



Remote controlled Haller–Bauer ring opening of bicyclo[2.2.2]octenones

Odón Arjona,* Rocío Medel and Joaquín Plumet*

Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense 28040 Madrid, Spain

Received 11 September 2000; accepted 8 December 2000

Abstract—A new, unprecedented case of the Haller–Bauer reaction in bicyclo[2.2.2]octenones, easily obtained from the Diels–Alder reaction, provides effective and stereocontrolled access to highly substituted cyclohexene derivatives. © 2001 Elsevier Science Ltd. All rights reserved.

The base-induced C–C bond cleavage of non-enolizable ketones to give a carboxylic acid derivative and a neutral fragment is known as the Haller–Bauer reaction¹ and constitutes one of the relatively scarce synthetic methods based on C–C bond cleavage compared with the large amount of synthetic methods based on C–C bond formation.

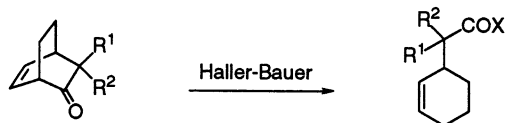
In the case of bicyclo[2.2.2]octenones this reaction should give functionalized cyclohexene derivatives and thus be an appealing possibility for the synthesis of these type of compounds (Scheme 1). However, to the best of our knowledge the reaction has been studied only in the case of the corresponding benzoderivatives, giving the expected tetrahydronaphthalene derivative in moderate yield (Scheme 2).²

Recently³ we have reported a new synthesis of functionalized bicyclo[2.2.2]octenones **1** via the inverse electronic demanding Diels–Alder reaction of masked *o*-benzoquinones⁴ with enol and thioenolethers as dienophilic partner (Scheme 3).

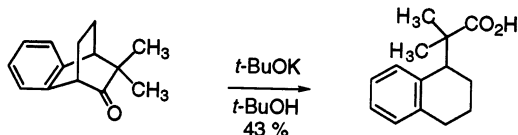
With these compounds in hand, we speculate that the Haller–Bauer reactions performed on **1** should give cyclohexene derivatives **2**. In this way, reaction of compounds **1(a–d)** with MeONa/MeOH at 0°C affords compounds **2(a–d)** in relatively good yield⁷ (Table 1). It is noteworthy that there is no experimental observation concerning the elimination of EtO[−] or EtS[−] in these reactions.

It should be pointed out that the presence of the ester group attached to the double bond in the starting material is mandatory for the success of the reaction. Thus, when compound **1e** was subjected to the reaction conditions only hemiacetal **3** was obtained (even in more severe reaction conditions: 0°C to rt, 24 h) (Scheme 3). Thus, the remote attracting group determines the feasibility of the reaction according to the proposed anionic mechanism (Scheme 4).⁵

In summary, a new unprecedented case of Haller–Bauer reaction in bicyclo[2.2.2]octenones is reported and constitutes a new synthetic application of these versatile bicyclic intermediates.⁶



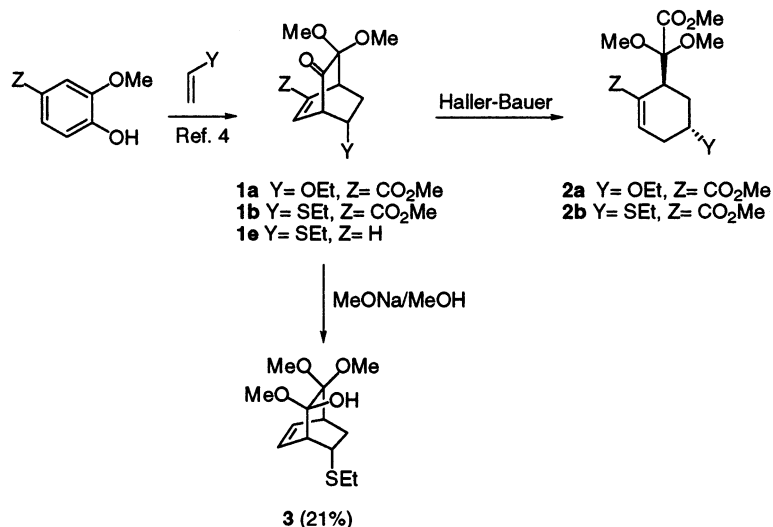
Scheme 1.



Scheme 2.

Keywords: Haller–Bauer; bicyclo[2.2.2]octenones; cyclohexene derivatives.

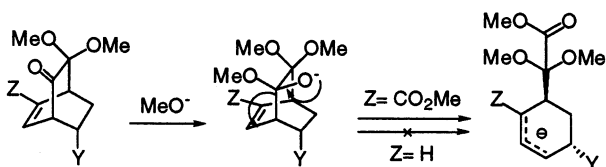
* Corresponding authors.



Scheme 3.

Table 1. Haller–Bauer reaction of substituted bicyclo[2.2.2]octenones 1^a

Starting Material (1)	Product (2)	Isolated yield (%)
1a, Y= OEt	2a, Y= OEt	78
1b, Y= SEt	2b, Y= SEt	52
1c	2c	81
1d	2d	50 ⁷

^a All reactions were conducted at 0°C during 2 h.

Scheme 4.

Acknowledgements

Financial support was obtained from the Ministerio de Ciencia y Tecnología, Spain, through grant no. BQU2000-0653. R.M. thanks Ministerio de Educación y Cultura for a predoctoral fellowship.

References

- (a) Haller, A.; Bauer, E. *Compt. Rend.* **1908**, 147, 824; (b) For selected reviews, see: Paquette, L. A.; Gilday, J. P. *Org. Prep. Proced. Int.* **1990**, 22, 167; (c) Mehta, G.;

- Venkateswaran, V. *Tetrahedron* **2000**, 56, 1399.
- (a) Muir, D. J.; Stothers, J. B. *Can. J. Chem.* **1993**, 71, 1290; (b) See also: Cheng, A. K.; Stothers, J. B. *Can. J. Chem.* **1977**, 55, 4184.
- (a) Arjona, O.; Medel, R.; Plumet, J. *Tetrahedron Lett.* **1999**, 40, 8431; (b) See also: Gao, S. Y.; Lin, Y. L.; Rao, P. D.; Liao, C. C. *Synlett* **2000**, 421.
- Chu, C. S.; Lee, T. H.; Liao, C. C. *Synlett* **1994**, 635.
- See Ref. 1c, p. 1400 and references cited therein.
- For the synthetic applications of bicyclo[2.2.2]octenones in natural product synthesis see: Quideau, S.; Pouségu, L. *Org. Prep. Proced. Int.* **1999**, 31, 617.
- Compound **2e** was isolated in 16% yield. The stereochemistry of **2d** was established by NOE experiments.

