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Copper-catalyzed additions of organic polyhalides to olefins: a versatile synthetic tool

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Abstract - New carbon-carbon σ-bonds between olefins or dienes and organic polyhalides bearing at least two geminal halogen atoms on an sp^3 carbon can easily be formed using catalytic amounts of Cu(I)-compounds. This article reviews the Cu(I)-catalysed additions carried out in our laboratories since 1972 as well as selected examples from the literature. It emphasises the usefulness of the polyfunctionalized 1:1-adducts for the selective syntheses of an array of more complex compounds such as 2-pyrones, aromatics, pyrethroid acids, pyridines, halogenated α-amino acids and 2-pyrrolidinones.

INTRODUCTION AND MECHANISTIC CONSIDERATIONS

Copper and its d^{10} compounds are outstanding in the transition element series for the variety and usefulness of their applications in organic synthesis. This is documented in a monograph (ref. 1) and several review articles (ref. 2) covering different aspects. While the generality of the Cu-catalysed reaction between an olefin or a conjugated diene and an organic polyhalide to form a 1:1-adduct was formulated as early as 1963 (ref. 3), organic chemists have not yet fully appreciated the preparative importance of this fundamental and broadly applicable reaction. Traditionally either organometallic or telomeric aspects of the reaction were explored, rarely the adducts as synthetic intermediates or as target molecules in their own right. Many interesting results remain hidden in the patent literature. So far, the title reaction has not been reviewed.

The structure of the organocopper species involved in the reaction and the mechanisms by which they react are still only vaguely understood. Originally, Asscher and Vofsi (ref. 3a, 4) advanced a redox-transfer chain mechanism in which the catalyst (e.g. Cu(I)Cl) participates in the chain propagation as a chlorine atom transfer agent, being in its oxidised form a much more reactive chlorine donor than the organic polyhalide (eq. 1-3).

$$Cu(I)Cl + CCl_4 \rightleftharpoons Cu(II)Cl_2 + \bullet CCl_3 \quad (1)$$

$$\bullet CCl_3 + C{=}C{-}X \longrightarrow CCl_3{-}C{-}\underset{\bullet}{C}{-}X \quad (2)$$

$$CCl_3{-}C{-}\underset{\bullet}{C}{-}X + Cu(II)Cl_2 \longrightarrow CCl_3{-}C(Cl){-}C{-}X + Cu(I)Cl \quad (3)$$

1 → 2

A number of facts, however, indicate that neither $\bullet CCl_3$ nor radical 1 enters the bulk of the solution. If this were the case, a considerable amount of telomer formation would be expected with highly reactive olefins (monomers) such as styrene, alkyl acrylates and acrylonitrile, even at high organic polyhalide/olefin ratios (ref. 5). However, the exclusive

formation of 1:1-adducts is a prominent feature of this copper-catalysed reaction. Furthermore, the distribution and type of products obtained under free-radical initiation conditions, e.g. in the presence of benzoyl peroxide, are different to those obtained with Cu-catalysts (ref. 3a,6,7). The above facts suggest that the free radicals formed by the reaction of organic polyhalides with copper salts are different from "normal" free radicals such as 1 and $\bullet CCl_3$ due to coordination or interaction with the metallic species. However, the question is still open whether CuCl cleaves the carbon-halogen bond by an overall one-electron change to generate a carbon radical and Cu(II) species (eq. 1) or by an overall two-electron change to generate a Cu(III) species 3 (eq. 4) (ref. 8), followed by insertion of the olefin into the carbon-copper(III) σ-bond of 3 and halogen ligand transfer (reductive elimination) within the new Cu(III) species 4 thus formed.

$$Cu(I)Cl + CCl_4 \longrightarrow \underset{3}{\left[CCl_3Cu(III)Cl_2\right]} \xrightarrow{+\ C{=}C} \underset{4}{\left[CCl_3\text{-}C\text{-}C\text{-}Cu(III)Cl_2\right]}$$

$$4 \longrightarrow CCl_3\text{-}C\text{-}C\text{-}Cl + Cu(I)Cl \qquad (4)$$

In fact, the $CCl_3Cu(III)Cl_2$ complex 3 (eq. 4) and the species on the right side of eq. 1 may only represent two extreme ways of writing a transient Cu(II)/Cu(III) complex, which (a) certainly contains additional ligands, (b) influences the intermolecular reactivity of radical 1 (e.g. by suppressing its ability to start polymerisation) and (c) keeps 1 in the metal coordination sphere until the halogen ligand transfer occurs. It is known that reactions of aliphatic free radicals with $Cu(II)_{aq}$ and Cu(II)-peptide complexes yield relatively long lived intermediates with Cu(III)-carbon σ-bonds (eq. 5) (ref. 9). Nevertheless, the interaction between the $Cu(II)Cl_2$(ligands) complex and radical 1 must be rather

$$Cu(II)_{aq} + \bullet RH \longrightarrow \left[Cu(III)\text{-}RH\right]_{aq} \xrightarrow{H_2O} Cu(I)_{aq} + RHOH \qquad (5)$$

weak, since 1 can acquire a planar trigonal configuration on C(1) and rotate freely around the C(1)-C(2) σ-bond as shown by the complete lack of diastereoselectivity in the addition of CCl_4 to methyl (Z)-β-[^{2}H]-acrylate (ref. 10). Furthermore, 1 can undergo typical intramolecular radical reactions, such as displacement of a β-thioalkyl radical (ref. 11), capture by a β-cyano group (ref. 7b) and cyclisation involving δ,ε-double bond to form 5- or 6-membered rings (ref. 11, 12). Because of the considerable variation of the Cu-catalyst and experimental conditions described in the literature to date, and thus the range of possible contributing factors, it would be unwarranted to draw detailed mechanistic inferences.

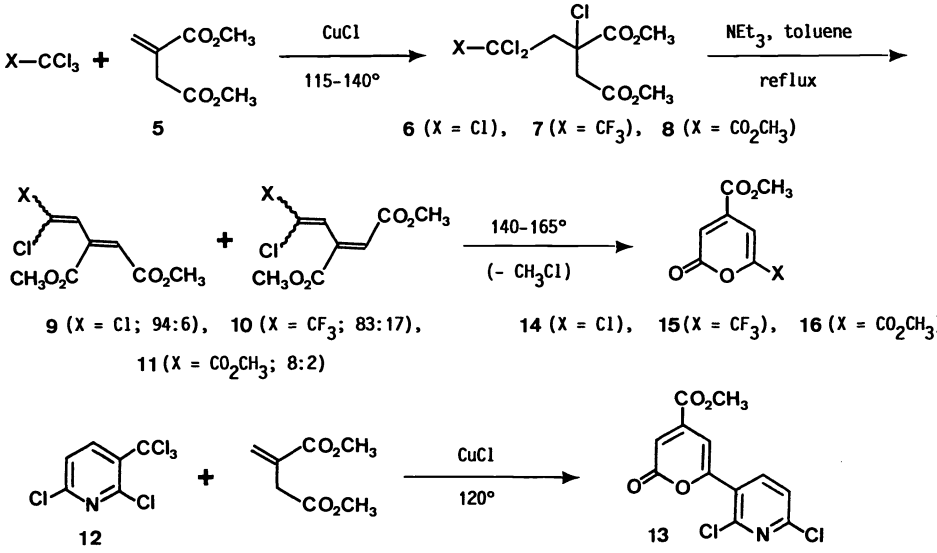
Notwithstanding this mechanistic uncertainty, the formation of a new carbon-carbon σ-bond between many types of terminally unsubstituted olefins or conjugated dienes and a variety of organic polyhalides can very easily be accomplished. Typically, heating of both components in a 1:1 to 1:3 ratio in an aliphatic nitrile solvent to 100-130° in the presence of 1-5 mol % of Cu(I) salts, preferably CuCl, affords 1:1-adducts in good to excellent yields. If Cu(II) salts are used as catalysts, 10-100 mol % of amines or their hydrochlorides are often added to solubilize and to reduce the Cu(II) to Cu(I) (ref. 13) and so to establish a high concentration of the catalytically active Cu(I) species in the reaction medium.

The 1:1-adducts exhibit functionality of sufficient versatility to allow considerable synthetic manipulation. It is the purpose of this paper to show several Cu(I)-catalysed addi-

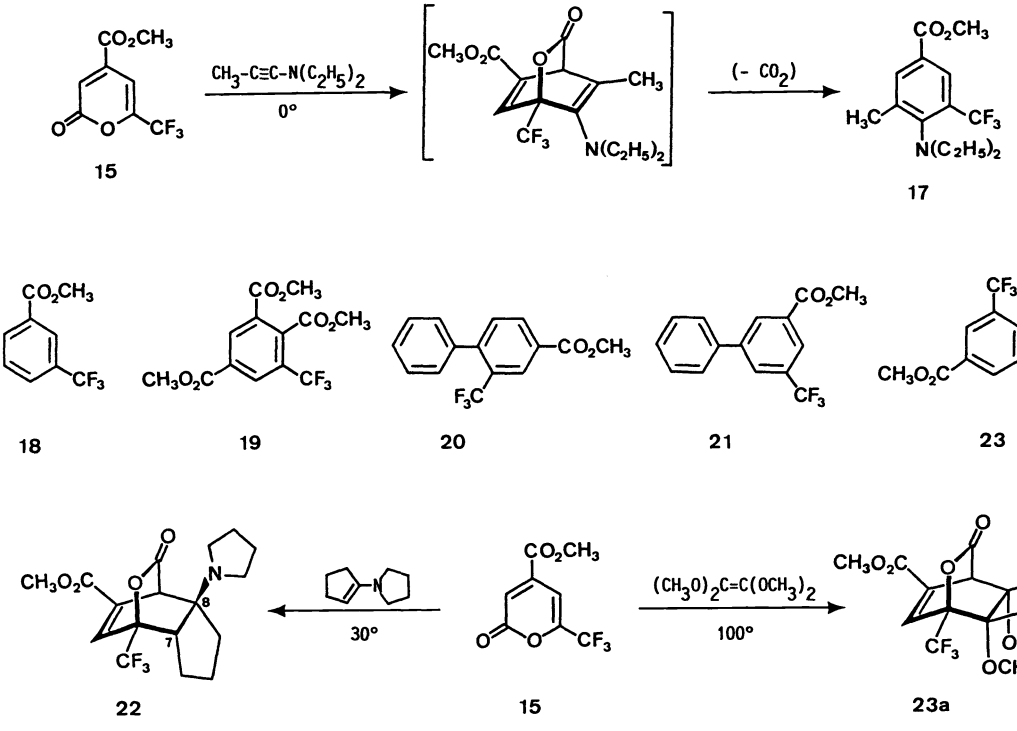
tions carried out in our industrial laboratories since 1972, to demonstrate the usefulness of the 1:1-adducts as synthetic intermediates, as well as to exemplify selected examples from the literature.

ADDITIONS OF ORGANIC POLYHALIDES TO ALKYL ITACONATES

In connection with a programme directed towards the synthesis of new maleic and fumaric acid derivatives there was a need to prepare their halovinyl derivatives. It was envisaged that in analogy to the reported Cu-catalysed additions of organic polyhalides to alkyl methacrylates (ref. 14, 15) and α-methylideneglutarates (ref. 16) the additions to alkyl itaconates should give rise to high yields of the corresponding 1:1 adducts. In fact, the Cu-catalysed (5 mol % CuCl in 200 ml acetonitrile) reactions of 1.5 mol CCl_4, CCl_3CF_3 or $CCl_3CO_2C_2H_5$ with 1 mol of dimethyl itaconate (5) at 115-140° afforded after 8 h the 1:1-adducts 6 (93 % yield), 7 (57 %) and 8 (90 %) (ref. 17). Double dehydrochlorination of 6-8 with triethylamine gave the desired isomeric mixtures of butadienes 9 (92 %), 10 (78 %) and 11 (89 %). However, the analogous Cu-catalysed reaction of 2,6-dichloro-3-trichloromethylpyridine (12) with 5 did not stop at the level of the corresponding 1:1-adduct or butadienes. Instead, the 2-pyrone derivative 13 was isolated in 18 % yield. This result stimulated the successful syntheses of the 2-pyrones 14-16: heating of the butadienes 9-11 in refluxing mesitylene (165°) brought about ring closure with elimination of methyl chloride, e.g. 10 → 15 (64 %) (ref. 17).



The 2-pyrones 14 and 15 are versatile synthetic intermediates. The 6-chloro substituent in 14 can be replaced by a great variety of nucleophiles. A noteworthy feature of 15 is its ability to undergo Diels-Alder reactions with acetylenes. The cycloadducts spontaneously lose CO_2 to form a benzene ring bearing the trifluoromethyl group. The substitution pattern is determined by the regioselectivity of the [4+2]-cycloaddition step. Thus, the reaction of 15 with 1-(N,N-diethylamino)-1-propine takes place at temperatures as low as 0° to produce 17 as a single isomer in 68 % yield. Less electron rich acetylenes require 140° to 200°. Treatment of 15 with acetylene leads to 18 (91 %). With dimethyl acetylenedicarboxylate 19 is formed (67 %). Phenylacetylene affords a 3:2 mixture of biphenyls 20 and 21 (39 %).



In most cases the [4+2]-cycloadducts of 15 with electron rich olefins do not eliminate CO_2. E.g. the reaction of 15 with N-pyrrolidino-1-cyclopentene at 30° gives rise regioselectively to the bicyclic lactone 22 (92 %). When 22 is treated with HCl/dioxane, the indane derivative 23 is obtained (51 %). Reaction of 1-trimethylsilyloxy-1-cyclopentene with 15 at 180° leads directly to 23 (90 %). Many other [4+2]-cycloadducts of 15 with olefins can be isolated in yields of 70 to 90 % (ref. 18); the first Diels-Alder adduct of tetramethoxyethylene with a cyclic diene 23a (71 %) is worthy of special mention.

The merits of this sequence of facile reactions, starting with a Cu-catalysed addition of CF_3CCl_3 to methyl itaconate are obvious: no exotic or aggressive reagents are needed for the regioselective introduction of a trifluoromethyl group of inexpensive Freon origin into useful aromatic compounds.

ADDITIONS OF ORGANIC POLYHALIDES TO ACRYLIC ACID AND ITS DERIVATIVES

Among the modern insecticides, the esters of halovinylcyclopropane acids (pyrethroids) were found by Elliott (ref. 19) to be the most promising class of compounds owing to their extraordinarily high potency, low mammalian toxicity and increased photostability compared with the esters of chrysanthemic acid. Consequently, there have been numerous synthetic approaches to the most important precursor, 2,2-dimethyl-3-(2',2'-dichlorovinyl)-cyclopropane-1-carboxylic acid (30). A short, conceptually unprecedented synthesis of 30 takes advantage of the ready availability of the key 2,4,4,4-tetrachlorobutyric acid chloride 25 either by CuCl-catalysed addition of CCl_4 to acryloylchloride (79 % yield; Table 1) or via the 1:1-adduct 24 of CCl_4 with acrylic acid (Table 1). Alternatively, 25 can be prepared by CuCl-catalysed addition of dichloroacetylchloride to 1,1-dichloroethylene, albeit in lower yield (51 %; see Table 2).

TABLE 1. Addition of Perhalogenated Methanes and Ethanes to Acrylic Acid and its Chloride and Esters (ref. 20e, 22)[a]

Organic Polyhalide	Olefin	Reaction time, Temperature	1:1-Adduct Yield %
CCl_4	CH_2=CHCOCl	24 h, 115°	76
	CH_2=CHCOOH	24 h, 115°	79[b]
	CH_2=CHCOOMe	24 h, 115°	85
CBr_4	CH_2=CHCOCl	6 h, 115°	33
	CH_2=CHCOOH	6 h, 140°	50
$CBrCl_3$	CH_2=CHCOCl	6 h, 120°	31
	CH_2=CHCOOH	6 h, 135°	80
CF_3CCl_3	CH_2=CHCOOH	4 h, 140°	40
CF_2ClCCl_3	CH_2=CHCOOEt	1 h, 150°	51

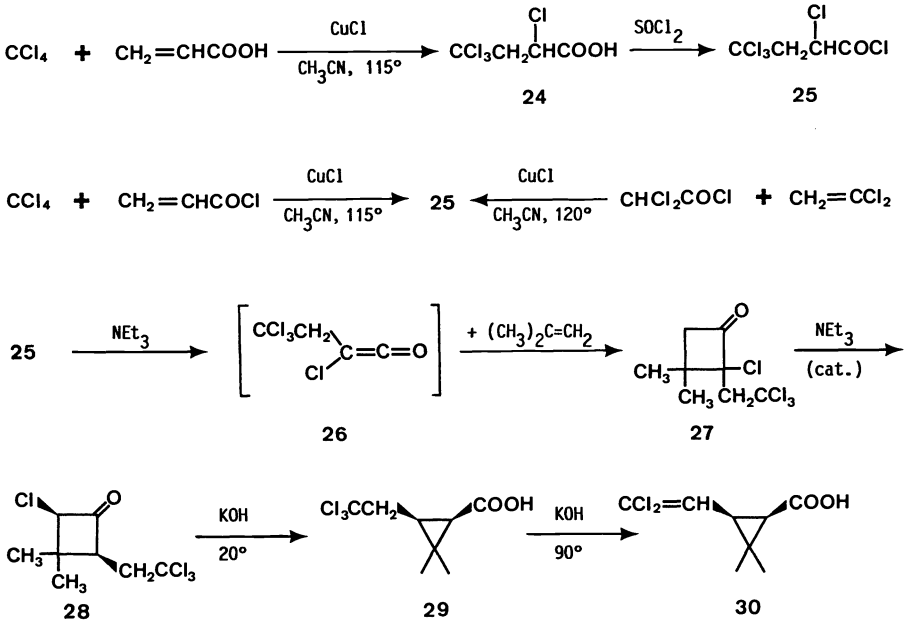
[a] Conditions: 1 mol olefin, 300 ml organic polyhalide, 200 ml acetonitrile, 6 mol % CuCl.
[b] Contains 5-7 % $CCl_3CH_2CH_2COOH$

TABLE 2. Addition of Dichloro- and Trichloroacetic Acid Chlorides and Esters to Halogenated Olefins (ref. 20e)[a]

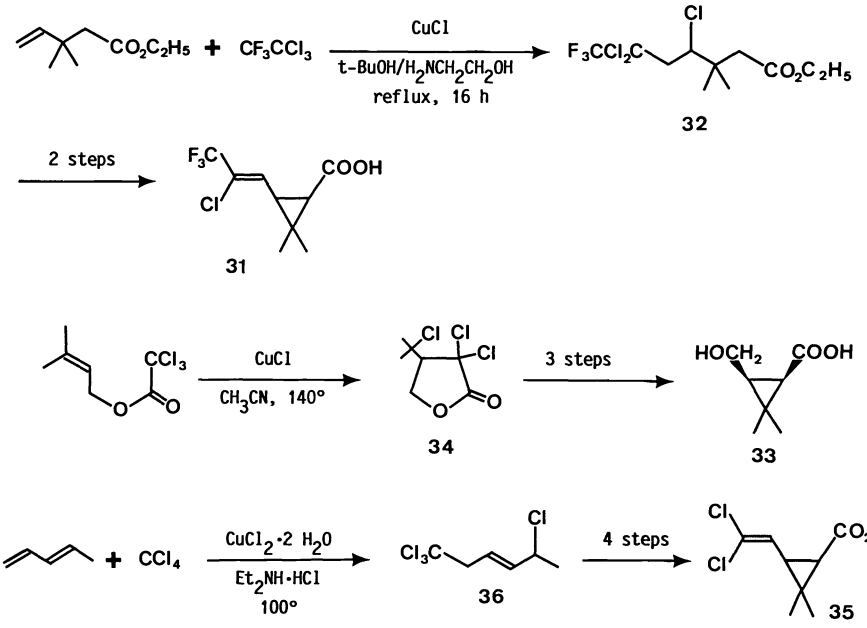
Olefin	Organic Polyhalide	Reaction time, Temperature	1:1-Adduct Yield %[b]
$CCl_2=CH_2$	CCl_3CO_2Me	24 h, 115°	53 (23)
	CCl_3COCl	4 h, 140°	45 (35)
	$CHCl_2COCl$	30 h, 120°	51
$CHCl=CH_2$	CCl_3CO_2Et	4 h, 140°	79
	CCl_3COCl	6 h, 160°	32 (18)
	$CHCl_2CO_2Et$	6 h, 160°	20
$CF_2=CH_2$	CCl_3CO_2Et	8 h, 160°	52
	$CHCl_2CO_2Et$	8 h, 160°	7
$CHF=CH_2$	CCl_3CO_2Et	6 h, 150°	60
	$CHCl_2CO_2Et$	6 h, 160°	14

[a] Conditions: olefin/organic polyhalide 1:1,25, acetonitrile, 3 mol % CuCl. [b] In brackets the yields of "twofold" addition products are given.

The synthetic potential of 25 can be realised on an industrial scale (ref. 20). Dehydrochlorination of 25 by triethylamine in hexane produces the new, very reactive chlorotrichloroethylketene 26, which is trapped in situ by isobutylene to give the cyclobutanone 27 in 67 % yield. The novel cine rearrangement 27→28 is achieved using a catalytic amount of triethylamine in toluene at 120°. The 28 thus formed in 90 % yield is the thermodynamically preferred 2,4-cis isomer. Its straightforward transformation to 30 via 29 proceeds largely under retention of configuration to give the desired acid 30 (82 % yield) containing over 80 % of the biologically more interesting cis isomer. Since (a) a large variety of cyclobutanones of type 27 can readily be prepared using 1,1-dialkyl-substituted ethylenes in place of isobutylene, (b) all 1:1-adducts cited in Table 1 can be transformed into haloketenes of type 26, and (c) cyclobutanones of type 28 can easily be resolved into their optical isomers (ref. 21), the Cu-catalysed addition of organic polyhalides to acrylic acid and its derivatives proves to be an excellent new entry into cyclopropanecarboxylic acids of type 30 (ref. 20), which can e.g. also be applied for synthesis of 31 (ref. 22).

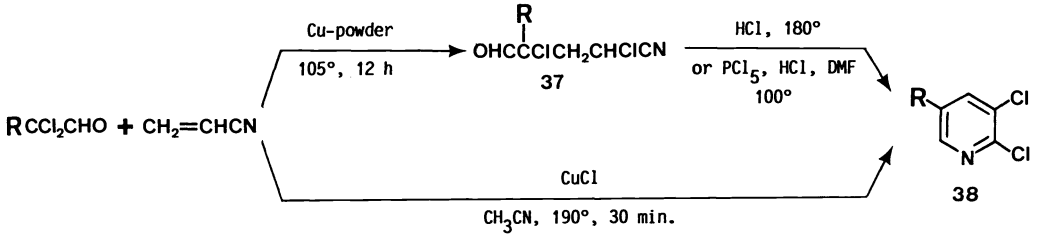


The recent syntheses of cyclopropanecarboxylic acids 31 (cis:trans 1:1) (ref. 23) and 33 (ref. 24) as well as the ester 35 (ref. 25) also deserve mention as all of them are based on a successful Cu-catalysed addition in the first step of the synthetic sequence. The polyfunctionalized 1:1-adducts are formed in 83 % (32), 57 % (34) and in 85 % yield (36), resp.



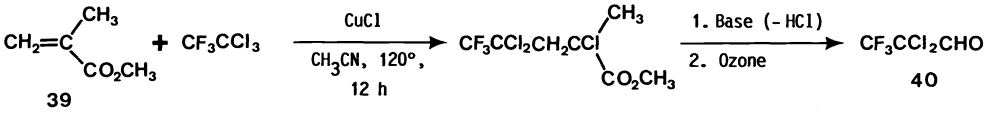
ADDITIONS OF α-HALOSUBSTITUTED ALDEHYDES TO ACRYLONITRILE

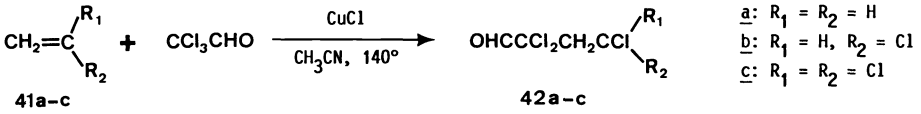
Chlorinated pyridines, especially 2,3-dichloro-5-substituted pyridines, e.g. 38, R = Cl or CF_3, have recently attracted considerable interest because very active pesticides containing these structures began appearing in the late 1970's (ref. 26). When we first considered 38 (R = Cl) as a synthetic target, we set as our goal the development of a strategy that would not only allow the introduction of chlorine but also of any alkyl group in the 5-position of the pyridine 38. This requirement was realised by taking advantage of the facile Cu-catalysed addition of chloral or α,α-dichloroaldehydes to acrylonitrile. In the first step the open-chain adducts 37 are formed which already contain all the necessary substituents and carbon atoms of the target pyridine.



Thus, addition of chloral to acrylonitrile in the presence of 8 mol % of copper powder as catalyst leads to 4-formyl-2,4,4-trichlorobutyronitrile (37; R = Cl) in over 70 % yield (ref. 17, 27). Acrylonitrile serves in this case both as olefin and as ligand for the catalytically active Cu(I) species which probably arises from metallic copper during the re-

action because virtually the same yield is achieved using CuCl as catalyst. 37 contains now only one element of water more than the target pyridine 38. Subsequent exposure of 37 to HCl brings about the envisaged cyclisation to 38 in yields greater than 85 %. Following the approach to 37 (R = Cl), a great number of 4-formylsubstituted pyridine precursors 37 can be synthesised, starting from α,α-dihaloaldehydes. However, yields are often low because of the propensity of 37 for spontaneous HCl-elimination and ring closure during isolation. Nevertheless, these properties of 37 can be turned to advantage, thus allowing an extremely facile one-pot preparation of a great number of pyridines 38, simply by heating an acetonitrile solution of α,α-dichloroaldehyde and acrylonitrile in the presence of 6 mol % of CuCl for 30 minutes at 190° (ref. 17, 28). For example, using this direct procedure 2,2-dichloro-3,3,3-trifluoropropanal 40 furnishes 38 (R = CF_3) in 60 % yield and 2,2,4,4-tetrachlorobutanal 42b gives 38 (R = CH_2CHCl_2) in 57 % yield.





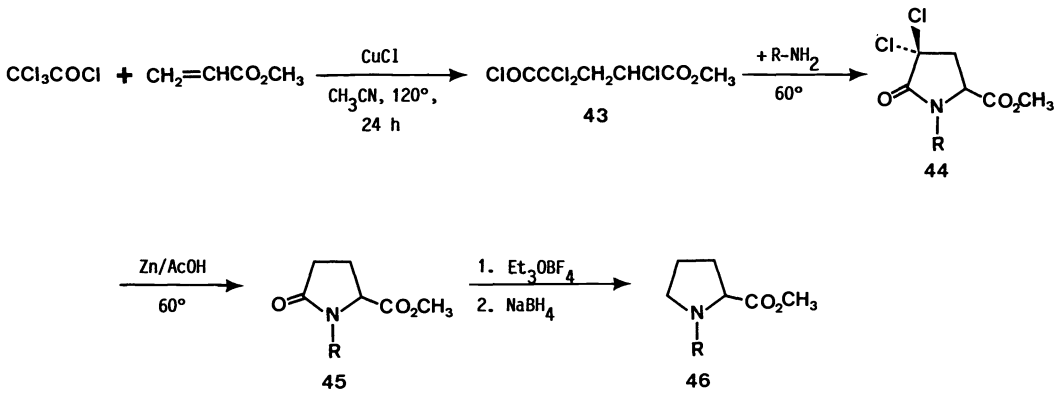
The aldehydes 40 and 42b are chosen to demonstrate a new access to α,α-dichloroaldehydes involving the Cu-catalysed addition of chloral to olefins such as 39 (ref. 15), 41a (68 % yield), 41b (71 %) and 41c (41 %) as shown. We believe that the underlying reactions may also have broad synthetic implications outside the pyridine field for the preparation of substituted aldehydes.

Feasible synthetic routes to 3-halomethyl-2,6-dichloropyridines and 1,8-naphthyridines (ref. 16) as well as to 2,3,5,6-tetrachloropyridine (ref. 29) which also utilise a Cu-catalysed first step to construct the carbon skeleton of the target heterocycle have been published. They use inexpensive, commercially available compounds, e.g. trichloroacetyl chloride and acrylonitrile in the latter case.

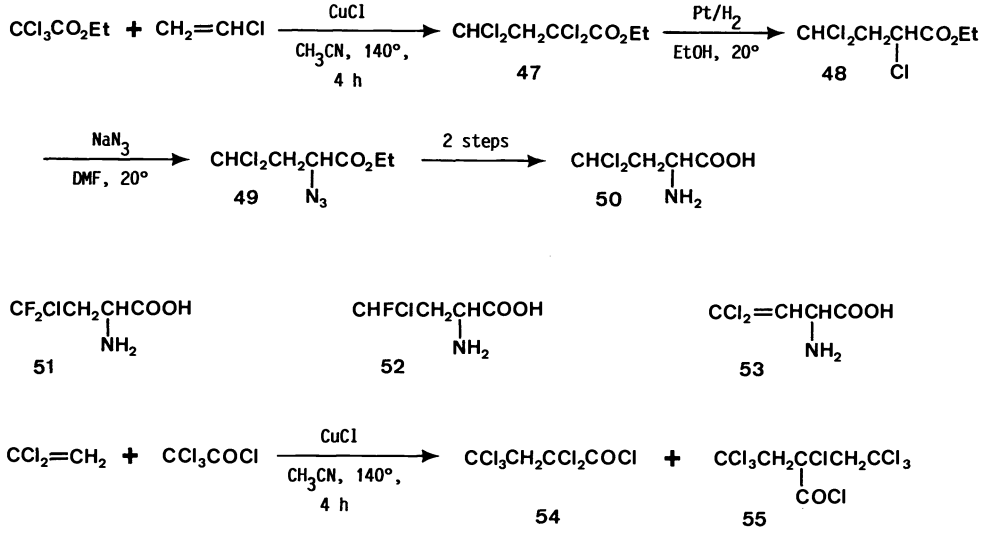
ADDITIONS OF DERIVATIVES OF HALOACETIC ACIDS TO OLEFINS

Intrinsically, this variant of the Cu-catalysed reaction is of special synthetic value, as it enables the introduction of a new functional group (i.e. an equivalent of a carboxy group) into the 1:1-adduct via an appropriately substituted organic polyhalide. The preparative application of some representative examples are given in this chapter.

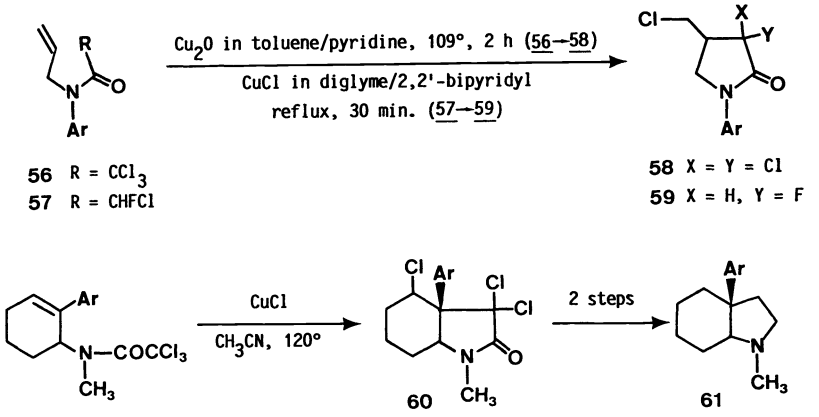
N-Aryl substituted pyrrolidin-2-ones (ref. 30) as well as their 4-carboxy (ref. 31) and 4-chloromethyl (ref. 32) derivatives exhibit a pronounced effect on plant growth. Their natural product related 5-carboxy analogues, i.e. derivatives of the cyclic amide of glutamic acid ('pyroglutamic acid') of type 45 were not investigated in that respect so far because of the lack of a suitable synthesis. Thanks to the Cu-catalysts a remarkably facile general synthesis is now available (ref. 17). The Cu-catalysed addition of trichloroacetyl chloride to methyl acrylate affords the 1:1-adduct 43 in 71 % yield. 43 reacts with a great variety of aliphatic and aromatic amines under simultaneous ring closure to give 3,3-di-



chlorinated pyroglutamates 44, mostly in excellent yields. With ammonia the open chain amide can also be isolated (at 6°) before cyclisation (at 80°) to the lactam 44 (R = H), a precursor for the preparation of the d,l-pyroglutamate 45 (R = H). Straightforward reduction steps now open an entry not only to the desired halogen-free pyroglutamates 45 (e.g. 84 % yield when R = 3-$CF_3C_6H_4$) but also to the N-substituted proline esters 46 (49 % yield when R = 3-$CF_3C_6H_4$). This latter result might be of considerable interest also in the field of biochemistry as it allows the preparation of a great variety of N-aryl prolines which are surprisingly unknown derivatives of this ubiquitous amino acid.



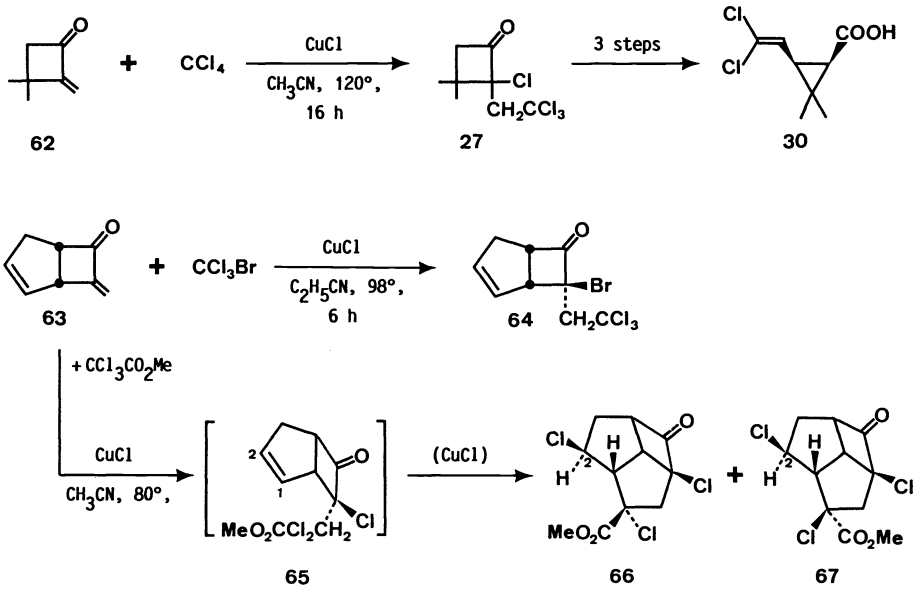
The high-yield synthesis of the known natural antibiotic α-amino acid d,l-armentomycin 50 is based on the selective α-monodechlorination of the 1:1-adduct 47 of ethyl trichloroacetate with vinylchloride (Table 2) (ref. 20e). The α-monochloro ester 48 thus formed in 82 % yield can easily be substituted by NaN_3 to give 49, which is transformed into 50 in conventional manner in an excellent overall yield of 60 %. This facile route also opens an approach to fluorinated and β,γ-unsaturated analogs of armentomycin e.g. 51, 52 and 53. The 1:1-adducts of ethyl trichloroacetate with 1,1-difluoroethylene (52 %) or vinylfluoride (60 %) (Table 2), and $CCl_3CH_2CHClCOOMe$ (Table 1) (ref. 33) serve as starting materials. Inspection of Table 2, footnote b, reveals that in some cases the 1:1-adduct can compete in the presence of Cu-catalyst with the organic halide for olefin to form also the "twofold" addition product in which the organic polyhalide moiety is incorporated in the middle of the new molecule, eg. 54→55 (see also ref. 34).



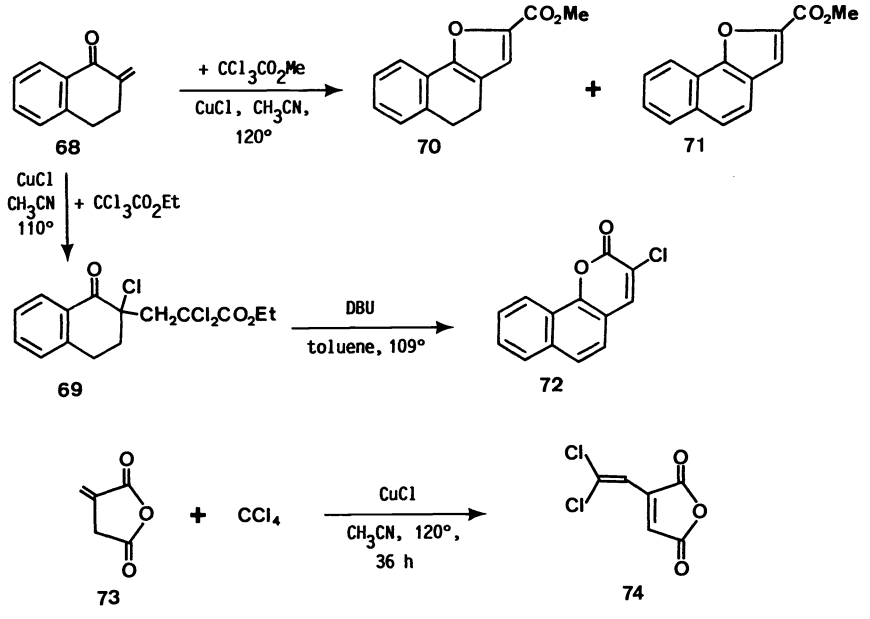
The efficient Cu-catalysed cyclisations of N-allyl di- and trihaloacetamides of type 56 and 57 were extensively used in industrial laboratories for the preparation of large numbers of 4-chloromethyl-2-pyrrolidinone derivatives of type 58 (73 % yield) (ref. 32a) and 59 (87 %) (ref. 32b), which are selective herbicides for weed control. Itoh's recent elegant stereoselective route to d,l-mesembrane 61 (Ar : 3,4-$(CH_3O)_2C_6H_3$), a known degradation product of mesembrine alkaloids, via trichlorolactam 60 (47 % yield of cyclisation) represents an interesting extension of the Cu-catalysed ring closure reaction into the field of natural product synthesis (ref. 35). Similarly, the studies of intramolecular Cu-catalysed cyclisations of allyl trichloroacetates (ref. 36) established a solid basis for Takano's facile synthesis of the chrysanthemic acid precursor 33 via γ-butyrolactones of type 34 (ref. 24).

ADDITIONS OF ORGANIC POLYHALIDES TO α-METHYLIDENE CARBONYL COMPOUNDS

The α-methylidene carbonyl unit is a key feature of many naturally occuring cytotoxic sesquiterpenes or antibiotics and for this reason, methods for its introduction and transformation are of considerable interest. Our interest in α-methylidene carbonyl compounds, however, was awakened by the possibility of an alternative access to the industrially important acid 30 via the Cu-catalysed addition of CCl_4 to α-methylidenecyclobutanone 62. In fact, the reaction 62→27 takes place under standard conditions with virtually quantitative yield. The cyclobutanone 62, now available by HCl-elimination from a [2+2]-cycloadduct of monochloroketene to 2-methyl-2-butene in 64 % yield (ref. 10), was originally not an easy compound to prepare. Therefore our first Cu-catalysed additions were attempted with the readily available α-methylidenecyclobutanone 63. The mild reaction with CCl_3Br gave rise to the desired 1:1-adduct 64 (61 %), which was stable under the experimental conditions. By contrast the 1:1-adduct of 63 with CCl_3CO_2Me was not isolable: the chlorines in the endo-$CH_2CCl_2CO_2Me$ moiety of 65 are apparently considerably more reactive towards the Cu-catalyst than those of the endo-CH_2CCl_3 moiety in 64, as seen in the very facile subsequent intramolecular addition to give the 2H-cyclobuta-[cd]pentalen derivatives 66 and 67 (9:1) in 87 % yield. According to X-ray analysis, in both isomers an exclusive trans-addition of the endo-$CH_2CCl_2CO_2Me$ moiety across the cyclopentene double bond occurred. Mechanistically this implies that if the cis-insertion reaction of type 3→4 involving the endo-face of the cyclopentene double bond applies, then the chlorine in the reductive elimination step (eq. 4) has not been delivered from the coordination sphere of the Cu(III)-species of type 4 to form 66 and 67 because of the complete absence of the C(2)-endo-chloro isomers.



The Cu-catalysed addition of organic polyhalides is by no means restricted to α-methylidenecyclobutanones. α-Methylidene-cyclohexanones, -lactones and -anhydrides are also excellently suited for this reaction (ref. 10). Under standard experimental conditions primary 1:1-adducts often escape isolation because subsequent elimination reactions readily take place. In this way, one step syntheses of interesting intermediates become possible: whereas the reaction of 68 with ethyl trichloroacetate at 110° leads to the expected 1:1 adduct 69 in 70 % yield, reaction with methyl trichloroacetate at slightly higher temperature (120°) surprisingly affords the dihydronaphthofuran 70 as the main product (40 %) along with 71 (6 %). The predominant formation of 70 remains mechanistically obscure. Treatment of 69 with base gives rise to the α-pyrone 72 (47 %). Itaconic anhydride 73 gives with CCl_4 dichlorovinyl maleic anhydride 74 (34 %), apparently by double HCl-elimination from the primary 1:1 adduct (ref. 10).



CONCLUSIONS

The Cu(I)-catalysed reaction described allows the formal insertion of an olefinic double bond into a halogen-carbon bond of an organic polyhalide to form a saturated 1:1-adduct. In spite of the fact that our mechanistic knowledge still lags behind synthetic developments, this first review attempts to illustrate a number of positive aspects of the reaction: (a) the simplicity of the reaction system, (b) the availability and great variability of the reacting components, (c) the predictability of the reaction products, and (d) their high degree of obvious or latent functionality which allows considerable manipulation. All this renders the Cu(I)-catalysed addition an exciting and versatile synthetic tool for both laboratory and industrial scale. A great deal of interesting new chemistry still remains to be found.

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