Tetrahedron Letters, Vol.31, No.51, pp 7501-7504, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

REACTION OF NON-ACTIVATED OLEFINS WITH CH-ACIDS; A NOVEL METHOD FOR THE PREPARATION OF ELECTROPHILIC CYCLOPROPANES

László Tőke[1]*, Gábor T. Szabó[1], Zoltán Hell[1] and Gábor Tóth[2]

Department of Organic Chemical Technology[1] and Department of General and Analytical Chemistry[2], Technical University of Budapest H-1521 Budapest, Hungary

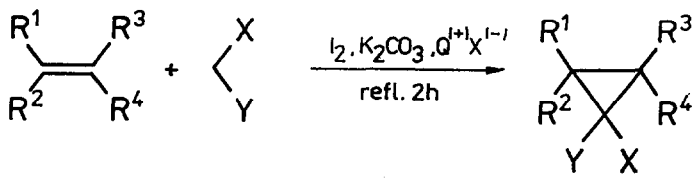
Abstract: Reaction of non-activated olefines with active methylene compounds was accomplished under solid-liquid phase-transfer conditions, in the presence of iodine, to give electrophilic cyclopropanes of a wide range of substituents. Several data to the mechanism of the reaction are also given.

Cyclopropane derivatives activated by two electronwithdrawing substituents at geminal position (electrophilic cyclopropanes) are useful intermediates in organic synthesis. Their inter- and intramolecular ring opening reactions by various nucleophiles or partial dealkoxy-carbonylation of the substituted cyclopropane dicarboxylic esters have been applied to the synthesis of natural products[1] or pyrethroid type insecticides[3]. The most important synthetic methods for these compounds are the reaction of 1,4-dibromo-2-alkenes or dimethyl vinyl sulphonium salts with anion of malonic esters, the reaction of gem-dibromocyclopropane derivatives with diethyl carbonate and butyllithium, the reaction of olefines with diazomalonic esters, with bromomalonic esters in the presence of copper (II) salts and amine, with dibromomalonic esters in the presence of copper or copper (I) salts or with bromomalononitrile[2,3].

Most of these syntheses are tedious or limited for the transformation of a certain type of olefins. Herein we report a novel, simple, one-pot method for getting geminally substituted cyclopropanes with a wide range of substituents. Alkyl or aryl substituted olefins react with dialkyl malonates, cyanoacetic ester, malono dinitrile, acetoacetic acid esters or acetyl acetone to give cyclopropane derivatives in fair to good yields if the CH-acids mentioned are added to the warm solution of the olefin in aprotic solvent containing two moles of solid potassium carbonate, catalytic amount of a lipophilic quaternary ammonium salt as a phase transfer catalyst ($Q^{(+)}X^{(-)}$) and one mole iodine per mole olefin (Table I).

No desired product was obtained by substituting iodine for bromine or chlorine, by omitting the phase transfer (PT) catalyst (most of the cases, tricapryl methyl ammonium chloride) or the base from the reaction mixture.

Table I.

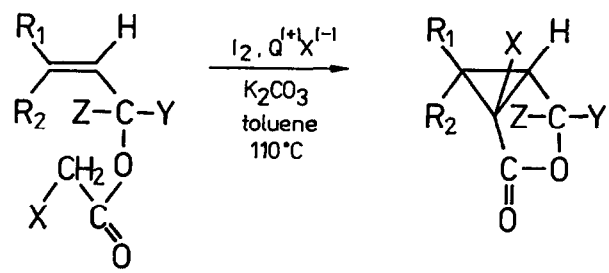


1 2 3

	R^1	R^2	R^3	R^4	X	Y	solv.	Yield* %	m.p. (b.p.**/Torr)	
a	CH_3 / CH_3 > =	H	Me	Me	CN	CN	THF	18	69-74	ref
b	Cl / Cl > =	H	Me	Me	EtOOC	EtOOC	toluene	52	(90/0.1)	ref
c	Cl / Cl > =	H	Me	Me	CN	CN	toluene	55	104-106	
d	Cl / Cl > =	H	Me	Me	CN	EtOOC	THF	11	(140/0.01)	
e	Cl / Cl > =	H	Me	Me	CN	H_3CCO	THF	18	160-162	
f	n-Bu	H	H	H	EtOOC	EtOOC	toluene	39	(140/0.01)	

All the products have satisfactory elemental analysis and/or MS data, IR and NMR spectra. * Isolated yields. ** Oil bath temperature.

Table II.



4 5

	R^1	R^2	X	Y	Z	Yield* %	^{o}C m.p.	^{o}C/Torr b.p.
a	H	H	COOEt	H	H	60	oil	
b	Me	Me	COOEt	CCl_3	H	90	58	115/0.1 (123-125/0.3 [7])
c	H	H	COOEt	Me	Me	65	80-80.5	
d	Me	Me	$COCH_3$	CCl_3	H	80	oil	
e	Me	H	COOEt	H	H	50	oil	
f	H	Me	COOEt	H	H	65	oil	

Experiments were run by adding diethyl bromo malonate to the solution containing olefin, potassium carbonate and a PT catalyst instead of using iodine and diethyl malonate but, again, formation of a cyclopropane derivative could not be observed.[4]

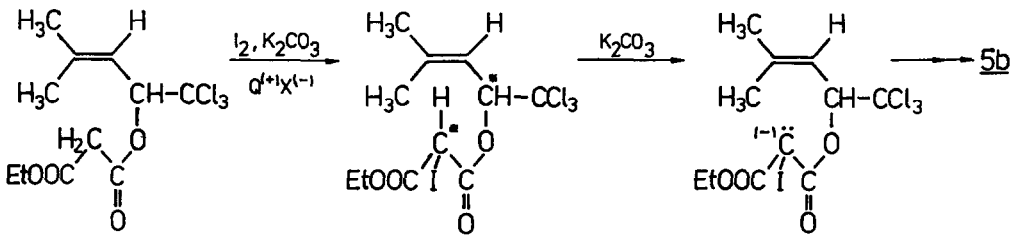
Potassium carbonate proved to be the base of choice except one case (3f) where aqueous sodium hydroxide was also working nicely. Triethylamine, pyridine, DBU or dimsyl anion are not suitable bases. The best solvents for running the reactions are boiling toluene, benzene or THF.

If the CH acid moiety is incorporated into the starting olefin at a favorable position, an intramolecular reaction might occur resulting in the formation of cyclopropane derivatives of 5 having a lacton ring opposite side to the X group (Table II). Compounds 5a,b,d are excellent starting materials for building up cis-or trans-1,2-disubstituted cyclopropane derivatives stereoselectively. Lacton 5b has already been synthetised, but for closing the ring a diazo group was first introduced into the malonic acid ester moiety of 4b by tosyl-azide[3,7].

Table II shows the experimental conditions for the reaction 4 to 5. Esters 4a-c were obtained from the corresponding alcohol by malonic ester-chloride in the presence of triethylamine, while 4d was prepared from the alcohol with diketene aceton compound[8] in the presence of p-toluenesulphonic acid (reflux, 3 h, see ref. 8).

Regarding the mechanism for the ring formation in 3 and 5, respectively valuable data have been obtained from the detailed study of the 4b→5b transformation in an NMR tube.

Fig 1.



After several minutes of heating in hexadeuterobenzene solution the starting 4b and the iodine disappears completely and not only the formation of several percent of the endproduct 5b but that of a new compound 6b are also detected. 6b could even be separated and purified as an oily product

if K_2CO_3-$KHCO_3$ mixture is removed by filtration because in the absence of K_2CO_3 6b → 5b conversion stops but restarts again if K_2CO_3 is added and heating is continued. The nature of the elemental step(s) from anion 6b to 5b is not known but the stereochemical integrity of the olefin is lost during this transformation as shown in the ring closure reaction of E-and Z-crotyl alcohol derivative 4e and 4f to 5e and 5f, respectively: the same diastereomeric mixture of 5e and 5f are formed from both starting material in mol-ratio of 40/60 with the isomer 5e dominating.

References and notes

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4. Reaction of diethyl bromomalonate with several olefins were examined and successfully accomplished by Japanese authors[2/b] although the reaction conditions used by them were completely different from ours.

   The olefinic double bond in 4b disappears during the reaction with bromine and K_2CO_3 and no further reaction can be observed.

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(Received in UK 23 October 1990)