SYNTHETIC COMMUNICATIONS, 22(14), 2043-2052 (1992)

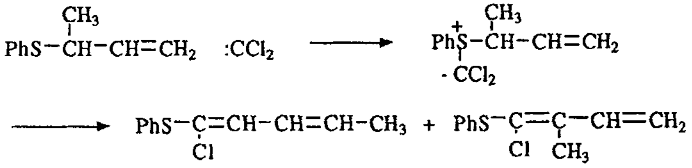
DIHALOCYCLOPROPANATION OF PHENYLTHIO OR BUTYLTHIOCYCLOALKENES UNDER PHASE TRANSFER CONDITIONS. OPENING OF CYCLOPROPANES UNDER MICROWAVE IRRADIATION.

Didier Villemin * and Bouchta Labiad,

Ecole Nationale Supérieure d'Ingénieurs de Caen
I.S.M.Ra, U.R.A.480 CNRS, F-14050 Caen cedex, France.

Abstract:
Dihalocarbenes (X=Cl,Br) generated under phase transfer conditions added to phenylthio or butylthiocylcloalkenes give corresponding 1,1-dihalo-2-thiobutyl or thiophenyl-cyclopropanes. The ring opening of dichlorophenylthiocyclopropanes (**2a**, **2b**, **2c**) was obtained by using silver tetrafluoborate on alumina under microwave irradiation.

Addition of dihalocarbenes to olefins is a widely used method in order to prepare cyclopropanes [1]. The addition of dihalocarbene to enolethers is similar to the addition to olefins [2]. With thioenol ethers the dihalocarbene (X= Cl, Br) which is a soft acid can react with sulfur atom or (and) with the π-carbon-carbon bond [3]. Reaction of dichlorocarbene with allylthioethers gave products due to a Stevens



$$\mathrm{PhS{-}\overset{\displaystyle CH_3}{\overset{|}{C}}H{-}CH{=}CH_2 \quad :CCl_2 \longrightarrow Ph\overset{+}{\underset{\displaystyle -CCl_2}{S}}{-}\overset{\displaystyle CH_3}{\overset{|}{C}}H{-}CH{=}CH_2}$$

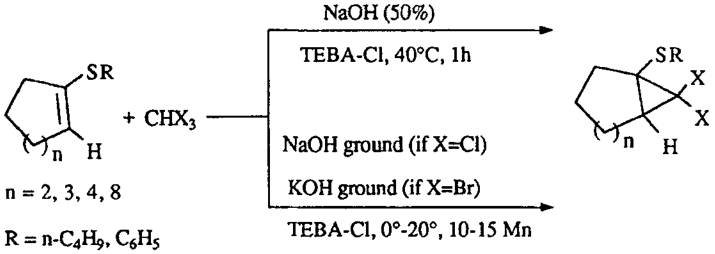
$$\longrightarrow \mathrm{PhS{-}\underset{Cl}{C}{=}CH{-}CH{=}CH{-}CH_3 + PhS{-}\underset{Cl}{C}{=}\underset{CH_3}{C}{-}CH{=}CH_2}$$

rearrangement of ylide resulting from a rapid reaction of dichlorocarbene with sulfur atom [4].

The reaction of dichlorocarbene with 9-thiomethylphenanthrene is also known to give abnormal products [5].

There are some examples of dichlorocarbene's addition with alkylthioethylene [6], alkylthiopropylene [6] and alkylselenoethylene [7], but until now the addition of dichloro and dibromocarbenes with thioether of cyclenes was not described although the synthesis of thioether of cyclenes is well established [8].

In this communication, we describe the dihalocyclopropanation of phenyl thio or butylthiocycloalkenes under liquid-liquid phase transfer (method A) and solid-liquid phase transfer (method B).



$n = 2, 3, 4, 8$

$R = n\text{-}C_4H_9, C_6H_5$

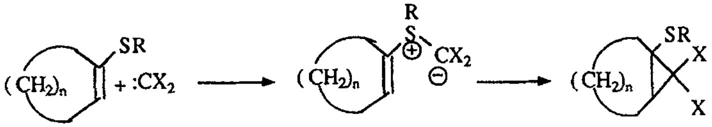
Under the liquid-liquid phase transfer according to Makosza (method A), the dihalogenocarbene was formed from haloform (chloroform, bromoform) with an aqueous solution of alkali hydroxide (50%) and a phase transfer agent (TEBA-Cl). Under the solid-liquid phase transfer (method B) the organic phase (haloform and enolthioether) was stirred with powdered alkali hydroxide in the presence of TEBA-Cl at room temperature. The method B is more rapid and gave better yields of dihalocyclopropane (75-95 %; Table). With iodoform as haloform a complex mixture of products was obtained.

We propose for these reactions a mechanism where the first step is the formation of sulfur ylide like in the case of thioalkylallyles [3], because dichloro or

Dihalogenocyclopropanation of ethers of enethiols by phase transfer : liquid - liquid (method A) and solid - liquid (method B)phase transfer

R	n	X	Product	Yield % (method)
C_6H_5	2	Cl	**1**	84 (A) 91 (B,10 Mn)
C_6H_5	3	Cl	**2**	90 (A) 95 (B,10 Mn)
C_6H_5	4	Cl	**3**	93 (B,15 Mn)
C_6H_5	8	Cl	**4**	73 (B,15 Mn)
C_4H_9	2	Cl	**5**	75 (A) 82 (B,15 Mn)
C_4H_9	3	Cl	**6**	85 (B,15 Mn)
C_6H_5	2	Br	**7**	78 (A) 85 (B,10 Mn)
C_4H_9	2	Br	**8**	72 (A) 78 (B,15 Mn)

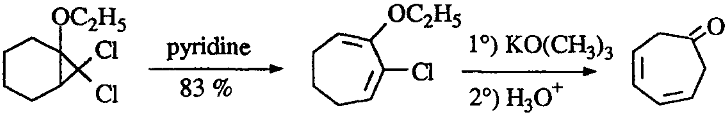
dibromocarbenes are soft base and react more rapidly with sulfur atom than with carbon-carbon double bond [1a, 4].



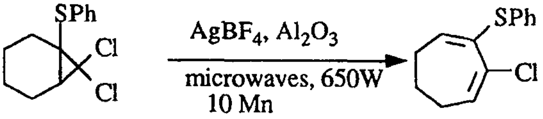
X= Cl, Br

Opening of cyclopropanes

The ring opening of dichloroalkoxycyclopropanes of cyclanes [9] is synthetically useful because this reaction allows ring expansion and functionalisation. The synthesis of tropolone [10a] from ethoxycyclohexene is a good illustration of the usefulness of this approach.



The phenylthio dichlorocyclopropanes (**1**,**2**,**3**) are very stable compounds. We have opened these compounds by reaction with silver tetrafluoborate in refluxing methanol into phenylthiochlorocyclodienes. The ring opening can be improved by using silver tetrafluoborate supported on alumina as reagent [11] without solvent (dry reaction) under microwave activation [12-13].



1 75% **10**

EXPERIMENTAL

Infrared spectra were recorded on a Perkin Elmer 684 IR spectrophotometer in KBr with absorptions in cm^{-1}. Proton NMR spectra (PMR) recorded in ppm downfield from internal Me_4Si were recorded on a Varian EM 360 instrument (60 MHz) from a solution in d^6 -DMSO of the product. ^{13}C NMR spectra in ppm downfield from internal Me_4Si were recorded on a Brucker WP 60. UV spectra were recorded on Beckman Acta M VI spectrometer. Mass spectra were recorded on a Nermag R10.10H spectrometer. Microwave irradiations were carried out with a commercial microwave oven Toshiba ER 7620 at 2450 MHz.

General Procedure

Dichlorocyclopropanation:

Method A (liquid-liquid phase transfer):

Thioether of cyclene (**1**, 10 mmol) and chloroform (30 mmol) are stirred with triethylbenzylammonium chloride (TEBA-Cl, 1 g). A solution of sodium hydroxide (50 %, 80 mmol) was added and the mixture was refluxed for 1 h. After cooling and acidification (H_2SO_4), the mixture was extracted with ether (2X 50 ml). The organic phase was dried on magnesium sulfate, and the residue after ether distillation was purified by Kugelröhr distillation or crystallization.

Method B (solid-liquid phase transfer):

Powdered sodium hydroxide (6 g) was placed in a round bottom flask (250 ml) and cooled with ice. A solution of thioether of cyclene (30 ml), TEBA-Cl (1 g) in chloroform (30 ml) was dropped. After addition, the mixture was stirred at room temperature for 15 Mn and the mixture was filtered on Celite. The product was purified by Kugelröhr distillation or crystallization.

7,7-dichloro-1-phenylthio [4.1.0] bicycloheptane (1)

Yellow liquid ; Bp 190° (0.7) ; IR (film) : 1580 (ν C=C) ,1480 , 1440 , 1025 (cyclopropane); PMR (CCl_4) δ : 1.10-2.40 (m, 9 H), 7.25 (m, 5 H, H arom.) ; ^{13}C NMR ($CDCl_3$) δ : 129.2, 129, 126.4, 72.0,37.7, 27.9, 20.6, 15.3, 18.5; MS (70 eV) : 274 (4.4), 272 (6.4, M^+), 239 (15), 237 (41.3), 207 (9.5), 205 (25.6), 201 (13.5),169 (12), 163 (12.4), 159 (11), 127 (29,8), 111 (13.5), 110 (16.1), 109 (32.4), 92 (10.7), 91 (100).

8,8-dichloro-1-phenylthio [5.1.0] bicyclooctane (2)

Yellow solid ; Mp= 78-80° (CH_3OH) ; IR (KBr) : 1580, 1480, 1470, 1180, 1120, 1080, 1020 (cyclopropane) ; PMR δ : 1.20-2.40 (m, 11 H), 7.25 (m, 5 H, Harom) ; ^{13}C NMR ($CDCl_3$) δ : 129.6 , 129.1 , 126.5, 74,5, 45, 39.5, 31.8 ; 30.4, 21.6, 21.1 ; MS (70 eV) m/e : 288 (11.7), 286 (16 M^+), 253 (37.5), 251 (100), 219

(44.6), 215 (31.2), 183 (13.2), 181 (12.2), 161 (23.3), 159 (25.4), 153 (10.4), 151 (38.4), 147 (24), 141 (39.1), 123 (22), 121 (19), 115 (25.8),113 (33.5), 111 (41.6), 110 (52.4), 109 (89.9).

9,9-dichloro-1-phenylthio [6.1.0] bicyclononane (3)

Yellow solid; Mp 58° (CH_3OH) ; IR (film) : 1580 (νC=C), 1480, 1440,1025 (cyclopropane) ; PMR(CCl_4) δ : 1.20-2.40 (m, 13 H), 7.25 (m, 5H, H arom) ; ^{13}C NMR ($CDCl_3$) δ : 130,128, 42.8, 38.4, 27.3, 26.3, 25.9, 25.5, 23.9 ; MS (70 eV), m/e : 302 (14.4), 300 (19.8 M^+), 265 (85.9), 229 (30.5), 195 (11.3), 151 (40.7), 135 (22.9), 110 (93.1), 109 (85.3), 91 (100).

13,13-dichloro-1-phenylthio [10.1.0] bicyclotridecane (4)

Viscous liquid ; IR (film) : 1580 (ν C=C), 1480, 1440, 1025 (cyclopropane) ; PMR (CCl_4) δ= 1.10-2.40 (m, 21 H), 7.25 (m, 5H, H arom.).**dichloro phenylthiocyclopropanocholestane (5)**

Yellow solid; Mp 128-130° (CH_3OH) ; IR (KBr) ; 1580, 1480, 1460, 1430, 1370, 1330, 1260, 1230, 1110, 1080, 1070, 1050, 990, 960 ; PMR ($CDCl_3$) : 0.40-2.40 (m, 50 H), 7.20 (m, 5 H, H arom.).

7,7-dichloro-1-buthylthio [4.1.0] bicycloheptane (6)

Yellow liquid; Bp 175 (0.4); IR (film): 2940 , 2860 , 1460 , 1380 , 1340 , 1280 , 1170 ,1150 , 1080 , 1050 , 1040, 980, 920 , 860 , 840 , 810; PMR ($CDCl_3$) : 0.9 (t , 3 H, CH_3) , 1.2 - 1.9 (m, 11 H), 2.1(m, 2 H) , 2.6 (t, 2 H, SCH_2).

8,8-dichloro-1-buthylthio [5.1.0] bicyclooctane (7)

Yellow liquid, Bp 180 (0,15); IR (film): 2940 , 2860 , 1460 , 1380 , 1250 , 1140 , 1025 , 830; PMR ($CDCl_3$): 0.95 (t, 3 H, CH_3) , 1.30 -1.90 (m, 13 H) , 2.1 (m, 2 H) , 2.60 (t, 2 H, SCH_2).

Dibromocyclopropanation:

The method A and the method B were similar but bromoform and potassium hydroxide were substituted respectively to chloroforme and sodium hydroxide.

7,7-dibromo-1-phenylthio[4.1.0] bicycloheptane (8)

Brown liquid; Bp 160 (0.35); IR (film) : 3070 ,3050 , 2920 , 2860 , 1580 , 1570 ; 1470 ; 1440 ; 1330 ; 1300 ; 1270 ; 1250 ; 1190 ; 1130 ; 1070 ; 1020 ; 1000 , 920 ,880 , 860 , 810 , 750 ,720 , 690; PMR (CCl_4) : 1.20 - 1.80 (m, 9 H) , 7.50 (m, 5 H, Harom.).

7,7-dibromo-1-butylthio [4.1.0] heptane (9)

Brown liquid ; Bp 180 (0.4) ; IR (film) : 2940, 2860, 2660, 1470, 1450, 1380, 1230, 1130, 1020, 870, 830, 790, 750 ; PMR (CCl_4)δ : 0.95 (t, 3H, CH_3) 1.55 (m, 10 H, CH_2) 2.10 (m, 2H, CH_2) 2.55 (t, 2H, SCH_2).

Ring opening of cyclopropanes:

Method A

The cyclopropane (2 mmol) and silver tetrafluoborate(6 mmol) were refluxed in a mixture water(20ml) and ethanol (25 ml) for 24 h. The mixture was filtered and the mixture was stirred with a saturated solution of sodium carbonate (20 ml) and extracted with ether (2 X 50 ml). The organic phase was dried on magnesium sulfate, and was purified by filtration on Florisil and then by Kugelrohr distillation.

Method B:

The cyclopropane (2 mmol) was adsorbed on silver tetrafluoborate (2 mmol) on alumina (8 g) was irradiated under microwave in an open Erlenmeyer flask with a commercial oven (2450 MHz, 650 W). After cooling, the products were extracted with acetonitrile (100 ml). The solvent was distillated and the residue was purified by filtration on Florosil (ether as eluent) and then by Kugelrohr distillation.

2-phenylthio-3-chloro-1,3-cycloheptadiene (10)

Obtained from (1) ,yellow liquid; Bp 210 (0.25); yield 75% (method B, irradiation 10 Mn),yield 20 % (method A); IR (film) : 1620 (νC=C) , 1580 ,1470 ,1440 , 1130 , 890 , 840 , 740 , 680; PMR($CDCl_3$) : 1.30 (m, 2 H, -CH_2-) , 1.70

- 2.15 (m, 4 H, CH_2-C=C) , 6.10 (m, 1H, CH=C) , 7.35 (m, 6 H, 5 Harom.and 1 Holef.); MS : 238 (22.7) , 237 (14.7) , 236 (62.7,M^+) , 218 (14.2) ,200 (11.3) , 110 (12.7) , 109 (18.4), 91 (100) , 77 (12,4); NMR^{13} C ($CDCl_3$) : 132.8 , 129.15 , 129 ,33.7 , 30.2 , 29.7 , 28.0 , 20.6 , 19. 25 ,18.5 ; UV (ethanol) λ max (log ε) : 290 (3.9) , 272 (3.8) , 255 (3.82) .

2-phenylthio-3-chloro-1,3-cyclooctadiene (11)

Obtained from (**2**) ,yellow liquid Bp 215 (0.15),yield 65 % (method B, irradiation 20 Mn), yield 15% (method A); IR (film) : 1610 (νC=C) , 1580 , 1470 , 1430 , 1080 , 860 , 810 , 730 , 680; PMR ($CDCl_3$) : 1.4 (m, 4 H, CH_2) , 1.8-2.6 (m, 4 H , CH_2-C=) , 6.3 (m, 1 H, CH=C)) , 7.3 (m, 6 H, 5 Harom. and 1 Holef.); MS: 250 (9.8, M^+) , 219 (52) , 215 (36.2) , 151 (35) , 141 (39) , 139 (9.7) , 110 (44,8),105 (75), 108 (5.7),77 (69).

2-phenylthio-3-chloro-1,3-cyclononadiene (12)

Obtained from (**3**) ,yellow liquid yield 62 % (method B, irradiation 15 Mn), IR (film) : 1610 (νC=C) , 1580 , 1480 , 1440 , 1080 ,860 , 730 , 690; PMR ($CDCl_3$) : 1.6 (m, 6 H, CH_2) , 2.2(m, 2 H , CH_2-C=) , 2.8 (m, 2 H , CH_2-C=) , 6.1 (m, 1 H, CH=C)) , 7.2-7.7 (m, 6 H, 5 Harom. and 1 Holef.).

REFERENCES

1)Kostikov R.R., Molchanov A.P., Khlebnikov A.F., *Russ. Chem. Rev.*, **1989**, *58*, 654; Keller W., "*Phase-Transfer Reactions* ", Fluka vol. 1-3, G. Thieme Verlag, Stuttgardt, **1986, 1987, 1991.**

2) Makosza M., Wawrzymwiez M., *Tetrahedron Lett.*, **1969**, 4659.

3) Ho T.L., *"Hard and Soft Acids and Bases"*, Academic Press N.Y., **1977**, Chap.9, p. 126.

4) Parham W.E. and Groen S.H., *J. Org. Chem.*, **1964**, *29* , 2214; Parham W.E., *Record. Chem. Prog.*, **1968**, *29* , 7 ; Parham W.E., Kajigaeschi S. and Groen S.H., *Bull. Chem. Soc. Jpn*, **1972**, *45* , 509; Andrews G., Evans D.A., *Tetrahedron Lett.*, **1972**, 5121.

5) Müller P., Bernardinelli G., Pauten N., *Tetrahedron Lett.* , **1988**, *29* , 5877.

6) (a) Parham W.E., Christensen L., Groen S.H., Dodson R.M., *J. Org. Chem.*, **1964**, *29* , 2214;(b) Arbuzov B.A., Salikhova A.M., Shostakoskii S.M. Vereshchagrin A.N. and Nikolskii N.S., *Izv. Akad. Nank. SSSR*, **1979**, 2786 ; *Chem. Abs.*, *92*, 128 301 s; (c) Kostikov R.R. Molchanov A.P., Amosova S.V. and Trofinov B.A., *Izv. Akad. Nank. SSSR, Ser. Khim.*, **1980**, 1354 ; *Chem. Abs.*, *93*, 204 104 s; (d)Weber A., Sabbioni G., Gallé R. and Nenenschwander M., *Chimia* , **1981**, *35* , 57 ; *Chem. Abs.* **94**, 191 738 v.

7) Comaneto J.V., Stefani H.A. and Silveira H.A. and Silveira C.C., *Synth. Commun.*, **1990**, *20* , 751.

8) Labiad B. and Villemin D., *Synthesis*, **1989**, 143 and references cited.

9) (a) Parham W.E., Soeder R.W.,Throckmorton, Kumel K., Dodson R.M., *J. Am. Soc. Chem.*, **1965**, *87*, 321; (b) Skattebol L.S., *J. Org. Chem.*, **1966**, *31*, 1554; (c) Parham W.E., *Record. Chem. Prog.*, **1968**, *29*, 7 ; (d) Barlet R., Vo-Quang Y., *Bull. Soc. Chim. Fr.*, **1969**, 3729.

10) "Preparative Chemistry using Supported Reagent", Laszlo P. Ed., Academic Press, San-Diego,1987.

11) Dry reactions under microwave irradiations: Ben Alloum A., Labiad B. and Villemin D.,*J. Chem.Soc. Chem. Comm.*,**1989**, 386 ; Guitterez E., Loupy A., G. Bram and Ruiz-Hitzky E., *Tetrahedron Lett.*, **1989**, *30* , 945; Villemin D., Labiad B. and Ouhilal Y.,*Chem. Ind.*,**1989**, 607 ; Bram G., Loupy A., Majdoub, *Synth. Commun.*, **1990**, *20* , 125; Villemin D.and Ben Alloum A., *Synth.*

Commun., **1990**,*20* , 925; Ipaktschi J. and Brück M., *Chem. Ber.*, **1990**, *123* , 1591; Villemin D. and Labiad B., *Synth. Commun.*, **1990**, *20* , 3207; **1990**, *20* , 3213; **1990**,*20* , 3333; Villemin D.and Ben Alloum A., *Synth. Commun.*, **1990**, *20* , 3325, **1991**, *21*, 63 ; Latouche R., Texier-Boullet F., J. Hamelin, *Tetrahedron Lett.*, **1991**, *32* ,1179; Villemin D., Lalaoui M. and Ben Alloum A., *Chem.Ind.(London)*, **1991**, 176; Bram G., Loupy A., Majdoub M.and Petit A., *Chem.Ind.(London)*, 396, **1991**; Alvarez C., Delgado F., Garcia O., Medina S., Marquez C., *Synth. Commun.*, **1991**, *21* , 619.

12) Review on microwave activation: Giguere R.J. in" *Organic Synthesis, Theory and Applications* ", Hudlicly Ed. , **1989**, vol. 1, 103; Mingos D.M.P., Baghurst D.R., *Chem. Soc. Rev.*, **1991**, *20* , 1.

(Received in UK 16 March, 1992)