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Reductions of Benzyl and Cyclohexyl Chloroformates with Tri-*n*-butyltin Hydride

Peter Beak* and Steven W. Mojé

Roger Adams Laboratory, University of Illinois, Urbana, Illinois 61801

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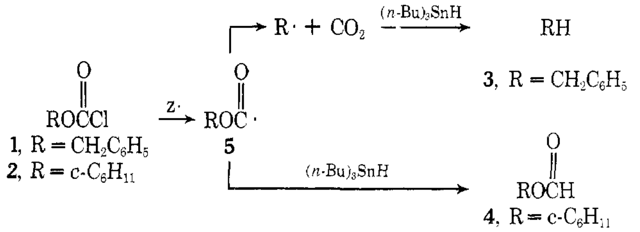
The lowering of transition-state energy provided by the generation of carbon dioxide in conjunction with the formation of carbonium ions and silver chloride in the reactions of chloroformates with silver ion[1] suggests that the same driving force might be available to promote the conversion of chloroformates to a formal chlorine atom, carbon dioxide, and a carbon radical. If the carbon radical could be reduced by a hydrogen-atom donor, such a process would be of synthetic value as part of a route for the deoxidation of alcohols alternative to other procedures.[2] In fact, Kuivila and Walsh have reported that benzyl chloroformate is reduced by tri-*n*-butyltin hydride to a 4:6 ratio of toluene and benzyl formate and that ethyl chloroformate gives solely ethyl formate under similar conditions.[3] It has been noted by a number of workers that the alkoxycarbonyl radical, an intermediate in the tri-*n*-butyltin hydride reduction,[4] while thermodynamically disposed to fragment to carbon dioxide and a carbon radical,[5] does have an appreciable activation energy toward such decomposition.

When the reaction of benzyl chloroformate (1) with tri-*n*-butyltin hydride and azobisisobutyronitrile (AIBN) as initiator is carried out for 22 hr in hexane at 36° at concentrations of less than 0.3 *M* in each reactant, the sole product is toleune (3) in 22% yield and less than 1% benzyl formate. Increase in the concentration of the hydride, however, leads to increasing amounts of benzyl formate at the expense of toluene. Reduction of benzyl chloride to toluene under the same conditions is *ca.* 1.6 times faster than the reduction of 1. However, no significant conversion of benzyl chloroformate to benzyl chloride occurs in the absence of the other reactants, and a methanol quench of a partial reaction showed an upper limit of 4% benzyl chloride present after a reaction of 13 hr.

Reaction of cyclohexyl chloroformate (2) under conditions similar to those which gave toluene from benzyl chloroformate produced only cyclohexyl formate (4) and less than 1% cyclohexane. Greater dilutions did not produce cyclohexane.

Rationalization of these results in terms of the alkoxycarbonyl radical 5 is consistent with previous studies which suggest that the rate of fragmentation of 5 is dependent on the stability of the radical formed.[3-6] The reciprocal relationship of toluene and benzyl formate as a function of hydride concentration suggests that fragmentation and reduction of the benzyloxycarbonyl radical can be competitive under these conditions. Apparently the stability of the benzyl radical is sufficiently influential to foster fragmentation, whereas a stabilized radical would not be produced by loss of carbon dioxide from cyclohexyloxycarbonyl radical, and it survives to be reduced. A related result and similar rationale have been reported for the conversions of benzyl and *n*-octyl formate to toluene and *n*-octyl alcohol, respectively, with palladium.[7] Conversion of the chloroformate function to a hydrocarbon may be of some specialized synthetic value for cases in which the intermediate radical is stabilized, although the present procedure would involve product isolation by gas chromatography. The formation of cyclohexyl formate from cyclohexyl chloroformate does suggest, however, that unless a stabilized radical is possible the present procedure does not offer an attractive general route for the deoxidation of alcohols by the reduction of chloroformates.



Numerous attempts were made to convert cyclohexyl chloroformate to cyclohexane by reduction with lithium aluminum hydride–aluminum chloride or triethylsilane and by photolysis with tri-*n*-butyltin hydride, triphenylsilane, and triethylsilane. In no case was a glpc peak corresponding to more than 5% cyclohexane observed. Attempted reductions of cyclohexyl chlorosulfite and cyclohexyl chloroglyoxylate with tri-*n*-butyltin hydride were also unsuccessful and gave destruction of starting material in exothermic reactions, but cyclohexane could not be detected.

Experimental Section

All reactions were run in a dry nitrogen atmosphere. Gas chromatography was performed on an Aerograph A90-P3, with a 3- or 10-ft column packed with 20% XF 1150 on 60/80 acid-washed, DMCS-treated Chromosorb P. Benzyl[8] and cyclohexyl[9] chloroformates and cyclohexyl chloroglyoxalate[10] were prepared by reaction of the purified alcohols with phosgene or oxalyl chloride and gave satisfactory C, H, and Cl microanalyses. Cyclohexyl chlorosulfinate[11] was prepared by reaction of cyclohexanol with thionyl chloride and by reaction of dicyclohexyl sulfite with thionyl chloride[12] and was characterized by ir and nmr spectroscopy. Tri-*n*-butyltin hydride was prepared by lithium aluminum hydride reduction of the chloride[13] and its purity was determined as >96% by refractive index, reduction of benzyl chloride, and titration.[14]

Reaction of Benzyl Chloroformate with Tri-*n*-butyltin Hydride. Reaction of benzyl chloroformate (52.6 mg, 0.308 mmol), tri-*n*-butyltin hydride (83.9 mg, 0.88 mmol), and azobisisobutyronitrile (AIBN, 1.5 mg, 0.01 mmol) in hexane (1.00 ml) with stirring for 22 hr at 36° showed 22% yield of toluene and less than 1% benzyl formate. AIBN initiator increased the rate of reaction. Increase in metal hydride or decrease in solvent quantity increased the percentage of benzyl formate formed at the expense of toluene; a reaction twice as concentrated as that described above gave a toluene:benzyl formate ratio of 24:1, while a reaction six times as concentrated produced the same products in a ratio of 2.3:1. Benzene or ether solvent did not appreciably change the rate of reaction but gave somewhat lower toluene yields. In no instance was a significant amount of benzyl alcohol formed. Toluene and benzyl formate were identified by collection from the gas chromatograph and comparison of infrared spectra with those of authentic samples.

Since benzyl chloride was found to reduce to toluene under conditions similar to those under which benzyl chloroformate is reduced, a control experiment was carried out by quenching the reaction with methanol after 13 hr. Benzyl chloroformate reacts with methanol to give benzyl methyl carbonate; benzyl chloride does not react with methanol under these reaction conditions. The carbonate/(carbonate + chloride) ratio exceeded 96%.

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Registry No.—**1**, 1885-14-9; **2**, 13248-54-9; **3**, 108-88-3; **4**, 4351-54-6; (n-Bu)$_3$SnH, 688-73-3.

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Carbon-13 Nuclear Magnetic Resonance Spectral Analysis Using Spin-Lattice Relaxation Data and Specific Deuteration. Thiamine Hydrochloride

Richard E. Echols[1a] and George C. Levy*[1b]

General Electric Corporate Research and Development, Schenectady, New York 12301

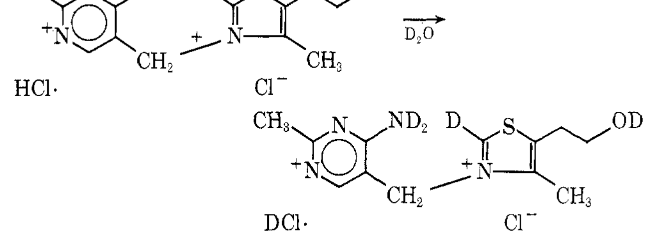
Received December 4, 1973

Carbon-13 spin-lattice relaxation data (the spin-lattice relaxation time, T_1, and nuclear Overhauser effect, NOE) can be useful parameters for organic spectral analysis.[2] In particular, ^{13}C–^{1}H dipolar T_1's (which account for ^{13}C relaxation in large organic molecules) can indicate the degree of proton substitution for each carbon in the molecule.[1b] ^{13}C T_1's for nonprotonated carbons in these molecules may also facilitate spectral assignments, since the efficiency of the dipolar relaxation mechanism for a given carbon depends strongly on the intermolecular distances between the carbon and nearby protons.[2c,d]

The sensitivity of T_1^{DD} (the dipolar T_1) to internuclear distances can be exploited in another way. When a carbon bearing protons is selectively deuterated, the ^{13}C T_1 for that carbon increases because the deuterium nucleus has a smaller magnetic moment than the proton. If all attached protons are replaced by deuterium nuclei, then T_1^{DD} for that carbon will increase by *ca.* tenfold (combining much less efficient ^{13}C–^{2}H dipolar relaxation with ^{13}C–^{1}H dipolar relaxation from nearby nonbonded protons). The effect of deuteration can also be seen on T_1^{DD} for nearby *nonprotonated carbons,* which depend on nonbonded protons for their relaxation.

The ^{13}C nmr spectrum of vitamin B$_1$, thiamine hydrochloride, has been published[3] but many of the assignments were listed as tentative. We report here a ^{13}C nmr spectral study of this compound. Most of the present resonance assignments were made by use of model compounds and standard chemical shift correlations.[4] However several lines could not be assigned on that basis.

^{13}C chemical shift and spin-lattice relaxation data for thiamine hydrochloride are given in Table I. Also in Table I are T_1 data for the partially deuterated compound separately prepared and redissolved in CD$_3$OD-D$_2$O. The exchange reaction results in pentadeuteration of the ion pair complex as shown (the "unusual" deuteration at C-2 is well known[5]).



A methanol-water solvent system was used in this work because a small solvent effect resulted in better separation of the closely spaced peaks corresponding to C-2′ and C-4′. Assignment of these closely spaced nonprotonated carbon resonances by conventional methods is not possible. Even the C-2′ and C-4′ T_1's (in the nondeuterated compound) do not distinguish between the two signals based on distances to nearby protons. Deuteration of the amino group in the exchange reaction affords definitive assignments, however. T_1^{DD} for the C-4′ carbon (α to the ND$_2$ group) increases by *ca.* 300% (see Table I) while the increase in T_1 for C-2′ is three times smaller. For the remaining carbons in the partially deuterated compound, smaller changes in T_1^{DD} can be noted (however, note that ΔT_1 is subject to considerable error since it is a difference between two derived quantities.).

The significant positive ΔT_1 value for C-4 is interesting, but as yet we have no certain explanation for this. We also have no explanation for the substantial negative ΔT_1 values observed for the two CH$_3$ carbons. Possibilities for the former effect include conformational considerations such as molecular stacking; the latter effect might indicate a reduced rate of CH$_3$ group rotation in the deuterated medium. Other, more easily interpreted molecular dynamics effects are indicated from the data in Table I. For example, T_1's for the 2′-CH$_3$ and 4-CH$_3$ carbons indicate that both CH$_3$ groups are spinning rapidly. The 5-α and 5-β CH$_2$ carbons and also the ring-bridging CH$_2$ group undergo some group segmental motion.[2c]