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gem-Dihalocyclopropane formation by iron/copper activation of tetrahalomethanes in the presence of nucleophilic olefins. Evidence for a carbene pathway

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Abstract—The activation of CBr_4 and CCl_4 by a bimetallic iron/copper couple in acetonitrile is a new, inexpensive, nontoxic and efficient procedure for *gem*-dibromo- and *gem*-dichloromethylenation of nucleophilic alkenes. This new route to *gem*-dihalocyclopropanes involves dihalocarbene species.
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The formation of *gem*-dihalocyclopropanes is already well documented, and most methods involve the addition of dihalocarbenes to an appropriate alkene.[1,2] Many routes have been reported for the generation of dibromo- and dichlorocarbenes. They are easily obtained by α-elimination of hydrogen halides from bromoform or chloroform under basic reaction conditions. The reaction of sodium methylate with ethyl dibromomalonate[3] or ethyl trichloroacetate[4] also gives dibromo or dichlorocarbene, respectively. Alternatively, the reduction of carbon tetrachloride either by $TiCl_4$/ $LiAlH_4$[5] or electrochemically at a lead cathode in a divided cell[6] has also been described. Other reported methods are less frequently used because of either the high cost (iron porphyrinate complexes[7]) or the toxicity (thermal decomposition of mercury complexes[2,8]) of the carbene precursors. The thermal decomposition of sodium trichloroacetate,[9] or of trichloro or trifluoro-(trichloromethyl)silane[1] is also used in the synthesis of

gem-dichlorocyclopropanes. Finally, another route to *gem*-dichlorocyclopropanes is the reductive cyclization of β-chlorotrichloromethyl radical adducts, which occurs, however, with poor selectivity.[10]

We have previously described a simple and efficient way for the activation of CBr_4 or CCl_4 by bimetallic iron/ copper or nickel/copper systems in dimethylform-amide.[11,12] This was used for the efficient conversion of primary alcohols into the corresponding alkyl bromides or chlorides,[11] and in the conversion of arylaldehydes into benzal bromides or chlorides.[12] The key step in these reactions is the reduction of CX_4 into the corresponding dihalocarbene, which reacts with DMF to produce a Vilsmeier type intermediate, which is the actual halogenating reagent[11–13] (Scheme 1).

On the basis of the possible formation of such a dihalocarbene, we thought it possible to use this method
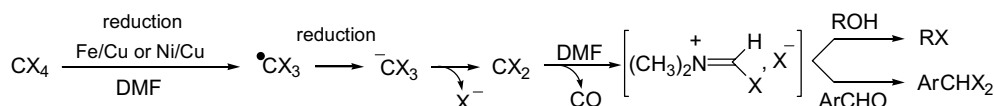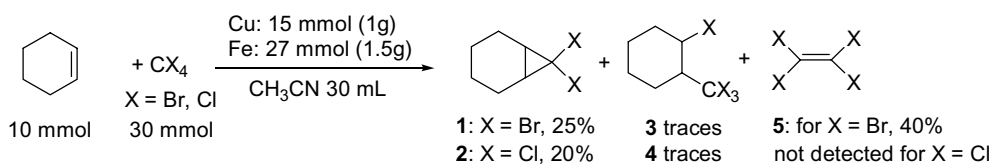
Scheme 1.

of activation for accessing dihalocyclopropanes starting with nucleophilic olefins if, on the one hand, the reaction could be conducted in a solvent other than DMF to prevent the formation of the Vilsmeier species and, on the other hand, the generated carbene or carbenoid is sufficiently electrophilic. The mechanism given in Scheme 1 raises, however, a complex question, since the reduction of CX_4 first produces a CX_3 radical, and it is well known that this radical readily adds to olefins. In addition, copper[14] as well as iron[15] are known to, independently, generate alkyl radicals from organic halides. What, therefore, would be the behaviour of the mixed copper/iron system in the presence of olefin/CX_4 couples?

With all these questions in mind, we started this investigation with cyclohexene as substrate and CBr_4 or CCl_4, according to the reaction conditions indicated in Scheme 2.[16] Dibromo- and dichloronorcaranes **1** and **2** were formed in moderate yields, along with small amounts of the corresponding adducts **3** and **4**, which result from a free-radical chain reaction. Thus, we can not rule out the formation of **1** and **2** by reduction of, respectively, **3** and **4**. It was important to ascertain the extent such a free-radical pathway contributes, if at all, to the formation of the dihalocyclopropane products.

There are typical processes, which can be used to check the possible occurrence of free-radical intermediates. We selected two unsaturated compounds, isopropenyl acetate and β-pinene, which should rearrange after the addition of a radical onto the olefinic bond, thus diverting the process from the formation of a cyclopropyl ring (Schemes 3[15] and 4[15,17]).

The reactions were carried out according to the conditions reported in Scheme 2. The results given in Table 1 clearly indicate that the major products are the cyclopropyl adducts.
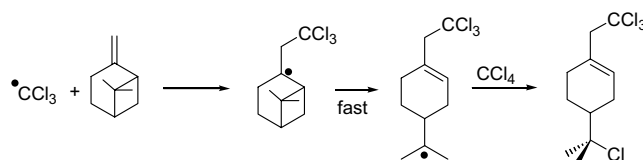
With isopropenyl acetate, yields are poor, probably because of the formation of telomers or polymers (Table
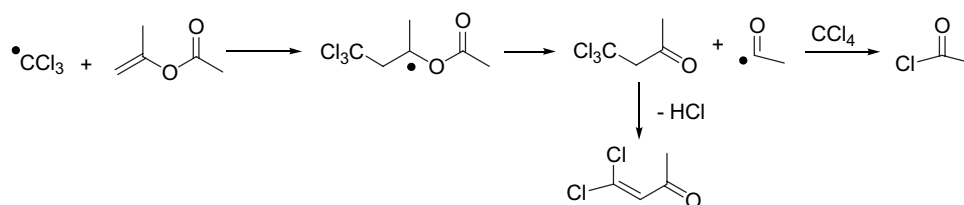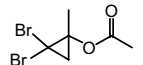
Scheme 4.

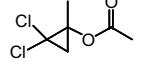1, entries 1 and 2). However, only the cyclopropanes **6** and **7** were isolated; no traces of 4,4-dichlorobut-3-en-2-one (Scheme 3) were found. The fragmentation in the case of isopropenyl acetate (Scheme 3) may, however, not be fast enough and may thus not provide clear-cut evidence for one way or the other. With β-pinene, cyclopropanes **8** and **9** were formed in good yields (Table 1, entries 3 and 4) and only traces of the radical adduct such as the one shown in Scheme 4 were detected.
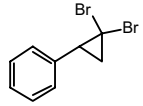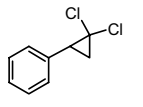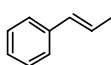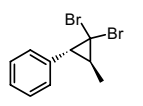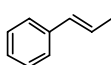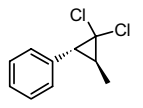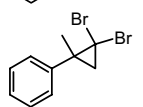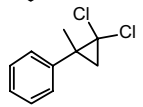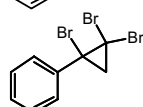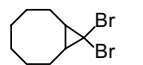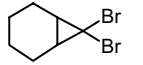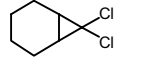
In order to definitely rule out any involvement of a radical pathway, we conducted the following additional experiment. We prepared an authentic free-radical adduct according to the method reported by Ghelfi,[15] that is the reduction of CCl_4 by iron in DMF in the presence of styrene. The adduct 1,1,1,3-tetrachloro-3-phenylpropane was isolated and then allowed to react with the copper/iron system in acetonitrile. The only product was the dimer of 1,1,1,3-tetrachloro-3-phenyl-propane, as characterized by GC–MS. So, it is clear that under our reaction conditions, the reduction of CX_4 only leads to the carbene species, perhaps under the guise of a metallocarbene.

Our process[16] was applied to the synthesis of dihalocyclopropanes from various alkenes using either CBr_4 or CCl_4. The results are reported in Table 2. The yield of cyclopropyl compounds range from poor to high in the case of nucleophilic olefins, and compare favourably with those given in most published procedures. Yields obtained with CBr_4 are generally of the same order as with CCl_4. In contrast, no cyclopropane was formed

Scheme 2.

Scheme 3.

Table 1. Reaction of CBr$_4$ or CCl$_4$ with isopropenyl acetate and β-pinene[a]
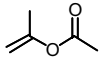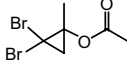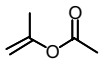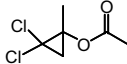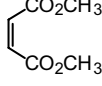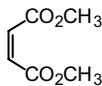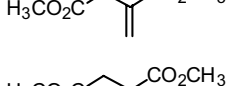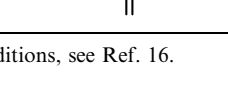
Entry	Olefin	Polyhalomethane	Product	Number	Isolated yield (%)
1		CBr$_4$		**6**	15
2		CCl$_4$		**7**	11
3		CBr$_4$		**8**	50
4		CCl$_4$		**9**	53

[a] Experimental conditions, see Ref. 16.

Table 2. *gem*-Dibromo- or dichlorocyclopropane formation by iron/copper activation of CBr$_4$ or CCl$_4$ and olefins[a]

Entry	Olefin	Tetrahalomethane	Product	Number	Isolated yield (%)
1		CBr$_4$		**10**	26
2		CCl$_4$		**11**	36
3		CBr$_4$		**12**	35
4		CCl$_4$		**13**	44
5		CBr$_4$		**14**	70
6		CCl$_4$		**15**	88
7		CBr$_4$		**16**	55
8		CBr$_4$		**17**	26
9		CBr$_4$		**1**	25
10		CCl$_4$		**2**	20
11		CBr$_4$		**8**	50
12		CCl$_4$		**9**	53

(*continued on next page*)

Table 2 (continued)

Entry	Olefin	Tetrahalomethane	Product	Number	Isolated yield (%)
13		CBr_4		**18**	57
14		CCl_4		**19**	50
15		CBr_4		**6**	15
16		CCl_4		**7**	11
17		CBr_4	—	—	—
18		CCl_4	—	—	—
19		CBr_4	—	—	—
20		CCl_4	—	—	—

[a] Experimental conditions, see Ref. 16.

with electrophilic olefins (Table 2, entries 17–20). This clearly indicates that the generated carbenoid species are electrophilic.

In conclusion, we have reported in this paper a new, inexpensive, nontoxic and efficient procedure for *gem*-dibromo- or *gem*-dichloromethylenation of nucleophilic alkenes. We have notably demonstrated that the key species is indeed a carbenoid.

References and notes

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16. A solution of CX_4 (CBr$_4$ or CCl$_4$, (30 mmol)) diluted in 5 mL of acetonitrile was added to a well-stirred mixture of copper powder (1 g, Aldrich, 99%, −200 Mesh), iron powder (1.5 g, Aldrich, 99.9+%, <10 μm) and the olefin (10 mmol) in acetonitrile (25 mL). The reaction was exothermic with CBr$_4$ and the temperature was controlled by an ice/water bath then stirring was continued at room temperature for half an hour. With CCl$_4$, the reaction mixture was refluxed for 1 h and cooled to room temperature. After the usual work-up, the product was isolated by column chromatography on silica gel (230–400 mesh) using pentane as eluent. The products were fully characterized by ^{1}H, ^{13}C NMR, MS and IR analysis. CAS registry numbers of the cyclopropanes: **1**: [2415-79-4], **2**: [823-69-8], **6**: [85653-77-6], **7**: [6498-46-0], **8**: [33889-86-0], **9**: [33889-85-9], **10**: [3234-51-3], **11**: [2415-80-7], **12**: [97552-09-5], **13**: [61883-02-1], **14**: [17343-73-6], **15**: [3591-42-2], **16**: [178425-56-4], **17**: [1196-95-8], **18**: [22715-57-7], **19**: [3141-45-5].
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