CATALYSIS OF THE DIELS-ALDER REACTION BY ORGANOTIN HALIDES

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Abstract Organotin halides catalyze the Diels-Alder reaction between isoprene and methyl vinyl ketone. The catalytic activity is a function of the number of proximate tin atoms in the molecule and the extent of halogen substitution on tin.

Introduction

In 1960 Yates and Eaton¹ reported that the Diels-Alder reaction between anthracene and maleic anhydride was greatly accelerated by the Lewis acid aluminum chloride. Since that time the catalytic effect of a number of Lewis acids has been studied. These include tin(IV) chloride^{2,3} and alkylaluminum chlorides^{3,4}. The most complete kinetic study was reported in a series of papers by Inukai and Kojima⁵. The catalytic properties of the Lewis acids and the increased regioselectivity in the presence of a Lewis acid has been treated theoretically by Alston and Ottenbrite⁶ and Houk and Strozier⁷. However, Carlson and coworkers⁸ found limited Diels-Alder catalytic activity for a number of tin(II) and tin(IV) halides. Likewise, tin(IV) chloride was not an effective catalyst for a Diels-Alder reaction with a stereofacially differentiated enone⁹. We wish to report catalysis of the Diels-Alder reaction by organotin halides containing one or more tin atoms. The diene and dienophile substrates chosen for study were isoprene, **1**, and 3-buten-2-one, **2** (MVK).

This system was amenable to analysis, by gas chromatography, of the progress of the reaction as a function of time. Using dodecane as an internal standard (with the appropriate detector response factors), the change in concentration of all three components of the system could be followed.

Materials and Methods

Isoprene, (**1**), 3-buten-2-one, (**2**), dichlorodimethylstannane, (**7**), tetramethylstannane, and dichlorodiphenylstannane, (**8**), were obtained from Aldrich and used without further purification. Chlorotrimethylstannane, (**4**), was prepared from the disproportionation of **7** and tetramethylstannane. The syntheses of **5**, **6**, **9** and **10** have been described previously¹⁰. Analysis of product mixtures by gas chromatography was performed isothermally at 160 °C on a Varian-Aerograph Model 90, fitted with a TC detector, using a 10' (0.25" column packed with 20% Carbowax 20M on Chromosorb P, 60/80 mesh. Detector response factors for each reactant and the products were determined using dodecane as the reference. Peak areas were integrated with a Columbia Scientific, Model CRS204, digital integrator. ¹H-NMR spectra, referenced to TMS, were obtained on a Varian, model EM-360 and IR spectra on PE Model 283-B spectrometer. Melting points were uncorrected.

Kinetic procedure In a typical reaction 1.0 mmol of catalyst was weighed into a Reacti-vial fitted with a Mininert valve and magnetic stirrer. Dodecane (852 mg, 5 mmol, 1.14 mL), isoprene (681 mg, 10 mmol, 1.00 mL) and MVK (701 mg, 10 mmol, 0.83 mL) were added by syringe in that order. The reaction mixture was placed in a water bath at 31 °C and 75 °C aliquots withdrawn at time intervals for gas chromatographic analysis. Each sample was transferred to a small conical tube, fitted with a septum cap, and containing approximately 15 mg of dry potassium fluoride. This amount constituted a five-fold excess for replacement of each chloride on tin by a fluoride. The tube was shaken to facilitate mixing, then centrifuged for about 30 seconds. A 1 µL sample was withdrawn for injection into the chromatograph. Each run was

carried out in triplicate and peak areas for the two reactants and the addition product were converted to mmols using appropriate detector response factors to dodecane.

Product Identification A reaction mixture similar to that above was prepared on a 0.1 mole scale. The amount of catalyst, $\text{MeSnCl}_3/\text{Me}_2\text{SnCl}_2$ (75/25), was increased to 0.08 mol of tin and the dodecane was eliminated. The reaction mixture was cooled in an ice bath and stirred magnetically. When the reaction was complete, as shown by gas chromatography, the reaction mixture was diluted with 20 mL of carbon tetrachloride, washed twice with 20 mL portions of water, the organic layer dried over magnesium sulfate and the solvent removed on rotary evaporator. The resulting oil was distilled under reduced pressure resulting in a 54% yield of acetylmethylcyclohexene, bp 91-93°C (20 torr); lit¹¹ (4-acetyl-1-methylcyclohexene) bp 90-92 °C (20 torr). The semicarbazone derivative was prepared, mp 149.5-150.5 °C; lit¹¹, semicarbazone of 4-acetyl-1-methylcyclohexene, mp 150-151 °C. ¹H NMR: (CCl_4); 1.5-2.6 (m, 13 H); 5.17 (m, 1 H). (When a small amount of $\text{Eu}(\text{tbd})_3$ shift reagent was added, the chemical shift of the olefinic proton did not change, nor was it broadened.) IR: cm^{-1} (neat); 3050 (m), 1720 (s), 1660 (w), 805 (s).

Results and Discussion

Analysis of the data shows that mono and ditin halides definitely catalyze the Diels-Alder reaction between isoprene and MVK, although the magnitude of catalysis is not dramatic at the ten mole percent level. Also, the presence of dodecane as a diluent diminishes the catalytic activity. The six tin compounds which were studied are shown in Table 1. The measure of catalytic activity is the time (in hours) necessary to produce a 50% yield of product. Also listed is a relative catalytic rate constant based on the times described above.

In order to preclude continued catalysis of the Diels-Alder reaction in the injection port of the chromatograph, the aliquot for analysis was treated with dry KF to convert the catalysts from tin chlorides to insoluble tin fluorides. The samples were then centrifuged and the supernatant liquid injected for analysis. Potassium fluoride was very successful in removing the tin catalyst in the case of Me_2SnCl_2 , Me_3SnCl , and $(\text{MeCl}_2\text{SnCH}_2)_2$ as shown by the absence of peaks due to the tin compounds in the NMR spectra of the centrifugates. This method was less successful with the bis-chloromethylstannylmethanes. Immediately upon mixing the reactants and catalyst, a sample was withdrawn to obtain values for the composition of the mixture at time-zero. When samples of the reaction mixture, untreated with KF, were analyzed early in the reaction, no product could be observed indicating that if catalysis does take place in the injection port, it is minimal.

The values for $k_{\text{cat}}^{\text{rel}}$ suggest the following features of the catalytic activity. The reactivity of the catalyst is a function of Lewis acidity of the tin compound. This can be seen by the order of reactivity 4<7<8 and 5<9. This is no surprise since catalysis undoubtedly involves a complex between the tin atom (Lewis acid) and the carbonyl oxygen of MVK (Lewis base).

A second interesting facet is illustrated by a comparison of $k_{\text{cat}}^{\text{rel}}$ values for 4, 5, 6, and 7. Dimethyltin dichloride, 7, is about twice as active as trimethyltin chloride 4. Bis-chlorodimethyl-stannylmethane, 5, is similar in activity to dimethyltin chloride even though each tin bears only one chlorine. Their proximity allows each tin to contribute to a complex containing a single MVK molecule. Thus the combined effect of the monochlorotins results in activity similar to 7. Bis-1, 2-chlorodimethyltannylethane, 6, exhibits similar catalytic activity to 5 and 7 and double that of 4. In this case, either the molecule assumes a conformation in which both monochlorotins complex with a single MVK molecules as in 5, or this is a statistical effect in which the molecule is acting as two separate monochlorotins (twice the effect of 4). This problem could presumably be resolved by moving the monochlorotins further apart on a carbon chain. Finally, a comparison of 9 and 10 indicates that the latter is more effective by factor of 1.5. In terms of electronic effects, the relative catalytic activity should be in reverse order with 9 the more active.

The $k_{\text{cat}}^{\text{rel}}$ experimental results can be explained in terms of a Thrope-Ingold Effect¹² operating in the formation of the complex with MVK. The *gem*-dimethyl groups compress the Sn-C-Sn bond angle resulting in more efficient coordination with the carbonyl oxygen. It should also be noted that the reaction involving 10 as the catalyst resulted in extensive polymerization of both isoprene and MVK, as evidenced by more rapid decreases in their concentrations than could be accounted for in the Diels-Alder product.

The regioselectivity of the catalyzed process is a question of interest. Lutz and Bailey¹³ reported in 1964 that the Diels-Alder reaction between isoprene and MVK, catalyzed by SnCl_4 (5 H_2O), resulted in 93% 4-acetyl-1-methylcyclohexene, 3a, and 7% 5-acetyl-1-methylcyclohexene, 3b. The Diels-Alder adduct was isolated from a number of kinetic runs as well as a preparative scale reaction catalyzed by a mixture of

$\text{Me}_3\text{SnCl}/\text{Me}_2\text{SnCl}_2$ (75/25). The NMR spectra were identical and were consistent for 4-acetyl-1-methylcyclohexene.

Table 1. Catalytic Activity of Organotin Halides

Catalyst	Time (hrs) ^a	$k_{cat}^{rel\ b}$
None	197	1
Me_3SnCl 4	104	2
5	48	4
6	45	4
Me_2SnCl_2 7	44	4
Ph_2SnCl_2 8	26	8
9	15	13
10	10 ^c	20

^aTime necessary to reach 50% yield of Diels-Alder product. ^bCatalytic activity relative to no catalyst. ^cExtensive polymerization of both isoprene and MVK was observed.

In conclusion, we report significant catalysis of a Diels-Alder reaction by organotin halides. It should also be noted that this system can also be utilized to measure the extent of Lewis acid coordination with α,β -unsaturated carbonyls.

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