

Reduction and carbonylation of gem-dihalogeno cyclopropanes with iron pentacarbonyl

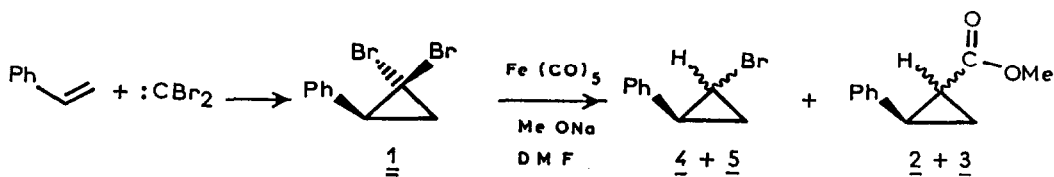
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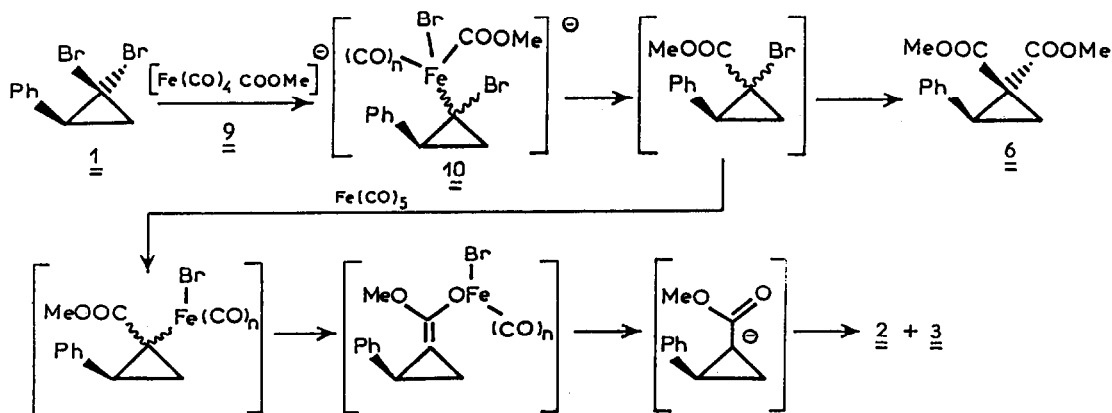
Abstract : Reductive carbonylation of a gem-dibromo cyclopropane to carbomethoxycyclopropane can be achieved with excess $\text{Fe}(\text{CO})_5$ in DMF and an added nucleophile such as MeOH or MeONa.

Carbonylation of vinylic halides (1) and cyclopropyl dihalides (2) has been observed with nickel tetracarbonyl. On the other hand, carbonylation of benzylic halides can easily be achieved with iron pentacarbonyl under mild conditions, especially under phase transfer conditions (3). It has also been reported that $\text{Fe}(\text{CO})_5$ is able to reduce vinylic halides (4) and extensive studies have been carried out on the reductive dehalogenation of bromoketones with the same reagent (5).

As gem-dihalogeno cyclopropanes are obtained in high yields by carbene addition on double bonds (6) it was tempting to achieve directly their reductive carbonylation with iron pentacarbonyl. Such a reaction would provide an easy access to chrysanthemic acid derivatives (7).



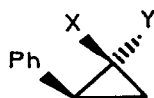
Indeed dibromocyclopropane **1** reacts with iron pentacarbonyl (8) in presence of an added nucleophile such as methanol or better sodium methoxide (16) to yield cyclopropane methyl esters **2** and **3** along with monobromocyclopropanes **4** and **5**, diester **6** and dimethoxy cyclopropane **7**. As indicated in the Table, the proportions of the different products depend on experimental conditions. In all the reactions described herein, the products were recovered after decomplexation, by reacting the crude reaction mixture with a Ce^{IV} solution for 12 hours (9).



(Intermediate complexes have not been isolated)

Carbonylation of halogeno cyclopropane **1** with iron pentacarbonyl in DMF in presence of added MeOH or MeONa.

TABLE



1 :	X = Y = Br	5 :	X = Br, Y = H
2 :	X = H, Y = COOMe	6 :	X = Y = COOMe
3 :	X = COOMe, Y = H	7 :	X = Y = OMe
4 :	X = H, Y = Br	8 :	X = COOMe, Y = Br

Entry	Starting Material	MeONa n equiv.	Yields			
			2+3	4+5	6	7
1 ^a	1	0	10	35	-	-
2	1	1	16	24	10	-
3	1	5	28	15	7	-
4 ^b	1	5	36	10	5	-
5	1	10	-	-	-	15
6	8	0	30	-	-	-
7	8	5	48	-	7	-

a) All the reactions were run in presence of MeONa except the one corresponding to entry 1, where 5 equivalents of MeOH have been used instead.

b) Reaction time is 24 hours in all cases except for entry 4 (72 hours).

Examination of the data (13) reported in the Table shows that when methanol is introduced into the reaction mixture, monobromo derivatives **4** and **5** are the major products accompanied by the two esters **2** and **3** formed by reductive carbonylation (entry 1). When sodium methoxide is used instead of methanol, the relative ratio of the two later derivatives is increased and the formation of a significant amount of diester **6** is observed (entry 2

and 3). Time has some influence on the product distribution (compare entry 3 and 4) and the use of an excess of sodium methoxide completely suppresses the reduction and the carbonylation processes (entry 5) ; the unique reaction product is then dimethylketal 7 which is known to form under such conditions (14). Although never isolated in the reaction medium, bromoester 8 is likely to be an intermediate. Compounds 2, 3 and 6 are indeed formed when this - independently prepared - bromo ester is submitted to the carbonylation reaction (entry 6 and 7).

These results provide some insight on the reaction mechanism which is likely to be involved in the carbonylation of dibromoderivative 1. As the latter does not react with iron pentacarbonyl alone, it is quite unlikely that the carbonylation reaction initially proceeds by an oxidative addition of this reagent on a carbon-bromine bond. On the other hand, nucleophilic substitution of the S_N2 type are quite seldom on cyclopropyl halides (15). The presence of nucleophiles such as MeOH or MeONa is required in the reaction medium in order to observe reduction, carbonylation or reductive carbonylation reactions. These are precisely the experimental conditions which are needed to form an active species such as 9 (16) which does not act as a nucleophile, but oxidatively is inserted into one of the C-Br bonds of 1 to yield intermediate 10. The latter can give rise to 4 and 5 during the isolation procedure, and to the bromo ester 8 by a sort of reductive elimination step. This bromo ester can be further carbonylated to 6, or reduced into a mixture of 2 and 3, probably via an iron enolate quite similar to the one postulated by Hirao (2) when $Ni(CO)_4$ is used instead of $Fe(CO)_5$. Monohalogenated cyclopropanes - which can be obtained by stereoselective reduction (17) of the corresponding dihalogenated derivatives - do not react under such conditions.

Further investigations are in progress to fully understand the mechanisms involved, particularly in order to have a better control of the reductive carbonylation reaction, possibly under catalytic and(or) phase transfer conditions.

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