Letter to the Editor

On a novel dihalocyclopropane–dihalomethylvinyl rearrangement: Additional mechanistic evidence

Christopher K. Jankowski ^{a,*}, Antoun BouLaouz ^a and Eduardo Diaz-Torres ^b

^a *Département de chimie et biochimie, Université de Moncton, Moncton, N.-B., E1A 3E9, Canada*

^b *Instituto de Quimica, UNAM, Cd Universitaria, 04510 Mexico, DF, Mexico*

Abstract. Some additional evidences on the mechanism of new rearrangement of dihalocyclopropane–dihalomethylvinyl reaction assisted by Hiyama reagent $\text{Cr}^{+2}/\text{Cr}^{+3}$ are discussed.

Dear Editor,

Following some discussion about the precise nature and the novelty of the title rearrangement reaction applied to the transformation of dihalocyclopropane rings (**1**) into dihalomethylvinyl compounds (**2**), we would like to make several comments concerning the possible mechanism of this transformation.

In our previous two papers, we have shown that this rearrangement proceeds via a unique pathway of a Hiyama-like system, where the presence of two neighbouring oxidation state metal cations is necessary [1,2]. This reaction did not follow the Makosza pathway of ring extension, which would lead, in the case of for example bicyclic compounds such as cis-fused 7,7-dichlorocarenes (**1**) (with gem-dichlorocyclopropane ring condensed on the cyclohexane frame), to halogenated cycloheptene (**3**) compounds [3,4]. The presence of these compounds was often associated with the phase transfer catalysis used to synthesize the dihalocyclopropane moiety from various olefins. In that procedure, it is believed that the dihalocyclopropane derivatives, after their formation *in situ*, will often spontaneously undergo further rearrangement into such an expanded-ring structure [5,6].

In our previous work we have also successfully applied the Hiyama reagent to the transformation of terpenic exo-double-bond unsaturated γ -lactones into the corresponding allenic compounds [7]. Incidentally, it was originally expected that our alleged novel reaction will follow the same pathway into direction of the allenic compounds, even for simple cyclohexene–dihalocyclopropane starting materials.

In the discussion of this problem and related questions we also compared, and rejected, the possibility of the mechanisms of many other known rearrangement reactions [8].

In our last study [2], we discussed the three most plausible mechanistic pathways and concluded that, under Hiyama conditions, the overall results tend to indicate the absence of the ionic intermediates.

*Corresponding author. Tel.: +1 506 858 4331; Fax: +1 506 858 4541; E-mail: jankowc@umoncton.ca.

In the literature, the presence of dihalomethylvinyl products are mentioned for 2,3-dihydro-1,4-dioxane only (4, 5), apparently as a result of the thermal insertion from the carbene adduct; however, this insertion does not lead to analogous structures for 2,5-dihydrofurane derivatives [9–11]. In general the insertion is observed for the C–H activated bond [11]; these reactions were catalysed by ironcarbonyl compounds and often lead to ketals [12,13].

Careful examination of the literature on some peripheral aspects of the subject also led to the conclusion that, on the path to the rearranged products and their hydrolytic transformations into the alpha, beta-unsaturated aldehydes and then to acids, one can also achieve the formation of useful and interesting monohalocyclopropene (6) intermediate products, resulting from the elimination of HCl from the dihalocyclopropane product [10].

This full pathway is, however, difficult to achieve for the bicycloproduct in our series, due to two difficulties: firstly, the absence of activated hydrogen on the cyclohexane moiety supporting the bicyclic structure, and secondly, the genuine difficulty of forming the cyclopropene on the fused ring in the direction of the bridgehead close to the violation of Bredt's rule, as an intermediate.

A solution was then proposed: a possible Cr^{+2} -assisted rearrangement, with a hydrogen shift from the relatively deactivated position on the junction of two cycles, which would induce the transformation with the cyclopropane ring cleavage, but without the formation of the cyclopropene intermediate (Scheme 1).

The cyclopropene-intermediate hypothesis, in particular, was advanced by Crossland and previously discussed by Billups and co-workers [9,10], and finally supported by isotopic labelling experiments of Prestein and Gunter [11].

When the 1,1-dichloro-2-phenyl cyclopropane or its perdeuterated derivative is reacted in basic conditions, the elimination–addition–elimination reaction takes place and the atropaldehyde diethyl acetal is obtained, after the quenching of intermediary aldehyde by ethanol [11].

We considered two possible routes for the rearrangement: ionic, and radical. The first should proceed via the opening of the C2–C3 bond lengthened by the presence of large halogens on C1 atom of the cyclopropane. In a case of the cis-fused rings, as in 7,7-cis-carene, the disrotatory electrocyclic ring opening of the cyclopropane, leading to the formation of the allyl cation thusly stabilised, is expected. This pathway is believed to be dependent on the conformational mobility of the entire system in a given solvent [11,12]. The formation of the allyl cation under Lewis acid catalysis should have resulted in some specific products formation, which was not observed [7,9,10].

The second mechanistic pathway, that is, the biradical, has the evident advantage of better fitting the final results obtained in our case; as well, it easily justifies the formation of either the rearranged product observed once the cyclopropane peripheral bond ring opening is realised under chrome-cation reductive conditions, or the bridgehead bond which leads to the Makosza cycloheptene structure (Scheme 1).

Under these conditions, the conrotatory opening of cis-fused starting reagent leads to an isomerised radical intermediate; the reaction is thought to then follow the solvolytic route.

- (a) Seen from this perspective, the lack of hydrolysis under Hiyama conditions is then related to the immediate reduction of the formed aldehyde to the alcohol, in absence of the acetalisation reagents. The formation of the alcohol was not observed.
- (b) The presence of hydride is another element of difference in this reaction. As well as playing a reductive role relative to the Cr^{+3} , the hydride is the nucleophile in either solvent, and can help the elimination.

In such a way the Hiyama mechanism involving the Lewis acid catalyst is necessary to break the cyclopropane ring and activate the hydrogen on the junction of the cyclopropane and cyclohexane rings,

Scheme 1. On the dihalocyclopropane–dihalomethylvinyl rearrangement: some additional mechanistic evidences.

as in the case of the carene-type molecules of our studies. There are then two possible hydrogen shift possibilities remaining: either those of the aforementioned junction hydrogens or, as in the Makosza mechanism, the hydrogen on the carbon α to cyclopropane, which earns its acidity from the “hyperconjugation” to the cyclopropane [14–16].

In the case of 7,7-dichlorobicyclo[4,1,0]heptane or hept-3-ene, this second hypothesis was then ruled out as a result of carbon-13 labelling experiments.

Because the presence of the second double bond in the benzocyclopropene has been shown [10] to further increase the acidity of this mobile hydrogen, it seems even less possible that the mechanism of our reaction with the Lewis acid catalysis is related to that route; rather, the hydrogen shift is observed from the junction of these two rings toward the dichloromethyl carbon of rearranged dihalocyclopropane–dihalomethylvinyl system.

Although the problem of the exact mechanism of this reaction under a Lewis acid system $\text{Cr}^{+2}/\text{Cr}^{+3}$, in basic conditions with the solvent change (DMF-THF), remains open, our observations on the necessary role played by this system indicate its unique character, close to the heavily solvent-dependent

Hiyama rearrangements. In our series of experiments we never observed the formation of cyclopropene derivatives.

In this way our claim for a novel character of the rearrangement observed under Hiyama catalyst conditions remains intact. The precise mechanism of this reaction, certainly worth of more studies, should eventually be clarified with selected (though expensive) isotopic labelling experiments. Of three hypotheses for the mechanism, as discussed [5], only the radical mechanism remains a plausible choice; the other two possibilities should be considered less probable in light of presented evidence.

The claim of our Hiyama-type rearrangement's novelty is thus supported, as the reaction is different enough from those quoted in a rich bibliography on the transformations of bridged systems in particular. None of the bibliographic additional data discussed in this letter contradict this specific point.

The reaction could also be used as another way to obtain α, β -unsaturated aldehydes or acids, and in that respect is one more method of synthesis of α, β -unsaturated carbonyl compounds from various unactivated olefins. Under rigorously controlled hydrolytic conditions, we were able to halt the reaction at the aldehyde stage [2,8]. In some cases allenic structures are also available.

The production and characterization of relatively stable dihalomethylvinyl product, for cyclic system of low chemical activity (such as cyclohexane) is incidentally the best proof for the initial biradical step necessary to achieve the rearrangement. Finally, the role of the Lewis acid is enough to distinguish this reaction from, in particular, the Crossland synthesis, to support our claim of novelty.

Acknowledgements

We are indebted to Environment Canada and the Faculty of Research and Graduate Studies (FESR, U de M) for continuous support of this project.

References

- [1] C.K. Jankowski, A. Bou Laouz, D. Lesage and E. Diaz, *Spectroscopy* **17** (2003), 735.
- [2] C.K. Jankowski, A. Bou Laouz, E. Diaz-Torres, D. Lesage, J.M.R. Bélanger and J.R.J. Paré, *Spectroscopy* **19** (2005), 171.
- [3] T. Hiyama, Y. Okude, K. Kumura and H. Nozaki, *Bull. Chem. Soc. Japan* **55** (1982), 561; T. Hiyama, *J. Amer. Chem. Soc.* **99** (1977), 3179.
- [4] M. Makosza and M. Wawrzynkiewicz, *Tetrahedron Lett.* **4659** (1969).
- [5] P.G. Gassman, S. Han and L.J. Chyall, *Tetrahedron. Lett.* **39** (1998), 5459.
- [6] T.C. Shields and P.D. Gardner, *J. Am. Chem. Soc.* **89** (1967), 5425; T.C. Shields, W.E. Billups and A.R. Lepley, *J. Am. Chem. Soc.* **90** (1968), 4749.
- [7] M. Fedorynski, *Chem. Rev.* **103** (2003), 1099.
- [8] A. Bou Laouz, Dihalocyclopropanation de quelques oléfines et leur réarrangement : prenylation en mode thermique et assistée par micro-ondes, Thesis, Département de chimie et biochimie, Faculté des sciences, Université de Moncton, 2003 Moncton NB, Canada.
- [9] W.E. Billups, T.C. Shields, W.Y. Chow and N.C. Deno, *J. Org. Chem.* **37** (1972), 3676; W.E. Billups, K.H. Leavell, E.S. Lewis and S. Vanderpool, *J. Am. Chem. Soc.* **95** (1973), 8096.
- [10] L. Skattebol and B. Boulette, *J. Org. Chem.* **31** (1966), 81; S. Skattebol, *J. Org. Chem.* **31** (1966), 1554.
- [11] I. Crossland, *Acta Chem. Scand. B* **41** (1987), 310; I. Crossland, *Org. Synth.* **7** (1990), 12.
- [12] J. Prestien and H. Gunther, *Angew. Chem. Internat. Edit.* **13** (1974), 276.
- [13] G.-A. Lee, C.-S. Shiau, C.-S. Chen and J. Chen, *J. Org. Chem.* **60** (1995), 3565.
- [14] K.-O. Hensling, D. Quast and P. Weyerstahl, *Chem. Ber.* **110** (1977), 1027.
- [15] F. Nerdel, J. Buddrus, W. Brodowski, P. Hentschel, D. Klamann and P. Weyerstahl, *Justus Liebigs Ann. Chem.* **710** (1967), 36; S.W. Tobey and R. West, *J. Am. Chem. Soc.* **89** (1966), 5425.
- [16] W.E. Billups, W.Y. Chow, K.H. Leavell, E.S. Lewis, J.L. Margrave, R.L. Sass, J.J. Shieh, P.J. Werness and J.L. Wood, *J. Am. Chem. Soc.* **95** (1973), 7878; T.C. Shields and W.E. Billups, *Chem. Ind. (London)* (1967), 1999.