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Iron Lewis Acid Catalyzed Reactions of Ethyldiazoacetate with Styrene and α-Methylstyrene: Formation of Cyclopropanes with Cis Selectivity

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Abstract: The iron Lewis acid, $(\eta^5\text{-}C_5H_5)Fe^+(CO)_2(THF)BF_4^-$ catalyzes the reaction of ethyldiazoacetate with styrene and α-methylstyrene to provide cyclopropanes with a preference for the cis isomer.

The use of transition metals to catalyze cyclopropanation of diazo-compounds and alkenes is a well precedented procedure.[1] Previously, the catalysts most used were soluble and insoluble copper complexes.[2] Recently, the group VIII metals have been extensively utilized for this reaction.[3] The most successful catalyst used to date is the rhodium carboxylates.[4] Although selectivities have been low, Doyle has improved the selectivity of the rhodium catalyzed cyclopropanation to a viable synthetic route in organic chemistry.[5] Doyle's catalyst along with most metals used preferentially give trans cyclopropanes when ethyldiazoacetate is treated with alkenes.[6] Here, we report the first example of an iron Lewis acid catalyzed decomposition of ethyldiazoacetate with styrene and α-methylstyrene to provide cyclopropanes with predominantly cis selectivity.

The Lewis acid, $(\eta^5\text{-}C_5H_5)Fe^+(CO)_2(THF)BF_4^-$, **1** was prepared by the protonation of the known methyl complex, $(\eta^5\text{-}C_5H_5)Fe(CO)_2CH_3$ at -78°C in tetrahydrofuran.[7] The methyl complex was easily synthesized in two steps with a high yield from the commercially available iron dimer.[8] Normally, less than one equivalent of $HBF_4.OEt_2$ was used in the synthesis of the Lewis acid, which was then recrystallized several times from CH_2Cl_2/THF to insure that no HBF_4 was left as an impurity to contaminate the reaction.

The results of Lewis acid catalyzed cyclopropanation of ethyldiazoacetate in the presence of styrene and α-methylstyrene are summarized in Table 1. Runs 1-14 were performed to determine the optimum concentrations and temperature for the highest yield of cyclopropane from ethyldiazoacetate and styrene; a 10 mole% catalyst concentration at 40°C with 5 equivalents of styrene was found to be the best (runs 8, 11 and 12). Initially, the reactions were stirred for 24 h, later we observed 12 h reaction times provided similar results (compare 8 with 11 and 12). The reactions at -78°C gave no cyclopropanation products (runs 1 and 2). Reactions run at 4°C gave lower yields of cyclic products. No cyclopropane was obtained in the absence of the catalyst (runs 15, 16 and 17). The most important aspect of this reaction was the overwhelming cis selectivity in the product (runs 3-14). This result is the first example of a predominant preference for the cis cyclopropane from ethyldiazoacetate and styrene. The selectivity increased with decreasing of temperature but the yield was much lower at low temperature (compare run 3 with 11 and 12). The reaction with α-methylstyrene gave 60±2% of the corresponding cyclopropane with a 60:40 cis to trans ratio, a ratio higher than observed with other catalysts.[9]

TABLE 1: Isolated Yield of Cyclopropane from Reactions of Ethyldiazoacetate with Styrene and α-Methylstyrene Catalyzed by Iron Lewis Acid, $(\eta^5\text{-}C_5H_5)Fe^+(CO)_2(THF)BF_4^-$, 1.[a]

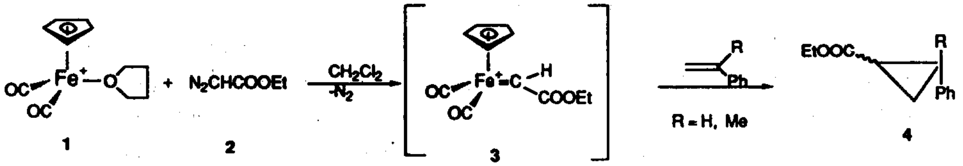
Run	Olefin	Catalyst mole%	Temp. °C	Time hr.	Yield[b] %	Cis/Trans[c]
1	styrene	10	-78	24	0	-
2	"	25	-78	24	0	-
3	"	10	4	24	10	97/3
4[d]	"	10	RT	24	11	80/20
5	"	10	RT	24	39	85/15
6[e]	"	10	RT	24	40	90/10
7[f]	"	10	RT	24	16	90/10
8	"	10	40	24	65	80/20
9,10	"	10	RT	12	40	84±2/16±2
11,12	"	10	40	12	68±3	85±3/15±3
13	"	5	40	12	30	84/16
14	"	25	40	12	71	85/15
15	"	0	4	24	0	-
16	"	0	RT	24	0	-
17	"	0	40	24	0	-
18,19	α-methyl-styrene	10	40	12	60±2	60/40

[a] 1 equivalent of ethyldiazoacetate and 5 equivalents of alkenes were used unless otherwise indicated. [b] Yields were based on ethyldiazoacetate. [c] Ratios were determined by GC. Cis and trans isomers from the reaction were isolated by column chromatography and identified by comparing their ^1H NMR spectra with data from the reported values[3i,j] and were used as authentic samples for the GC. [d] 1 equivalent of styrene was used. [e] 10 equivalents of styrene was used. [f] 50 equivalents of styrene was used.

In a typical experiment, the catalyst was dissolved in methylene chloride under nitrogen. To the stirred solution, the appropriate amounts of styrene and ethyldiazoacetate were added together. This solution was then placed in an oil bath, maintained at 40°C and stirred for 12 h. After this time, the solution was cooled to room temperature, the solvent was removed by rotary evaporation and the products were isolated by column chromatography (1% ethylacetate/hexane mixture on silica gel).

Yates first suggested that metal-catalyzed cyclopropanation could proceed through a transient metal carbene species.[10] Later, Doyle demonstrated that there was a linear correlation of both the relative reactivities and stereoselectivities for $Rh_2(OAc)_4$-catalyzed reactions of phenyldiazomethane with a variety of olefins and the stoichiometric reaction of these same olefins with the isolated tungsten carbene complex $(CO)_5W{=}CHPh$. This has led Doyle to suggest the involvement of carbene complexes in metal-catalyzed cyclopropanation reactions.[11] Despite the lack of concrete evidence for the intermediacy of a metal carbene,[12] Doyle's findings, observed formation of carbene dimers (diethyl fumarate and maleate)[13] and cis selectivity in cyclopropanation reactions[14] are consistent with the chemistry involving the iron carbene complex 3 (Scheme I).

Scheme I



The results of our work illustrate the first example of an iron Lewis acid catalyzed cyclopropanation with a preference for the cis isomer. The reaction also demonstrates the first catalytic cyclopropanation reaction involving an iron carbene complex.[15] The results also raise the possibility of synthesizing an iron carbene complex with an electron withdrawing group at a C_α position. Work is underway to determine the versatility of this method by utilizing a greater variety of alkenes. In addition, mechanistic studies of the reaction are being pursued.

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