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CHLOROACETYLENES AS MICHAEL ACCEPTORS. I.

MECHANISM OF ENOLATE DICHLOROVINYLATION.

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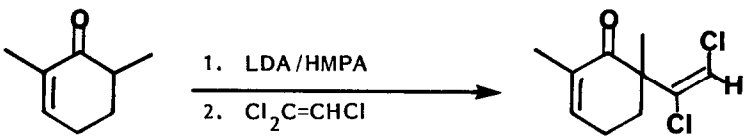
Summary The condensation of certain enolates with trichloroethylene to yield α-dichlorovinyl ketones has been shown to proceed by way of dichloroacetylene as an obligatory intermediate.

In a recent communication we described a novel condensation of certain enolates with Cl_2C=CHCl to yield α-dichlorovinyl ketones, illustrated in eqn 1.[1]



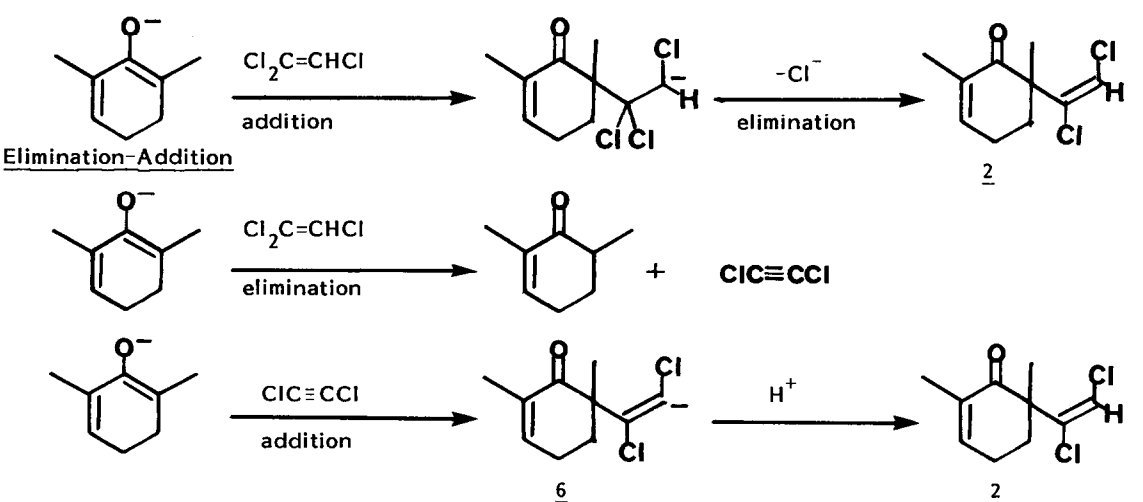
(1)

1 2

Although some limited synthetic applications of this reaction were shown, neither its scope nor its mechanism was understood. At least four discrete mechanisms could be proposed to rationalize the initial data, namely (1) transfer alkylation,[2] (2) $S_{RN}1$ radical chain,[3] (3) addition-elimination,[4] and (4) elimination-addition.[5] The complete absence of α-chloroketones (stable to reaction conditions) argued against transfer alkylation. Neither O_2, nor light, nor AIBN, nor t-Bu_2NO had effect on product yield, making a radical chain mechanism untenable.[3a] Differentiation between addition-elimination and elimination-addition (Scheme I.) was less obvious. The observed

SCHEME I

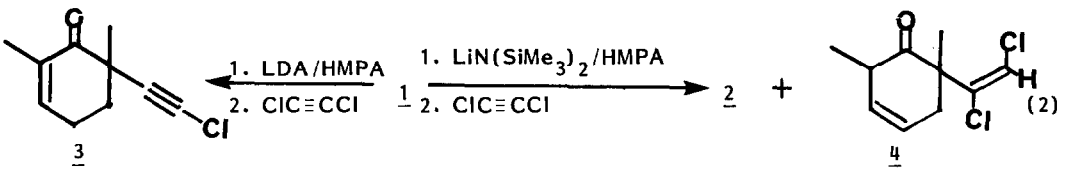
Addition-Elimination



formation of 1,2-dichlorovinyl rather than 2,2-dichlorovinyl products seemed to argue against addition-elimination since the 2,2-regiochemistry would be anticipated.[6] In addition, it has been shown that the reaction between $Cl_2C{=}CHCl$ and arylthiolate[7] or phenolate[8] nucleophiles proceeds through initial formation of $ClC{\equiv}CCl$. On the other hand, our limited knowledge of the substitution chemistry of $ClC{\equiv}CCl$ with carbon nucleophiles, based on the work of Ott with sodio diethyl ethylmalonate, would predict formation of the α-(2-chloroethynyl) derivatives from a dichloroacetylene intermediate rather than the observed dichlorovinyl products.[9]

To establish the possible role of $ClC{\equiv}CCl$ in our dichlorovinylations we undertook to generate $ClC{\equiv}CCl$ free of $Cl_2C{=}CHCl$ and to examine its reactions with enolates. None of the several published procedures for preparation of $ClC{\equiv}CCl$ were suitable in our hands for this purpose. That of Ott[10] gave unacceptable mixtures, and that of Kloster-Jenson[11] gave unreproducible results. We ultimately found that addition of a solution of $Cl_2C{=}CHCl$ in Et_2O at -78°C to a suspension of $LiN(SiMe_3)_2$ in hexanes, followed by warming to rt over 3 h and direct distillation at 30-36°C through a 12 cm Vigreux column reproducibly gave a distillate free of $Cl_2C{=}CHCl$ that contained (glc) ca 50% $ClC{\equiv}CCl$, 40% diethyl ether and 10% hexanes.[12]

When the kinetic enolate of 1 (from 1 and one equiv each of LDA and HMPA) was reacted in THF with freshly distilled $ClC{\equiv}CCl{\cdot}Et_2O$, prepared as above, (-78°C → rt, 3 h), no dichlorovinyl ketone 2 was formed. We obtained 64% of the α-chloroethynyl ketone 3; excess $ClC{\equiv}CCl$ or excess ketone gave a similar result. However, when the enolate of 1 was prepared using $LiN(SiMe_3)_2$ instead of LDA, the major product was 2 (40%) accompanied by a small amount of the isomer 4. (Eqn 2).

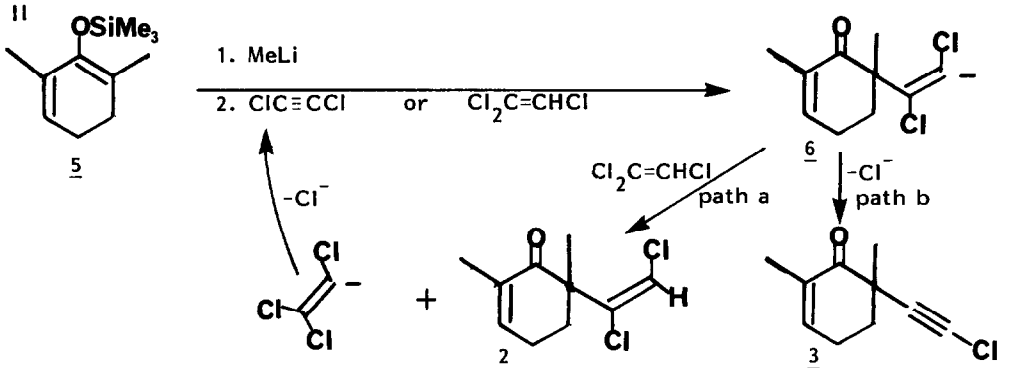


3 4

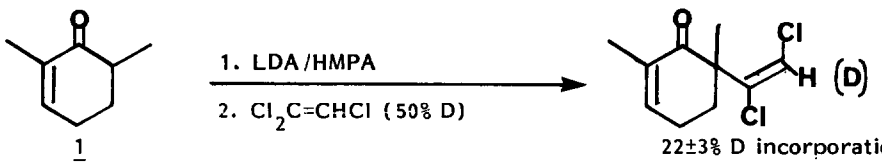
How can the choice of base lead to such distinctly different product types? As a working hypothesis, we considered that all of our data could be consistent with the intermediacy of $ClC{\equiv}CCl$ for the reaction depicted in eqn 1. In other words, mechanism (4), elimination-addition, could be operative, and the fate of the vinyl anion (cf 6) formed in these reactions would depend on competition between Cl^- elimination to form 3 vs. proton abstraction from a proton donor in the reaction mixture to yield 2. Our data suggested, further, that $Cl_2C{=}CHCl$ or $HN(SiMe_3)_2$ can serve as proton sources toward anion 6, whereas the starting ketone or the kinetically less acidic amine $HN(i\text{-}Pr)_2$ cannot. When $Cl_2C{=}CHCl$ serves as the proton source, the trichlorovinyl anion generated can eliminate Cl^- and regenerate $ClC{\equiv}CCl$. Consistent with this hypothesis were the observations that the TMS enol ether 5, upon treatment with one equiv. MeLi, followed by $ClC{\equiv}CCl$ gave only 3, whereas 5 with MeLi, then $Cl_2C{=}CHCl$ gave only 2 (Scheme II).

A reliable distinction between addition-elimination and elimination-addition was available from intermolecular competition in product formation using a mixture of $Cl_2C{=}CHCl$ and $Cl_2C{=}CDCl$ as reactants. Addition-elimination would predict only a small, secondary isotope effect, whereas the elimination-addition mechanism for enolate dichlorovinylation could lead to a potentially large primary isotope effect at the proton (deuteron) transfer step (path a, Scheme II) to form the observed product 2. A ten-fold excess of dry trichloroethylene containing 50±2% $Cl_2C{=}CDCl$, prepared by partial deuteration of $Cl_2{=}CHCl$ using $Ca(OD)_2$ in D_2O,[13] was reacted with the kinetic

SCHEME II



enolate in the usual manner. The resulting dichlorovinylation product 2 was analyzed by mass spectrometry and by 400 MHz nmr. Careful integration of the vinyl proton against the β-proton of the enone (duplicate determination on two separation reaction products, after calibration using two separate reaction products obtained with 100%-H Cl_2C=CHCl) showed .78±.03 out of 1.0 vinyl protons, corresponding to 22±3% deuterium incorporation (Eqn 3). To establish that loss of label did not occur after product formation, unlabeled 2 was mixed with 5 equiv. of 100% Cl_2C=CDCl in THF, then treated with LDA/HMPA. No exchange of vinyl protons (<1%) could be detected under the usual reaction conditions.



(3)

Calculations of the isotope effect using the method of Melander and Saunders[14] gave k_H/k_D= 3.7±0.5, a primary isotope effect comparable to those reported for E_2 eliminations[15] and clearly consistent with the elimination-addition mechanism for enolate dichlorovinylations.

We conclude from our data that the reaction of the enolate of 1 with trichloroethylene to yield 2 does indeed proceed through a dichloroacetylene intermediate. The fate of the initial adduct between ClC≡CCl and an enolate, such as vinyl anion 6, is determined by competition between unimolecular elimination of Cl^- and bimolecular proton abstraction. Hence, for eqn 1, an elimination-addition mechanism is operating, in which Cl_2C=CHCl acts as proton source in quenching vinyl anion 6, and regenerates ClC≡CCl in a propagative fashion. These conclusions, which are consistent with our recent observations in the hexachlorobutadiene series,[16] have important implications to the synthetic scope of haloacetylene chemistry for the ethynylation and vinylation of enolate systems. These synthetic studies are outlined in the accompanying communication.[17]

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