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# $Fe^0$ Initiated Halogen Atom Transfer Radical Addition of Methyl 2-Br-2-Cl-Carboxylates to Olefins

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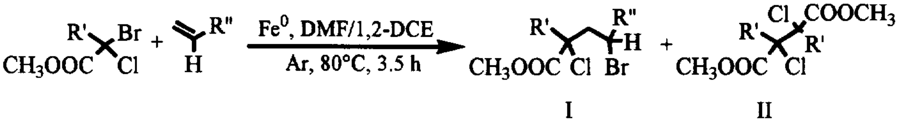
***Abstract***: The halogen atom transfer radical addition (HATRA) of methyl 2-Br-2-Cl-carboxylates to alkenes is obtained in good yields by catalytic amounts of iron filings in dimethylformamide/1,2-dichloroethane at 80°C under argon.

Inter- and intra-molecular radical addition reactions are powerful tools in synthetic organic chemistry.[1] One of the more used method to generate radical species is the reaction of halocompounds with metals, or their salts and complexes.[2] Metals, in particular, have found widespread use as promoters in radical homo-coupling reactions of halo-esters;[3] their application, however, in the Kharasch addition of esters to alkenes has been limited to some α-iodoesters.[4]

Recently,[5] we carried out the addition of methyl 2-Br-2-Cl-carboxylates to olefins in DMF/$CH_2Cl_2$ at room temperature by the combinate CuBr/$Fe^0$ as radical initiator, suggesting the iron metal as the active component.

Now we report that halogen atom transfer radical additions (HATRA) of methyl 2-Br-2-Cl-carboxylates to alkenes can be obtained in good yields by catalytic amounts of iron filings in dimethylformamide (DMF)/1,2-dichloroethane (DCE) at 80°C under Ar atmosphere (Scheme).



Scheme

On using at first a 100 mol% iron powder considerable amounts of homocoupled compounds **II** are produced, likely owing to the large number of carboxy chloromethyl radicals originated and their slow addition to the olefinic bond at room temperature. On reducing the amounts of $Fe^0$ the conversion is unsatisfactory at 25°C and is better at 80°C, because of higher efficiency of the radical chain.[1b] At 100°C with a 10 mol% iron powder the conversion is quantitative but homocoupling becomes too high. By the use of a coarse metal a smoother generation of radicals could have been expected. Iron filings (20 mol%) at 80°C, in fact, gave rise to the best conversion and product yield.

The representative results of the addition reactions from a variety of substrates are listed in the Table. In all cases the HATRA products **I** are obtained in good yields, significantly higher than the previous ones,[5] and in shorter reaction times. Besides little amounts of homocoupled adducts, however, transhalogenation and lactonization products are now detected, from further reactions of **I**. Terminal alkenes only are reactive:[6] 4-vinyl-cyclohexene, for example, chemospecifically reacts at the mono-alkylated olefinic bond (Table, entry 8). Starting from allyltrimethylsilane allylation product is recovered through the elimination of trimethylsilylbromide (Table, entry 9). 2-Monobromoesters, 2,2-dichloroesters and 2,2-dihaloamides are poorly reactive (conversions < 15%) under these conditions.

Table. The addition of methyl 2-Br-2-Cl-carboxylates to alkenes.[7]

| | | | | | product yields (mol/mol %)[a] | | |
|---|---|---|---|---|---|---|---|
| entry | R' | R" | t (h) | conversion[b] (%) | I[c] | II | other[d] |
| 1 | n-$C_4H_8$- | $CH_3(CH_2)_4CH_2$- | 3.5 | 98 | 74(60) | 6 | 7 |
| 2 | $CH_3$- | $CH_3(CH_2)_4CH_2$- | 3.5 | 98 | 82(62) | 5 | 4 |
| 3 | i-$C_3H_7$- | $CH_3(CH_2)_4CH_2$- | 7 | 99 | 75(58) | 7 | 8 |
| 4 | $C_6H_5$-$CH_2$- | $CH_3(CH_2)_4CH_2$- | 3.5 | 100 | 47(48) | - | 35 |
| 5 | $C_6H_5$- | $CH_3(CH_2)_4CH_2$- | 7 | - | -(-) | - | - |
| 6 | $CH_3$- | $CH_2$=$CH(CH_2)_4$- | 3.5 | 100 | 84(64) | 2 | 7 |
| 7 | $CH_3$- | $C_6H_5$-$CH_2$- | 3.5 | 99 | 73(60) | 6 | 5 |
| 8 | $CH_3$- | 4-cyclohexenyl | 3.5 | 99 | 75(58) | 5 | 5 |
| 9 | $CH_3$- | $(CH_3)_3Si$-$CH_2$- | 5 | 100 | 78(64)[e] | 2 | - |
| 10 | $CH_3$- | $CH_3$-CO-O-$CH_2$- | 5 | 100 | 75(37) | 7 | 13 |
| 11 | $CH_3$- | $(CH_3)_3Si$-O-$CH_2$- | 5 | 100 | 70 | 8 | 8 |

[a] Isolated yield are based on the starting ester. [b] Conversion of the starting ester monitored by GC. [c] In parenthesis are shown the yields previously obtained by the CuBr-$Fe^0$ combinate.[5] [d] Other addition products: methyl 2-Cl-2-alkyl-4-Cl-decanoates, methyl 2-Br-2-alkyl-4-Br-decanoates and corresponding γ-lactones. [e] Methyl 2-butyl-2-Cl-but-3-enoate.

Other solvents, ethanol, acetonitrile, dimethylsulfoxide, 2-propanol and dimethoxyethane, and other metal-solvent systems, such as $FeBr_2$ (generated in situ by reaction of CuBr and $Fe^0$)-DMF/DCE, $Ni^0$-ethanol,[8] $Cu^0$-acetonitrile,[9] $Cu^0$-DMF/DCE, $Mn^0$-DMF/DCE, have been tested, but with very poor results.

The addition of 1,4-dinitrobenzene (10 mol%), a single electron transfer scavenger, significantly reduces the conversion, while oxygen completely inhibits the reaction. These results agree with the previously suggested hypothesis,[5] of a free radical chain process initiated by a single electron transfer from $Fe^0$ to methyl 2-Br-2-Cl-carboxylates. As far as we know, the use of $Fe^0$ as the radical initiator in the Kharasch addition of halocompounds to alkenes is quite neglected, the addition of fluoroalkyl iodides being the only reported example.[10]

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6. 1-Alkynes are quite unreactive under these conditions.
7. The reactions were carried out at 80°C under argon in DMF/DCE (1:1, 2 ml); alkene, 10 mmol; ester, 2 mmol; $Fe^0$ filings, 20 mol% (based on the starting ester); workup according to ref. 5.
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