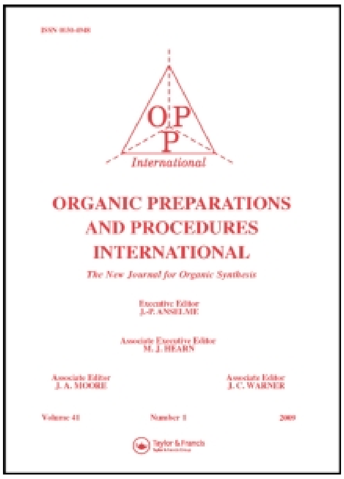

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# REACTIONS OF CARBON TETRACHLORIDE AND CARBON TETRABROMIDE WITH ANIONS AND CARBANIONS. A REVIEW

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# REACTIONS OF CARBON TETRACHLORIDE AND CARBON TETRABROMIDE WITH ANIONS AND CARBANIONS. A REVIEW

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# REACTIONS OF CARBON TETRACHLORIDE AND CARBON TETRABROMIDE WITH ANIONS AND CARBANIONS. A REVIEW

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## INTRODUCTION

Carbon tetrachloride ($CCl_4$) with boiling point 76-77° is a suitable organic solvent in different organic reactions, especially for halogenation reactions. Carbon tetrabromide ($CBr_4$) is a white solid melting at 88-90° seldom used in organic synthesis. Although a number of reviews have been published regarding the preparation of perfluorinated compounds,[1-6] not so much has been reviewed in the chemistry of carbon tetrachloride and carbon tetrabromide.[7-9] The reactions of $CCl_4$ and $CBr_4$ with anions and carbanions generated in the presence of a base have not been reviewed at all.

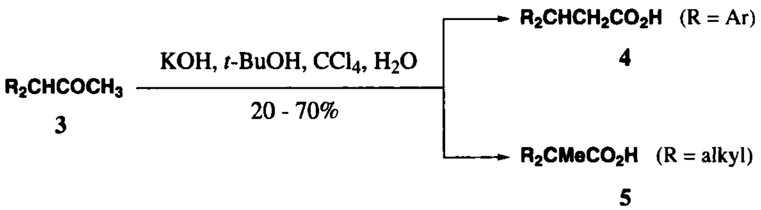
The main reaction of carbanions and anions with $CCl_4$ and $CBr_4$, which are excellent sources of positive halogen, is halogenation. The halogenated products often undergo subsequent transformations-reactions with nucleophiles, dimerization reactions, hydrolysis, etc. Sometimes in reactions of organic substrates in the presence of carbon tetrahalides and base, the formation of corresponding dihalocarbenes, as well as $CX_3^-$ ions is observed. The aim of the present work is to describe these reactions as they have practical significance in the synthesis of different types of compounds.

## I. REACTIONS OF CARBON TETRAHALIDES WITH CARBANIONS GENERATED FROM KETONES

$CCl_4$ and $CBr_4$ are strong electrophiles capable of reacting with many types of ketone enolates. The main reaction usually is chlorination of the carbanion, often followed by further transformations of the chlorinated products in the highly basic medium.

In 1969, Meyers[10-11] found that ketones containing α-hydrogens and lacking hydrogens in α'-position **1** are readily poly-α-chlorinated in the $CCl_4$/KOH/*t*-BuOH system and may subsequently be cleaved into carboxylic acids **2** (*Eq.* 1) while ketones with α- and α'-hydrogens **3** are transformed in situ into carboxylic acids **4** or **5** *via* Favorskii reaction (*Eq.* 2).

$$\underset{\mathbf{1}}{Me_3CCOCH_3} \xrightarrow[80\%]{KOH,\ t\text{-}BuOH,\ CCl_4,\ H_2O,\ 25\text{-}80^\circ} \underset{\mathbf{2}}{Me_3CCO_2H} \qquad (1)$$



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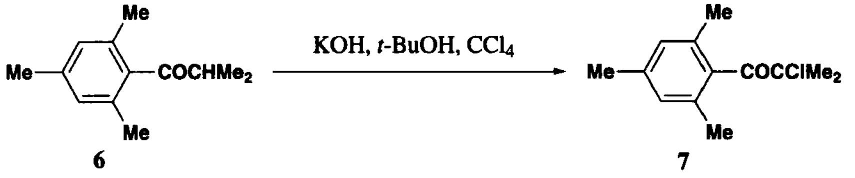
Further investigations [12] showed that sterically hindered ketone **6** underwent α-chlorination to give product **7** without further transformations (*Eq.* 3).



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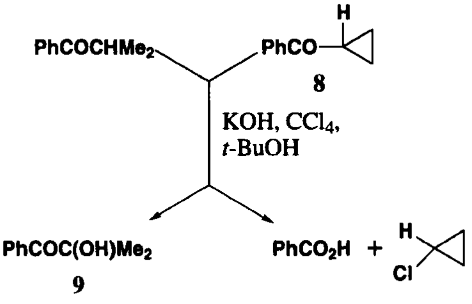
Ketones having only α-hydrogen **8** were usually converted to the α-hydroxy derivatives **9** or underwent cleavage (*Eq.* 4). Later it was shown that similar reactions also occurred when $CCl_4$ was replaced by other perhalomethanes. [13]



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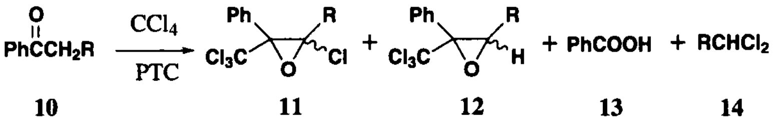
The generation of carbanions from ketones in two-phase catalytic systems considerably simplifies the reactions of these CH acids with $CCl_4$ and opens new synthetic possibilities.[14] It has been found that a similar reaction takes place under phase transfer catalysis (PTC) conditions using aq. NaOH/benzyltriethylammonium chloride (see *Eq.* 1).[15] The PTC reaction of benzyl methyl ketone with $CCl_4$ in the presence of the NaOH/$Bu_4NBr$ system gives a mixture of three products: $PhCHCl_2$, $PhCCl_3$ and 2-methyl-2-trichloromethyl-3-phenyloxirane.[16] Acetophenone under analogous conditions yields a mixture of 2-phenyl-2-trichloromethyloxirane (9% yield) and 2-phenyl-2-trichloromethyl-3-chlorooxirane (10%) and benzoic acid.[17] A detailed study of the reaction of ketones $PhCOCH_2R$ **10** (where R = H, $C_1$...$C_4$-alkyl, $PhCH_2$) with $CCl_4$ in the presence of 50% aq. NaOH and $Bu_4NBr$[18] has generally confirmed these findings, i.e. formation of epoxides **11** and **12**, benzoic acid (**13**), and $RCHCl_2$ (**14**) (*Eq.* 5).



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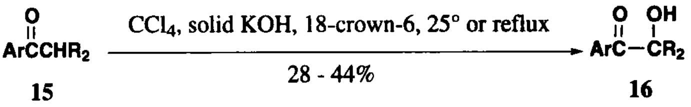
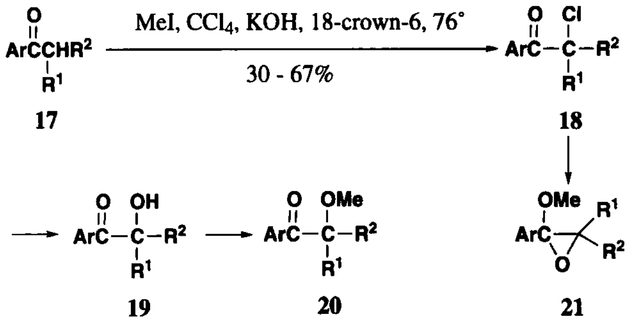
**10** **11** **12** **13** **14**

Only one product-the oxirane **12** (10.5%) was obtained from acetophenone using $CCl_4$/solid KOH/dibenzo-18-crown-6.[19] A similar PTC reaction was carried out with methyl and ethyl hetaryl ketones and the corresponding products, 2-hetaryl-2-trichloromethyloxiranes, were obtained in 8-22% yield.[20] The formation of oxiranes proceeds *via* chlorination of the carbanion with subsequent addition of $Cl_3C$-anion to C=O and intramolecular cyclization.[18-20] Sterically hindered aryl and hetaryl ketones **15** ($ArCOCHR_2$, where Ar = Ph, 2-furyl, 2-thienyl; R = Me, Et) in the presence of the $CCl_4$/solid KOH/18-crown-6 system gave the corresponding α-hydroxyketones **16** *via* α-chloroketones (*Eq.* 6), similar to the homogenous reaction.[20-21]


$$ArC(=O)CHR_2 \xrightarrow[28-44\%]{CCl_4,\ \text{solid KOH, 18-crown-6, 25° or reflux}} ArC(=O)-C(OH)R_2 \qquad (6)$$

**15** **16**

The reactions of sterically hindered ketones **17** ($Ar'COCHR^1R^2$ type, where Ar' = Ph, 2-furyl, 2-thienyl, 5-methyl-2-thienyl; $R^1$, $R^2$ = Me, Et, Ph) in the $CCl_4$/MeI/KOH/18-crown-6 system lead to α-methoxyketones **20** in 30-67% yield (*Eq.* 7).[22] According to gas chromatography data, the formation of products **20** proceeds through the intermediate α-chloroketones **18** and α-hydroxyketones **19**. As a rule, the process of α-methoxylation of ketones is selective-the main by-product was oxirane **21**, resulting from the cyclization of the intermediate **18**.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## II. REACTIONS OF ACTIVE METHYLENE COMPOUNDS WITH CARBON TETRACHLORIDE

Reactions of active methylene compounds with $CCl_4$ in the presence of 1,8-diazabicyclo-[5.4.0]undec-7-ene (DBU) give chlorinated derivatives and dimeric products. Thus, diethyl malonate (**22**), $CCl_4$ and DBU at room temperature under stirring for 5 h afford a mixture of dichloro **23** and dimeric **24** products (*Eq.* 8).[23] Similarly, benzylacetonitrile gives *trans*-dicyanostilbene in 70% yield.[23]

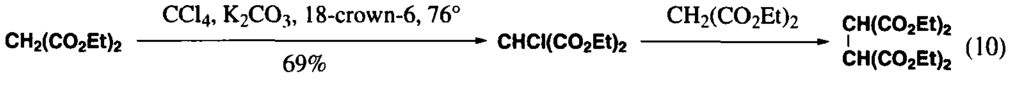
$$\underset{\mathbf{22}}{CH_2(CO_2Et)_2} \xrightarrow[5\ \text{h, rt}]{CCl_4,\ DBU} \underset{\mathbf{23}}{\underset{48\%}{CCl_2(CO_2Et)_2}} + \underset{\mathbf{24}}{\underset{26\%}{(EtO_2C)_2C{=}C(CO_2Et)_2}} \qquad (8)$$

Esters of malonic acid in the presence of $CBr_4$/DBU/THF at low temperatures (-78°) form the corresponding monobromo derivatives in yield up to 75%.[24]

Dimethyl methylmalonate (**25**) in the presence of $CCl_4/Bu_4NF$ affords dimethyl α-chloro-α-methylmalonate (**26**) in 99% yield (*Eq.* 9).[25]

$$\underset{\mathbf{25}}{\mathrm{MeCH(CO_2Me)_2}} \xrightarrow[99\%]{\mathrm{CCl_4,\ Bu_4NF,\ 10\ min,\ rt}} \underset{\mathbf{26}}{\mathrm{MeCCl(CO_2Me)_2}} \qquad (9)$$

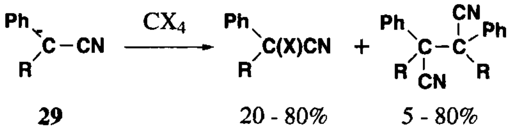
It has been found that diethyl malonate (**22**) in the presence of the $CCl_4$/solid $K_2CO_3$/18-crown-6 system gives dimeric product **28** in 69% yield (*Eq.* 10).[26] The formation of **28** proceeds *via* monochloro derivative **27**.



$$\underset{\mathbf{22}}{\mathrm{CH_2(CO_2Et)_2}} \xrightarrow[69\%]{\mathrm{CCl_4,\ K_2CO_3,\ 18\text{-}crown\text{-}6,\ 76^\circ}} \underset{\mathbf{27}}{\mathrm{CHCl(CO_2Et)_2}} \xrightarrow{\mathrm{CH_2(CO_2Et)_2}} \underset{\mathbf{28}}{\begin{array}{c}\mathrm{CH(CO_2Et)_2}\\ |\\ \mathrm{CH(CO_2Et)_2}\end{array}} \qquad (10)$$

## III. REACTIONS OF CARBON TETRAHALIDES WITH CARBANIONS GENERATED FROM CARBOXYLIC ACIDS, NITRILES AND ESTERS

Carbanions of phenylacetonitriles **29** obtained by the interaction with metallic potassium/*t*-BuOH or NaH/THF systems were halogenated by $CCl_4$ or $CBr_4$ and/or converted into symmetrically-substituted succinonitriles **31** (*Eq.* 11).[27] The halogenation occurs *via* the ionic process, and the formation of **31**-*via* the radical process.



(11)

**29** 20 - 80% 5 - 80%

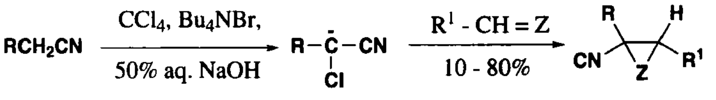
R = alkyl, aryl **30** **31**

Carbanions generated by the treatment of esters **32** (R=Me, allyl) with lithium diisopropylamide (LDA) in THF at -78° react readily with $CX_4$ thus producing α-haloesters **33** in high yields (*Eq.* 12).[28] The absence of dihalocarbenes in the system explains why no dihalocyclopropane derivatives were detected in the products derived from unsaturated esters.

$$\underset{\mathbf{32}}{\mathrm{Me_2CHCO_2R}} \xrightarrow[70\,-\,95\%]{\mathrm{LDA,\ -78^\circ}} \mathrm{Me_2\overset{-}{C}CO_2R} \xrightarrow{\mathrm{CX_4(X = Cl,\ Br)}} \underset{\mathbf{33}}{\mathrm{Me_2C(X)CO_2R}} \qquad (12)$$

Recently this ester halogenation method was used in the synthesis of halogenated derivatives of unprotected (1<u>H</u>-pyrrol-3-yl)propionates.[29]

A variety of carbanions generated from nitriles **34** in the aq. $NaOH/Bu_4NBr$ system with $CCl_4$ formed the chlorinated intermediates **35** capable of acting as nucleophiles in the presence of aldehydes or electrophilic alkenes (R -CH=Z type , where R =H, alkyl, aryl; Z=O, CHCN, CHCOO-*t*-Bu) to form oxirane or cyclopropane derivatives **36** [18,30] (*Eq.* 13). Diphenylacetonitrile in the absence of aldehyde or electrophilic alkene undergoes dimerization.[31]

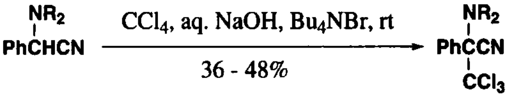


34 35 36

R = alkyl, aryl

(13)

Phenyl(dialkylamino)acetonitriles **37** also react with $CCl_4$/aq. NaOH/$Bu_4NBr$ to afford trichloromethyl derivatives **38** (*Eq.* 14).[18,30] The fact that these products are formed only from **37** implies a special role of amino function.



$$\underset{37}{\overset{NR_2}{\mathrm{PhCHCN}}} \xrightarrow[36-48\%]{CCl_4,\ aq.\ NaOH,\ Bu_4NBr,\ rt} \underset{38}{\overset{NR_2}{\underset{CCl_3}{\mathrm{PhCCN}}}} \qquad (14)$$

R = alkyl

There is only one example of direct α-chlorination of carboxylic acids by perhaloalkanes. Snider and Kulkarni [32] have shown that α-chloro acids were obtained by the treatment of the corresponding acids with LDA and reaction of the acid dianion with excess $CCl_4$.

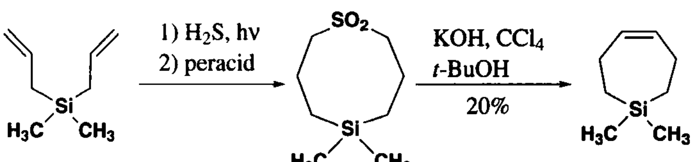
## IV. REACTIONS OF SULFONES WITH CARBON TETRAHALIDES UNDER BASIC CONDITIONS. THE RAMBERG-BACKLUND REACTION

Sulfones possessing α-H atoms are readily α-chlorinated by $CCl_4$ in the presence of base and *t*-BuOH and usually undergo Ramberg-Backlund reaction.[33] Thus, dibenzyl sulfones **39** , as well as di-sec-alkyl sulfones were converted to alkenes **40** (*Eq.* 15) or alkene dichlorocarbene adducts in 30-100% yields.[10,34] Allylic and cyclic sulfones having primary α-carbon atoms also provide simple alkenes.[34,35]

$$\underset{39}{\mathrm{PhCH(R)SO_2CH(R)Ph}} \xrightarrow{CCl_4,\ KOH,\ t\text{-}BuOH,\ H_2O} \underset{40}{\mathrm{PhC(R){=}C(R)Ph}} \qquad (15)$$

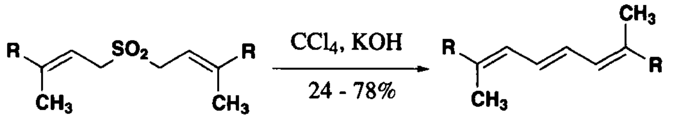
R = H, Me

The Meyers modification of the Ramberg-Backlund reaction was used in the synthesis of unsaturated organosilicon heterocycles **42** from dimethyldiallylsilane (**41**) (*Eq.* 16) [36] and *trans*-trienes **44** from diallylic sulfones **43** (*Eq.* 17).[37] The formation of products **42** and **44** proceeds *via* monochlorinated intermediates.



41 42

(16)



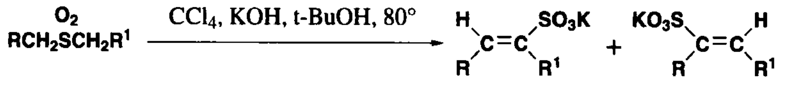
43 44

(17)

R = alkyl

Recently, the Ramberg-Backlund reaction was used in the preparation of paracyclophane derivatives[38] and in the decarboxylative 1,3-displacement of some α-isoprenyl sulfonyl carboxylic esters.[39]

Di-primary-alkyl sulfones were transformed into *cis*-dialkylethylene sulfonic acids *via* the dichlorosulfones. As expected, unsymmetric sulfones **45** provide two positionally isomeric alkenesulfonic acids **46** and **47** (*Eq.* 18). For example, ethyl n-propyl sulfone was converted into the mixture of potassium salts of *cis*-2-pentene-2-sulfonic acid (53% yield) and *cis*-2-pentene-3-sulfonic acid (47%).[34]

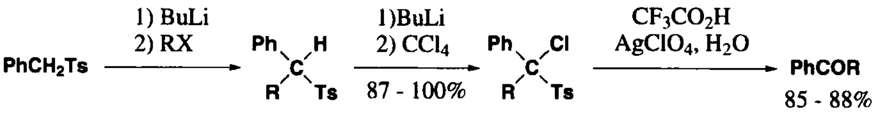


45 46 47

(18)

$R,R^1$ = alkyl

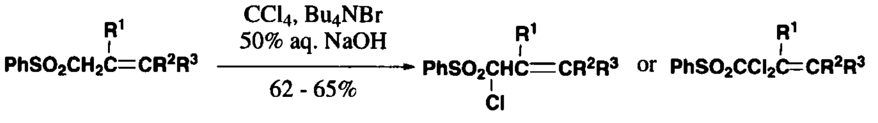
The cyclic sulfones having α- and α'-H atoms were lithiated by the treatment with BuLi and converted to α-mono, α,α'-di and α,α-dichlorinated products by the subsequent interaction with $CCl_4$ or $C_2Cl_6$.[40] Sulfones were also easily monohalogenated by $CX_4$ (X = Cl, Br) in the presence of the NaOH/DMF system at 0° and the products were isolated in 68-96% yields.[41] Carbanions of alkyl p-tolyl sulfones reacted with carbon tetrahalides to give corresponding polyhalogenated products in good yields. The chlorination of alkyl tolyl sulfone **48** with $CCl_4$ was successfully used for the synthesis of unsymmetric aromatic ketones. Thus, the alkylated intermediate **48**, without isolation, was lithiated again with BuLi followed by the addition of $CCl_4$ to obtain chlorinated sulfones **49**. The compounds **49** were treated with silver perchlorate in refluxing trifluoroacetic acid in water solution to afford the aromatic ketones **50** (*Eq.* 19).[42]



$$\mathrm{PhCH_2Ts} \xrightarrow{\text{1) BuLi, 2) RX}} \mathrm{PhCH(R)Ts} \xrightarrow[87-100\%]{\text{1) BuLi, 2) } CCl_4} \mathrm{PhCCl(R)Ts} \xrightarrow[85-88\%]{CF_3CO_2H,\ AgClO_4,\ H_2O} \mathrm{PhCOR} \quad (19)$$

R = alkyl X = Br, I **48** **49** **50**

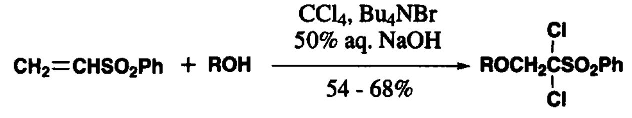
Allyl sulfones **51** in the presence of the $CCl_4$/50% aq. NaOH /$Bu_4NBr$ system afford mono- **52** or dichlorinated products **53** (*Eq.* 20), as well as their dichlorocarbene adducts.[43]



$$\mathrm{PhSO_2CH_2C(R^1){=}CR^2R^3} \xrightarrow[62-65\%]{CCl_4,\ Bu_4NBr,\ 50\%\ \text{aq. NaOH}} \mathrm{PhSO_2CHClC(R^1){=}CR^2R^3} \text{ or } \mathrm{PhSO_2CCl_2C(R^1){=}CR^2R^3} \quad (20)$$

51 $R^1, R^2, R^3$ = H, Me 52 53

It has been shown that phenyl vinyl sulfone **54** in the presence of an excess of alcohols **55** in $CCl_4$/aq. NaOH/$Bu_4NBr$ gives 2-alkoxy-1,1-dichloroethyl sulfones **56** in good yields (*Eq.* 21).[44]



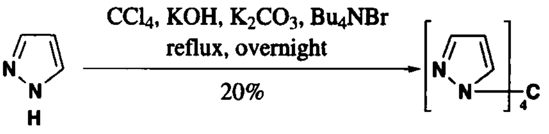
$$CH_2{=}CHSO_2Ph + ROH \xrightarrow[54-68\%]{CCl_4,\ Bu_4NBr,\ 50\%\ aq.\ NaOH} ROCH_2\overset{Cl}{\underset{Cl}{C}}SO_2Ph \qquad (21)$$

**54** **55** **56**

R = alkyl

## V. SYNTHESIS OF POLYAZOLYLMETHANES

The general PTC method of synthesis of polyazolylmethanes using $CCl_4$ has been developed. Thus, pyrazole (**57**) reacts with $CCl_4$ and a mixture of powdered KOH and anhydrous $K_2CO_3$ in the presence of catalytic $Bu_4NHSO_4$ to afford tetra(1-pyrazolyl)methane (**58**) (*Eq.* 22).[45]



(22)

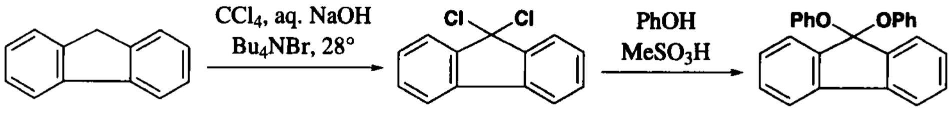
**57** **58**

## VI. REACTIONS OF CARBON TETRAHALIDES WITH HYDROCARBONS AND HALOGENATED HYDROCARBONS IN THE PRESENCE OF BASES

Some hydrocarbons having activated protons undergo deprotonation in the presence of strong bases and the subsequent halogenation of the carbanion with perhaloalkanes. Thus, diphenylmethane **59** deprotonated by $NaNH_2$ or $KNH_2$ in liquid $NH_3$ reacts with $CCl_4$ and alkali diphenylmethide to afford 1,1,2,2-tetraphenylethane (**60**) in good yields (*Eq.* 23).[46]

$$\underset{\mathbf{59}}{Ph_2CH_2} \xrightarrow[89\%]{MNH_2,\ (M = Na,\ K)} Ph_2CHM \xrightarrow{1)\ CCl_4\quad 2)\ Ph_2CHM} \underset{\mathbf{60}}{Ph_2CHCHPh_2} \qquad (23)$$

Fluorene **61** was sufficiently chlorinated in the presence of the $CCl_4$/aq. NaOH/$Bu_4NOH$ system to give 9,9-dichlorofluorene (**62**) which was easily converted to 9,9-bis(phenoxy)fluorene (**63**) by the reaction with PhOH and catalytic $MeSO_3H$ (*Eq.* 24).[47]

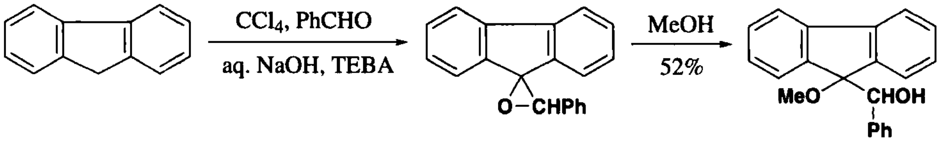


(24)

**61** **62** **63**

When **61** was stirred in the presence of benzaldehyde in the two-phase $CCl_4$/aq. NaOH/ $Et_3(PhCH_2)NCl$ (TEBA) system the formation of oxirane **64** occured. The latter undergoes ring opening in methanol to give 9-(α-hydroxybenzyl)-9-methoxyfluorene (**65**) (*Eq.* 25) [30]. 3-Methyl-2-

azafluorene and 4-azafluorene reacted similarly with benzaldehyde and $CCl_4$/aq. NaOH/TEBA to afford the corresponding oxiranes and dichlorinated adducts.[48]



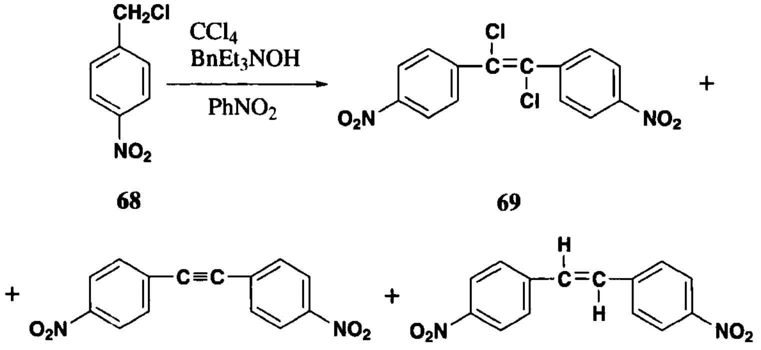
**61** **64** **65** (25)

Benzyl and benzal chlorides, as well as heterocyclic analogues (**66**) were sucessfully converted into the trichloromethyl derivatives **67** using the $CCl_4$/n-dodecyltrimethylammonium chloride or 18-crown-6/50% aq.NaOH or solid KOH systems in 27-91% yields (*Eq.* 26).[49,50]

$$\underset{\mathbf{66}}{\mathrm{Ar{-}CHCl_2}} \xrightarrow[27-91\%]{\mathrm{CCl_4,\ OH^-,\ PTC}} \underset{\mathbf{67}}{\mathrm{ArCCl_3}} \qquad (26)$$

Ar = Ph, substituted Ph, pyridyl, pyrazinyl

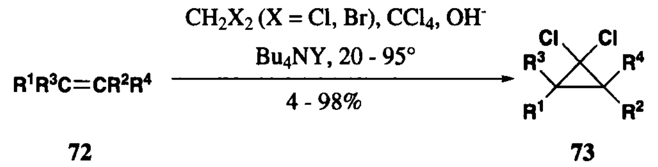
*p*-Nitrobenzyl chloride (**68**) and benzyltriethylammonium hydroxide in a mixture of $CCl_4$ and $C_6H_5NO_2$ (1:2) gave α,α'-dichloro-*p,p*'-dinitrostilbene (**69**) in up to 98% yield. Bis(*p*-nitrophenyl)acetylene (**70**) and *p,p*'-dinitrostilbene (**71**) were obtained as by-products (*Eq.* 27). It was also found that in the absence of nitrobenzene the yield of the main product was only 25%.[51]



**68** **69** **70** **71** (27)

## VII. REACTIONS OF ALKENES AND ACETYLENES WITH CARBON TETRAHALIDES UNDER BASIC CONDITIONS

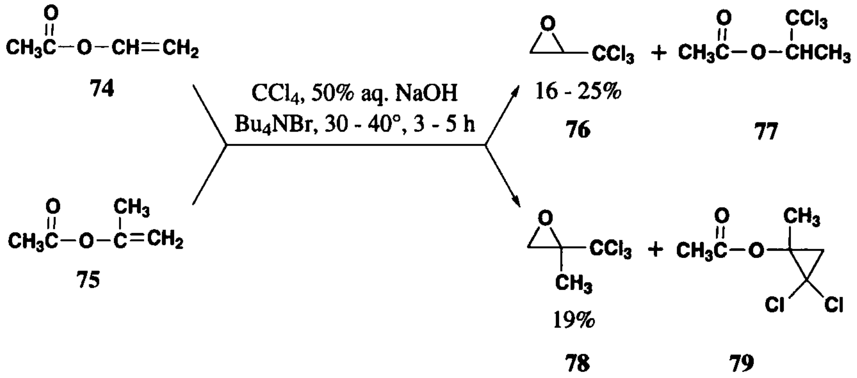
Under basic conditions $CCl_4$, $CBr_4$, $CCl_3Br$, $CCl_3CCl_3$ are able to induce halogenophilic reactions affording carbenes $:CCl_2$ or $:CBr_2$ via $CCl_3^-$ or $CBr_3^-$. The main reaction of these carbenes with alkenes is generally the formation of gem-dihalocyclopropanes. Thus, when $CCl_4$ or $CBr_4$ were treated with methyl or *n*-butyl lithium in the presence of excess cyclohexene in ether solution at -60° to room temperature olefin-carbene addition products were formed in 8-91% yields.[52] Later it was shown that similar carbenes could be generated by the interaction of perhaloalkanes with potassium *t*-butoxide in *t*-butanol/cyclohexene or potassium amide in anhydrous liquid ammonia /ether systems.[53] The PTC systems $CCl_4/CH_2X_2$ (X = Cl, Br)/60% aq.NaOH , 60% aq. KOH or solid $KOH/Bu_4NY$ (Y = Br, $HSO_4$) permit the preparation of gem-dichlorocyclopropanes **73** from alkenes **72** (*Eq.* 28). The reactions proceed *via* the formation of dichlorocarbene.[54] If bromoform is used instead of dihalomethanes gem-bromo(chloro)cyclopropanes were obtained as the main products in 48-53% yields.[55]



(28)

$R^1$ - $R^4$ = H, Ph, alkyl

It has also been found that trichloroethylene is very effectively chlorinated under PTC conditions to give tetrachoroethylene in 80% yield.[30] Enol esters in two phase catalytic systems afford trichloromethyl substituted oxiranes and other chlorinated products. Thus, vinyl acetate (**74**) in the presence of 50% aq. $NaOH/CCl_4/Bu_4NBr$ gives a 1 : 5 mixture of oxirane **76** and trichloromethylated adduct **77**. Isopropenyl acetate (**75**) with $CCl_4$ affords the oxirane **78** as main product and small amounts of the dichlorocarbene adduct **79** (*Eq.* 29).[56]



(29)

Phenylacetylene (**80**) was successfully chlorinated in the presence of the $CCl_4$ /50% aq.NaOH/TEBA system at 35° to afford phenylchloroacetylene (**81**) in 45% yield (*Eq.* 30) .[57] Substrate **80** was also successfully halogenated by the reaction of perhaloalkane in the presence of quaternary ammonium fluoride [58].

$$\underset{\mathbf{80}}{PhC\equiv CH} \xrightarrow[45\%]{CCl_4,\ 50\%\ aq.\ NaOH,\ TEBA} \underset{\mathbf{81}}{PhC\equiv CCl} \qquad (30)$$

Pyridylacetylenes were chlorinated under PTC conditions using $CCl_4$/solid KOH/18-crown-6 to afford the corresponding chloro derivatives in 40-52% yields.[59] Additionally, mild and selective bromination of terminal acetylenes **82** can be accomplished using $CBr_4$/solid KOH/18-crown-6.[60, 61] It has been found that 0.75 equivalent of $CBr_4$ with 1 equivalent of phenylacetylene or other terminal acetylenes is an optimal amount of brominating agent for the synthesis of **83** (*Eq.* 31).

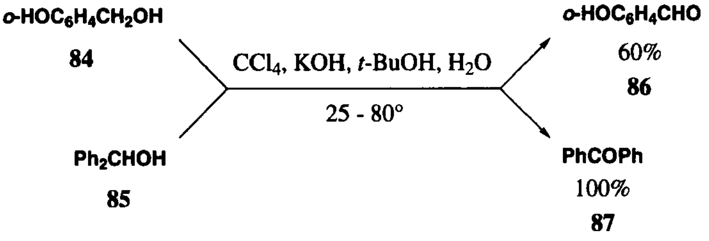
$$\underset{\mathbf{82}}{RC{\equiv}CH} \xrightarrow{CBr_4,\ KOH,\ 18\text{-crown-6},\ 20^\circ} \underset{\mathbf{83}}{RC{\equiv}CBr} \qquad (31)$$

R = alkyl, aryl, hetaryl

Method of synthesis for the novel class of biologically active substances *O*-(ω-bromopropargyl)oximes by bromination of *O*-propargyloximes in the presence of $CBr_4$ has also been elaborated.[61] Bromination of *E*-ketoxime and aldoxime *O*-propargyl ethers proceeds stereoselectively giving only *E*-isomers of brominated products.

## VIII. REACTION OF ANIONS GENERATED FROM ALCOHOLS AND NITROPROPANE AND 1,2-DIBENZYLHYDRAZINES WITH CARBON TETRACHLORIDE

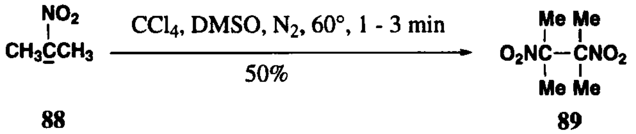
The reactions of alcohols with carbon tetrahalides under basic conditions have been described only in a few articles. In 1969, Meyers et.al showed that primary alcohols **84** in the presence of $CCl_4$/KOH/*t*-BuOH/$H_2O$ are oxidized to the corresponding aldehydes **86** if the latter are resistant to alkali (*Eq.* 32). The aldehydes may subsequently undergo aldol condensations leading to polymers or the Cannizzaro reaction leading entirely to carboxylic acids. Secondary alcohols **85** are oxidized to ketones **87** (*Eq.* 32). If the latter have α-hydrogens they react further to form carboxylic acids. Tertiary alcohols are essentially unreactive.[10]



(32)

An unusual dehydrogenation/oxidation of benzyl alcohol to benzaldehyde was observed in the $CCl_4$/$Na_2CO_3$/quaternary ammonium salt PTC system in the presence of $RuCl_3$• triphenylphosphine complex.[62]

The lithium and potassium salts of 2-nitropropane anion (**88**), prepared *in situ* from nitropropane and potassium *tert*-butoxide, react with $CCl_4$ in DMSO to afford 2,3-dinitro-2,3-dimethylbutane (**89**) in 50% yield (*Eq.* 33).[63]



$$\underset{\mathbf{88}}{CH_3\overset{NO_2}{\overset{|}{\underset{-}{C}}}CH_3} \xrightarrow[50\%]{CCl_4,\ DMSO,\ N_2,\ 60^\circ,\ 1-3\ min} \underset{\mathbf{89}}{O_2N\overset{Me}{\underset{Me}{C}}{-}\overset{Me}{\underset{Me}{C}}NO_2} \qquad (33)$$

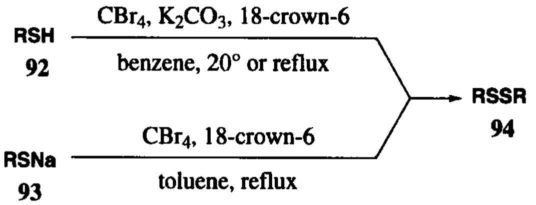
1,2-Dibenzylhydrazines **90** in the $CCl_4$/$Na_2CO_3$/$H_2O$/$Et_3(PhCH_2)NCl$ system undergo oxidation to the corresponding unsaturated derivatives **91** (*Eq.* 34).[64]

$$\underset{\mathbf{90}}{ArCH_2NHNHCH_2Ar} \xrightarrow[Et_3PhCH_2NCl]{CCl_4,\ H_2O,\ Na_2CO_3} \underset{\mathbf{91}}{ArCH_2N{=}NCH_2Ar} \qquad (34)$$

## IX. REACTIONS OF ANIONS OF THIOLS WITH CARBON TETRAHALIDES

Aliphatic, aromatic and heteroaromatic thiols **92** in the $CBr_4$/solid $K_2CO_3$/18-crown-6/benzene PTC system or sodium mercaptides **93** in the $CBr_4$/18-crown-6/benzene system underwent dimerization to disulfides **94** isolated in 67-88% yields (*Eq.* 35).[26]

In all cases bromoform was formed. It has been suggested that the reactions of dimerization proceed *via* brominated thiols (RSBr), not detectable due to the rapid changes. The described method for the synthesis of disulfides is convenient and simple expecially for the heterocyclic ones which are difficult to obtain otherwise.



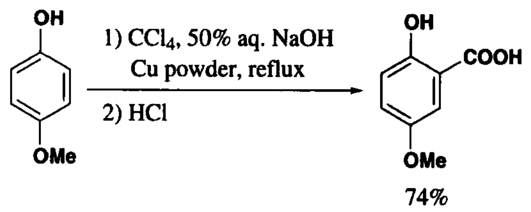
(35)

Synthesis of thioureas **96** by the three component reaction of amines **95**, $CCl_4$ and sulfide ions was described. Thiophosgene, carbon disulfide and trithiocarbonates were detected as an intermediates in this conversion (*Eq.* 36).[65]

$$\underset{\mathbf{95}}{RNH_2} + Na_2S \xrightarrow{CCl_4,\ NaOH} \underset{\mathbf{96}}{RNHCSNHR} \qquad (36)$$

## X. REIMER-TIEMANN REACTION IN THE PRESENCE OF CARBON TETRAHALIDES

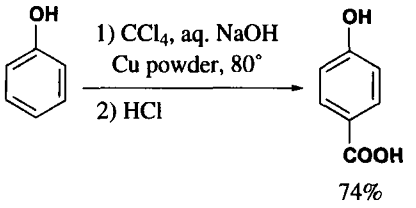
The carboxylation of phenols by carbon tetrachloride under alkaline conditions was reported in 1876 by Reimer and Tiemann [66] and reviewed in 1960 by Wynberg.[67] The excellent catalytic effect of copper metal was reported later in the preparation of 2-hydroxy-5-methoxybenzoic acid **98** from hydroquinone monomethyl ether (**97**) (*Eq.* 37).[68]



**97** **98**

(37)

Low yields and selectivity are considered the main disadvantages of this method. However, the *para*-carboxylation of phenol **99** has been ilustrated.[69] The direction of attack of trichloromethyl cation (generated by copper catalyst from $CCl_4$) on phenolate was found to be strongly dependent on the concentration of aqueous sodium hydroxide used. The selective formation of *p*-hydroxybenzoic acid (**100**) was observed under very mild conditions (*Eq.* 38).

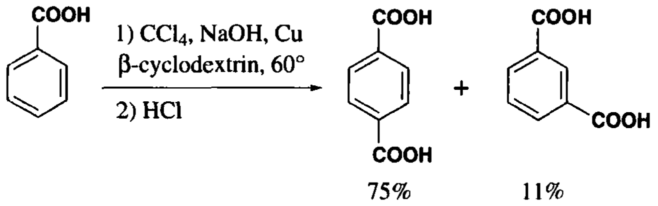


(38)

**99** **100**

Komiyama and Hirai observed that in the presence of β-cyclodextrin the carboxylation reaction of phenols selectively led to the para product.[70] *p*-Aminobenzoic acids were prepared selectively by the reaction of anilines $R^2C_6H_4NRR^1$ (where $RR^1$ = H, alkyl; $R^2$ = alkyl, halo, $NO_2$, COOH, $NH_2$) with $CX_4$ (X = halogen) in aqueous alkali in the presence of cyclodextrin and Cu powder [71].

Benzoic acid (**13**) upon heating with $CCl_4$ in aqueous NaOH in the presence of copper powder and β-cyclodextrin selectively gives terephthalic acid (**101**) in good yield (*Eq.* 39).[72]



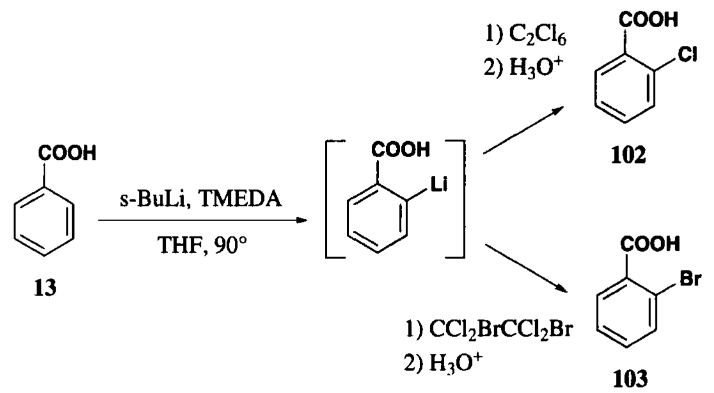
(39)

**13** **101**

4-Biphenylcarboxylic acid under similar conditions selectively afforded 4,4′-biphenyldicarboxylic acid.[73]

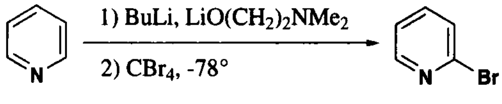
## XI. HALOGENATION OF AROMATIC AND HETEROAROMATIC COMPOUNDS WITH PERHALOALKANES *via* LITHIATION

The direct lithiation and ortho lithiation of substituted aromatic compounds is a method for the preparation of synthetically useful aryllithium intermediates.[74,75] The interaction of lithium intermediates with perhaloalkanes gives the halogenated products. Thus, benzoic acid (**13**) undergoes ortho lithiation with s-BuLi/TMEDA in THF at -90°. Treatment of the Li-salt with perhaloalkanes (hexachloroethane or 1,2-dibromotetrachloroethane) affords 2-chloro- (**102**) or 2-bromobenzoic acid (**103**), respectively (*Eq.* 40).[76]



(40)

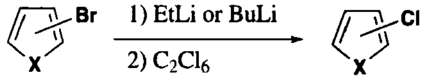
Pyridine (**104**) is metallated at -78° with BuLi.LiO$(CH_2)_2NMe_2$ complex and treated with $CBr_4$ to give selectively 2-bromopyridine (**105**) in 85% yield (*Eq.* 41).[77]



**104** **105**

(41)

Chlorofurans and chloroselenophenes **107** are prepared *via* metallation of the corresponding bromo derivatives **106** followed by treatment with with $C_2Cl_6$ (eq 42).[78]



**106** X = O, Se **107**

(42)

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