The formation of cyclic tertiary alcohols other than five-membered ring alcohols was studied with some unsaturated ketones under similar conditions (Table II).[3] As is shown in Table II, alcohols other than the five- and six-membered ring alcohols were not produced by the present electroreduction method. The theory that the carbonyl carbon always attacks the inner carbon atom of the terminal double bond is shown in Tables I and II. The exclusive formation of a five-membered ring product **5** (yield 40%) from the unsaturated ketone



4 5

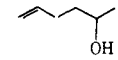
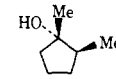
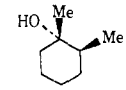
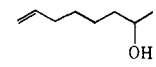
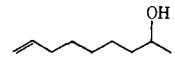
4 again supported this theory. The alkyl substitution on the inner carbon atom of the double bond inhibited the cyclization.

(2) H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, **81**, 247 (1959).

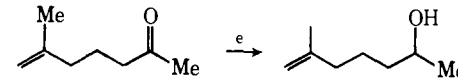
(3) Although the starting olefinic ketone was almost consumed, the alcohols listed in Table I and a tarry substance were the only products detected in the reaction mixture. The formation of pinacol under the present reaction condition seemed to be unlikely, since relatively high ketone concentration is needed for the formation of pinacol.[4]

(4) A. Yamura, T. Sekine and K. Sugino, *J. Electrochem. Soc. Jap.*, **34**, 110 (1966).

Table II. Reduction of $CH_2{=}CH(CH_2)_nCOR$

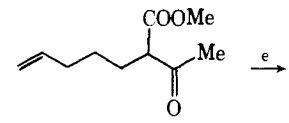
R	*n*	Product	Yield, %
Me	2		33
Me	3		66
Me	4		50[a]
			10[a]
Me	5		25
Et	9	None	

[a] Isopropyl alcohol was used as the solvent and the cathodic potential was −2.8 V *vs.* sce.

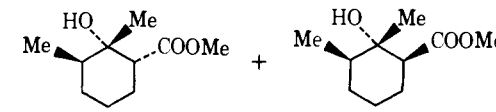


(yield 12%)

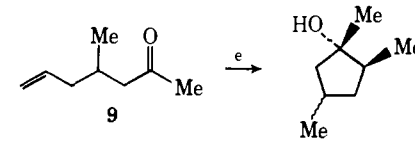
On the other hand, a functional group located on the carbon atom between the double bond and the carbonyl group (as in **6** and **9**) did not obstruct the cyclization.[5]



6

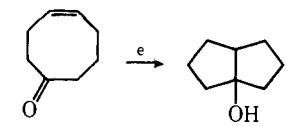


7 (yield 30%) 8 (yield 8%)



9 10 (yield 40%)

A cyclic olefinic ketone such as **11** was also cyclized to a bicyclo compound **12**[6] (yield 64%).



11 12

(5) The stereoconfigurations of **7**, **8**, and **10** (except **4**-Me) were tentatively assigned on the basis of their nmr spectra.

(6) A. C. Cope, J. M. Grisar, and P. E. Peterson, *J. Amer. Chem. Soc.*, **82**, 4299 (1960).

This investigation is currently being extended to ascertain in more detail the scope and mechanism of these reactions.

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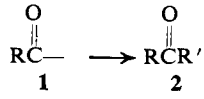
Received April 29, 1971

Anions of Protected Cyanohydrins as Acyl Carbanion Equivalents and Their Use in a New Synthesis of Ketones

Sir:

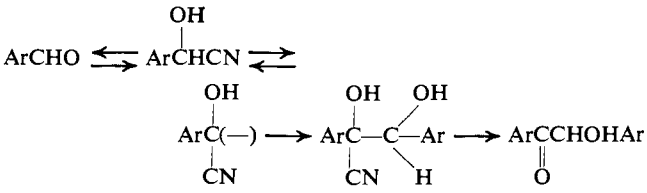
The obvious utility of acyl carbanion equivalents (*cf.* **1**) in the formation of a variety of carbonyl-containing systems by reaction with electrophilic reagents (*e.g.*, **1** → **2**) has prompted considerable synthetic



1 **2**

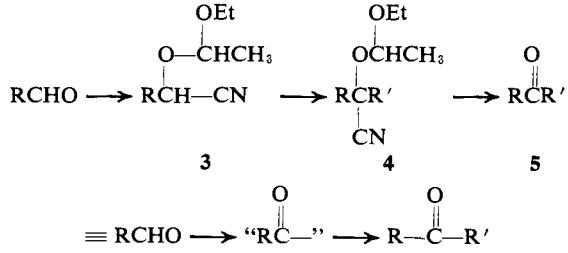
work, of much ingenuity, toward the synthesis of species equivalent to **1**.[1] We now wish to report a new and generally useful type of acyl carbanion equivalent and its use in the synthesis of ketones.

It occurred to us that a simple solution to the problem would be at hand if one could generate and alkylate the carbanions derived from suitably protected aldehyde cyanohydrins. Indeed, a special case of such a process is implicated in the long-known benzoin condensation of *aromatic* aldehydes.[2] It is obvious from the occur-



rence of this reaction, *without protection of the cyanohydrin hydroxyl*, that the aryl ring provides considerable additional stabilization for the α-cyano carbanion. A general synthesis would require finding conditions which would allow the alkylation of cyanohydrin in derivatives of *aliphatic* aldehydes as well as aromatic ones.

We have found that aldehyde cyanohydrins, suitably protected as their easily prepared reaction products, **3**, with ethyl vinyl ether,[3] can indeed be transformed into their anions with lithium diisopropylamide under carefully controlled conditions (*vide infra*). Addition



3 **4** **5**

(1) For a good review, see D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **8**, 639 (1969).
(2) *Cf.* K. Wiberg, *J. Amer. Chem. Soc.*, **76**, 5371 (1954).
(3) H. J. Sims, H. B. Parseghian, and P. L. DeBenneville, *J. Org. Chem.*, **23**, 724 (1958).

of an alkyl halide then produces a high yield of the protected cyanohydrin (**4**) of a ketone (**5**) which is then easily liberated, quantitatively and in a few minutes, by successive treatment with dilute sulfuric acid and dilute aqueous base.

The general procedure is described below.

A. Alkylation (3 → 4). To a solution of 0.022 mol of lithium diisopropylamide (from butyllithium and diisopropylamine) in 5–10 ml of dry tetrahydrofuran, under nitrogen and cooled to −78° in Dry Ice–acetone, a solution of 0.021 mol of freshly distilled **3** in 4.2–4.5 g of dry hexamethylphosphoramide is added dropwise, with vigorous stirring. After stirring for an additional 5 min, the halide R′X (0.025–0.030 mol) is added dropwise (5–10 min) followed by rinsing with an additional 10 ml of tetrahydrofuran. Stirring is continued for another 1–2 hr in the cold and 1 hr at room temperature. Addition of water, removal of solvent, and extraction (methylene chloride or ether) are followed by drying (Na_2SO_4), removal of solvents on the water pump, and percolation of the residue dissolved in 1:1 hexane–benzene through 25 g of silica gel. The product **4** can either be purified by distillation or used directly in the next step.

B. Regeneration of Ketone (4 → 5). To a mixture of 0.003–0.005 mol of **4** in 2–3 ml of methanol and 1 ml of 5% aqueous sulfuric acid enough methanol (2–5 ml) is added to make the mixture almost homogeneous. Disappearance of starting material (tlc) occurs after 5–10 min of stirring a room temperature. Removal of volatile components *in vacuo*, extraction with ether, and washing (saturated brine) leads to the crude cyanohydrin which can be isolated, if needed. Normally, the ketone is produced from the cyanohydrin by vigorous shaking of its ether solution with 20 ml of 0.5 *N* sodium hydroxide solution for 5–10 min. The ketone is then recovered from the ether solution in the usual way.

We wish to point out a number of features which make this new synthetic method of considerable interest. (a) Primary bromides (and iodides) give excellent yields in the alkylation of **3** to **4**. For instance, from the readily available **3** (R = CH_3), *n*-butyl, *n*-hexyl, and *n*-decyl bromides give the corresponding **4** in 80–85% yield.[4a] (b) Secondary bromides often give excellent yields with little dehydrohalogenation: **3** (R = CH_3) gave with isopropyl and cyclopentyl bromides the corresponding **4** in 80% yield. The easily dehydrohalogenated cyclohexyl bromide still gave an acceptable 41% yield.[4b] (c) Halides of the homoallylic type, which are often easily dehydrohalogenated, give good yields: **3** (R = CH_3) gave with 2-phenylethyl bromide and *cis*-3-hexenyl iodide the corresponding **4** in 84 and 61% yields,[4c] respectively. (d) Especially reactive halides such as allyl bromides and chloromethyl ether, as well as notably unreactive ones such as diethyl bromoacetal, give the respective **4** in 76, 71, and 59% yields.[4d] (e) Although most of our work has been with acetaldehyde cyanohydrin (thus leading to methyl ketones) the homologs can, of course,

(4) (a) (R = CH_3) R′ = *n*-butyl, bp 97–99° (9 mm); R′ = *n*-hexyl, bp 75–80° (0.05 mm); R′ = *n*-decyl, bp 120–130° (0.09–0.11 mm); (b) R′ = *i*-Pr, bp 85–86° (9 mm); R′ = cyclopentyl, bp 69–70° (0.05 mm); R′ = cyclohexyl, bp 93–95° (0.1 mm); (c) R′ = *cis*-3-hexenyl, bp 75–76° (0.05 mm); (d) R′ = allyl, bp 59–62° (0.15 mm); R′ = CH_3OCH_2–, bp 92–94° (7 mm); R′ = $(C_2H_5O)_2CHCH_2$–, bp 90–91° (0.08 mm).