Tetrahedron Letters,Vol.29,No.49,pp 6497-6500,1988 0040-4039/88 $3.00 + .OC
Printed in Great Britain Pergamon Press plc

1,4-REGIOSELECTIVE IODOFUNCTIONALIZATIONS OF 1,3-BUTADIENE

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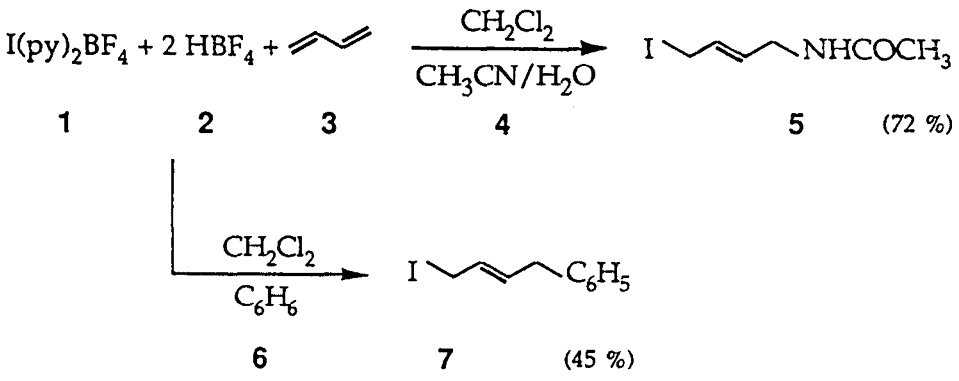
Summary: Addition reactions of benzene and acetonitrile to 1,3-butadiene are described. This new iodofunctionalization process proceeds "via" iodonium ion-allylic cation equilibrium and gives regioselectively 1,4-adducts, which can be alternatively obtained by acid treatment of the 1,2-derivative **8**.

Regiochemistry in electrophilic additions to conjugated dienes is a tool to check kinetic "versus" thermodynamic control [1]. An important drawback looking for synthetic applications of many of these processes is the lack of regiocontrol shown [2].

In previous papers, we described the preparation and reactivity of $I(py)_2BF_4$ towards several unsaturated substrates [3], and organometallic transformations of some of the resulting addition products [4]. In particular, $I(py)_2BF_4$ allows the regioselective iodofunctionalization of conjugated dienes; thus, we found that terminal dienes leads 1,2-addition products, and internal ones give the corresponding 1,4-derivatives [3b].

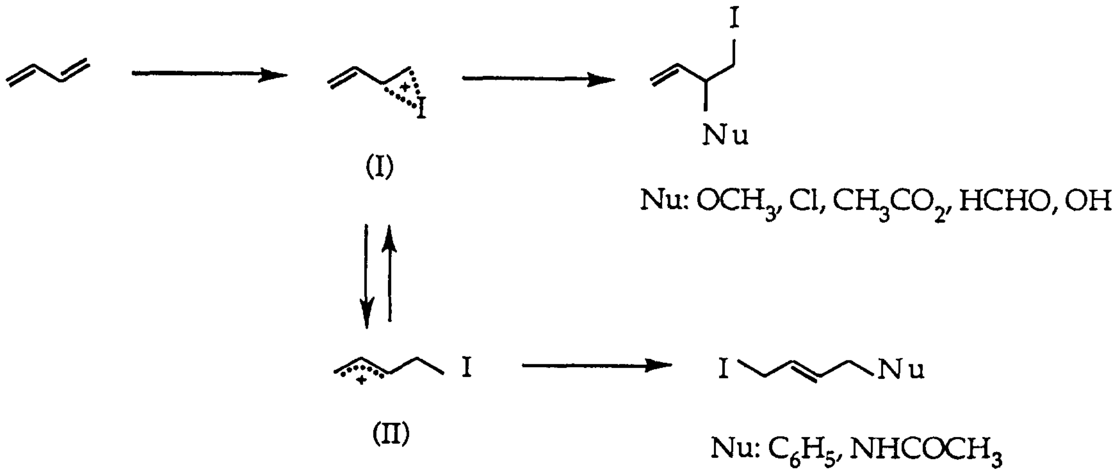
In this paper, in connection with addition reactions to 1,3-butadiene, we are going to report new results being an exception to the preceding behaviour. In this way, when the reaction is carried out in the presence of benzene or acetonitrile as nucleophile, the iodofunctionalization takes place [5], yielding in both cases the *E*-1,4-regioisomer as the only product, unlike the previously reported 1,2-iodofunctionalization of butadiene [3b]. The stereochemistry of the double bond has been found to be *E*, by ^{1}H-NMR (300 MHz) and/or IR analyses [6]. These results are summarized in Scheme 1.

A noteworthy feature of these new reactions is that only one isomer is obtained in all instances. The carbon-carbon bond formation by reacting benzene and butadiene, leading to a synthetically valuable structure, is also remarkable.



Scheme 1

To justify the 1,4-regiochemistry observed in these iodofunctionalizations in comparison with the earlier 1,2-additions [3b], we now propose that 1,2-regioisomers derived from butadiene are obtained through a three-membered iodonium ion involving a non-symmetrical charge distribution (I); a subsequent nucleophilic attack to the allylic position gives, "via" ring-opening, 1,2-derivatives (the kinetically controlled addition products), as depicted in Scheme 2.

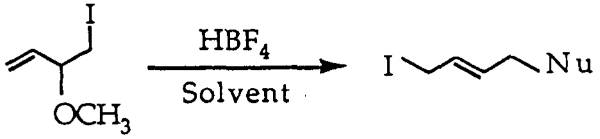


Scheme 2

As no 1,4-regioisomers have been found in the reaction crudes, the participation of allylic cation (II) may be ruled out. Analogous arguments were previously used to explain similar results with other electrophiles [7].

Nevertheless, when poorer nucleophiles such as benzene or acetonitrile are employed, the initially formed iodonium ion (I) can lead to the allylic cation (II) and give 1,4-products, according to a thermodynamic control. Other alternatives, like nucleophilic attack involving allylic participation, cannot be excluded to account for the formation of 1,4-derivatives on the basis of the available experimental results.

In good agreement with these assumptions we have observed that, after protonation, 1,2-regioisomers can act as a source of 1,4-derivatives. In this way, the treatment of a solution of 4-iodo-3-methoxy-1-butene with an ethereal solution of HBF_4, in acetonitrile, benzene or methanol as solvent, affords a crude containing the corresponding 1,4-iodofunctionalized substratum **5**, **7** or **9**, as the major product; 1,2-derivative is not detected in the crude mixture (in accordance with ^{1}H-NMR, 300 MHz, and ^{13}C-NMR analyses) [8].



8

CH_3CN/H_2O	Nu = $NHCOCH_3$	(**5**)
C_6H_6	Nu = C_6H_5	(**7**)
CH_3OH/CH_2Cl_2	Nu = OCH_3	(**9**)

Scheme 3

As an important advantage of the procedures above described, it should be pointed out that they provide us with a way to obtain 1,4-derivatives, substituted by carbon, nitrogen and oxygen from 1,3-butadiene, which were inaccessible by other methods. The acid conversion of 1,2- into 1,4-substrata, allows to perform both iodofunctionalizations in a regioselective mode.

Acknowledgements: Financial support of this work by Comisión Asesora de Investigación Científica y Técnica (CAICYT), is gratefully acknowledged. One of us (José Manuel González) wishes to thank Ministerio de Educación y Ciencia for a predoctoral scholarship.

REFERENCES AND NOTES

[1] March, J, *Advanced Organic Chemistry: Reactions, Mechanisms and Structure*, (3rd ed.), J. Wiley & Sons, Inc.: New York, 1985, pp 668–670.

[2] Pattenden, G. In *Comprehensive Organic Chemistry*, Barton, D., Ollis, W.D. Eds.; Pergamon Press: Oxford, 1979, Vol. 1, Chap. 2.3, pp 177–178.

[3] (a) Barluenga, J.; González, J.M.; Campos, P.J.; Asensio, G. *Angew. Chem.*, **1985**, *97*, 341; *Angew. Chem. Int. Ed. Engl.*, **1985**, *24*, 319. (b) Barluenga, J.; González, J.M.; Campos, P.J.; Asensio, G. *Tetrahedron Lett.*, **1986**, *27*, 1715. (c) Barluenga, J.; Rodríguez, M.A.; González, J.M.; Campos, P.J.; Asensio, G. *Tetrahedron Lett.*, **1986**, *27*, 3303.

[4] Barluenga, J.; Rodríguez, M.A.; Campos, P.J.; Asensio, G. *J. Amer. Chem. Soc.*, **1988**, *110*, 5567.

[5] The following represents the typical experimental procedure for the preparation of **5** and **7**: A solution of 1,3–butadiene (6 mmol, 0.5 ml, previously condensed at low temperature and dried through KOH) in the appropriate solvent (acetonitrile containing a 0.1 % of water or dried benzene), is cooled at – 5 ° C (5 ° C, to prepare **7**), treated with HBF_4 (10 mmol, 1.4 ml of a commercially available 54 % ethereal solution), and a 0.5M solution in dried CH_2Cl_2 of $I(py)_2BF_4$ (5 mmol, 1.86 g), is immediately added under argon atmosphere. After stirring further 15 minutes (4 hours for **7**), the mixture is diluted with CH_2Cl_2 and washed with water. The organic phase is dried over anhidrous Na_2SO_4. For the acetonitrile reaction, removal of solvents gives a solid, which is the amide **5** essentially pure (72 % yield). Attempts to recrystallize **5**, lead spontaneously to its partial conversion into 2–methyl–5–vinyl–4,5–dihydrooxazol. From a synthetic viewpoint, that could be fully accomplished by stirring in DMSO at room temperature. For **7**, removal of solvents and chromatography on silica gel, eluting with n–hexane as solvent, affords to pure *E*–1–iodo–4–phenyl–2–butene (45 % yield).

[6] All spectral data agree with the assigned structure and all compounds have provided satisfactory combustion analysis and/or mass spectra.

[7] (a) Barluenga, J.; Pérez–Prieto, J.; Asensio, G. *J. Chem. Soc., Perkin Trans. I*, **1984**, 629. (b) Mueller, W.H.; Butler, P.E., *J. Chem. Soc., Chem. Commun.*, **1966**, 646.

[8] To a solution, cooled at 0 ° C, of HBF_4 (6 mmol, 0.84 ml) in acetonitrile or benzene is added a 1M solution of **8** (5 mmol, 1.06 g) in the same solvent. The temperature is allowed to raise 20 ° C. The resulting mixture is stirred for another 3 hours and then hydrolyzed to give, after removal solvents, a crude containing the corresponding 1,4–derivatives **5** and **7** as main products, respectively. In the preparation of **9** from **8**, solvolytic methods did not yield satisfactory results, and the following has been applied. A solution of **8** (5 mmol), at 0 ° C, in dried CH_2Cl_2 (20 ml), was succesively treated with dried methanol (25 mmol, 1.1 ml) and HBF_4 (6 mmol, 0.84 ml). After 10 minutes, solvents were removed and the spectral analysis of the crude shows the complete isomerization of **8** to 1,4–isomer **9**. Standard work–up allows us to obtain pure **9**.

(Received in UK 13 October 1988)