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Catalytic oxaziridinium-mediated epoxidation of olefins by Oxone®. A convenient catalyst excluding common side reactions

Luis Bohé* and Majed Kammoun

Institut de Chimie des Substances Naturelles, CNRS, Avenue de la Terrasse, 91198 Gif sur Yvette, France

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Abstract—The nicely crystalline, easily prepared and handled, 3,3-dimethyl-3,4-dihydroisoquinolinium salt **6**, is a convenient catalyst for the oxaziridinium-mediated epoxidation of alkenes by Oxone®.

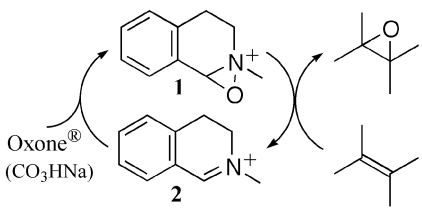
Oxaziridinium chemistry was introduced in the middle seventies and it was early established that oxaziridinium salts are electrophilic oxygen atom transfer agents towards nucleophiles.[1] Subsequently the oxygenation of alkenes,[2] thioethers[3] and *N*-nucleophiles[4] with the isolated oxaziridinium salt **1**[5] has been described. Concerning olefins, epoxides are produced in good yields by the action of 1 equiv. of the isolated oxaziridinium salt **1**[2] (Scheme 1).

Owing to their high reactivity, oxaziridinium salts generally are not easily isolable compounds but it was shown that they may be conveniently generated from the corresponding iminium salt in the presence of an olefinic substrate. As the oxygen transfer onto the olefinic bond regenerates the iminium salt, X. Lusinchi et al. have developed an oxaziridinium-mediated catalytic epoxidation method using the iminium salt **2** as catalyst and Oxone® as the oxygen source[6] (Scheme 1). The suitability of the catalytic method for performing asymmetric epoxidation was then established using an enantiomerically pure iminium salt.[7] Thereafter, this promising method has deserved growing interest. Accordingly, some other cyclic[8,9] and acyclic[10–12] iminium salts have been tested for their potential as asymmetric or racemic epoxidation catalysts.

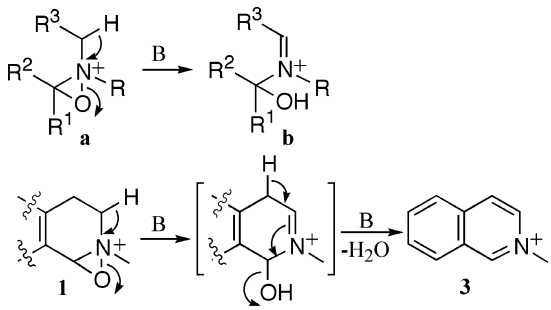
Two factors lowering the catalytic efficiency of the epoxidation process have been outlined:

– the hydrolysis of the iminium salt in the reaction medium. This (directly) catalyst-consuming side reaction affect principally the catalytic oxaziridinium-mediated epoxidations involving acyclic iminium salts as catalysts.[10–12]

– the loss of active oxygen from the intermediate oxaziridinium, in a reaction which does not regenerate the iminium, i.e. (Scheme 2) the irreversible base-catalyzed isomerization of oxaziridinium salts having protons α to the nitrogen atom (**a**), into α-hydroxy-iminium salts (carbinol–iminium salts, **b**) which evolve further according to their structure. In particular, the carbinol iminium salts resulting from the isomerization of oxaziridiniums of the 3,4-dihydroisoquinolinium family lead to the corresponding isoquinoliniun salts through a dehydration process.[2,6]



Scheme 1.



Scheme 2.

* Corresponding author. E-mail: bohe@icsn.cnrs-gif.fr

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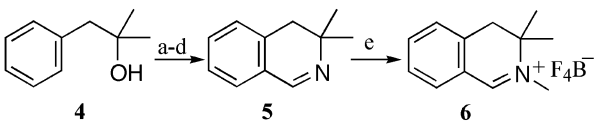
We considered that the efficiency of the catalytic oxygen-transfer process should be improved by preventing this (indirectly) catalyst-consuming aromatization reaction to occur. In consequence we decided to prepare a 3,3-disubstituted-dihydroisoquinolinium salt in order to evaluate its catalytic capabilities, with the unsubstituted iminium salt **2** as standard.

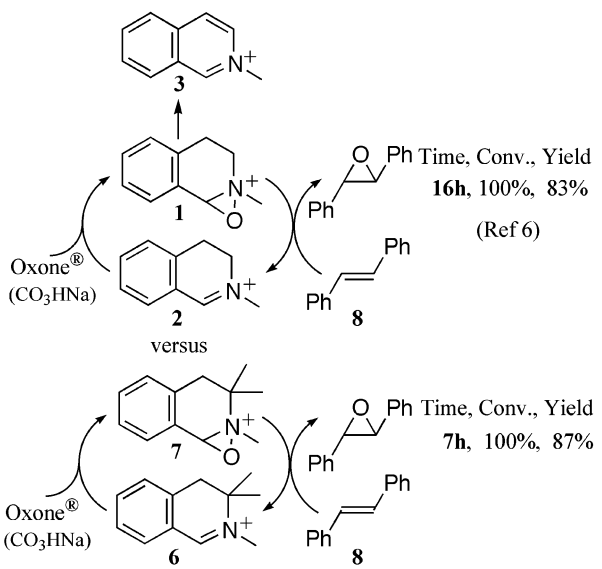
Thus, we have prepared the 3,3-dimethyl-dihydroisoquino-linium salt **6** and we report herein that it is a convenient catalyst with regard to the oxaziridinium-mediated epoxidation system.

The iminium salt **6**, an easily handled crystalline solid,[13] was synthesized from the commercially available tertiary alcohol **4** as indicated in Scheme 3. The formamide from step (a)[14] was cyclized, following a three-step sequence,[15] into the dihydroisoquinoline **5**[16] which was finally alkylated with the Meerwein's salt trimethyloxonium tetrafluoroborate.

With oxaziridinium **7**, derived from iminium **6**, as the active oxidizing agent in the epoxidation system (Scheme 4), an aromatization pathway as the one observed in the iminium **2** catalyzed system is not possible. In order to estimate the effect of the (endocyclic) α-disubstitution on the catalytic efficiency, we performed the epoxidation of *trans* stilbene **8** (widely used as model substrate for these epoxidation reactions) under the same conditions as previously described with the unsubstituted iminium salt **1**.[6] The results from both systems are indicated in Scheme 4. The epoxidation of *trans* stilbene in the 3,3-disubstituted iminium's system is notably faster than in the reference system involving salt **1**. Since the electrophilicities of both intermediate oxaziridinium species (**7** and **2**, respectively) are most probably very similar, the exclusion of the aromatization path (**1**→**3**, Scheme 4) by the disubstitution of the endocyclic α position allows to improve the catalyst turnover and consequently enhances the efficiency of the oxaziridinium-mediated catalytic epoxidation systems operating with dihydroisoquinolinium-derived iminium salts as catalysts.



Scheme 3. (a) KCN, SO_4H_2–AcOH, rt; (b) oxalyl chloride, Cl_2CH_2; (c) $FeCl_3$; (d) MeOH, SO_4H_2, reflux; (e) Me_3O^+ F_4B^-, Cl_2CH_2; rt.



Scheme 4.

The results of the oxaziridinium-mediated oxidation of a variety of olefinic substrates (Fig. 1) by Oxone® using the iminium salt **6** as catalyst are given in Table 1. Under the conditions used for *trans* stilbene **8**, di- and trisubstituted alkenes **9**–**16** are quantitatively converted into the corresponding epoxides, which may be isolated in good yields (entries 1–8), while incomplete epoxidation was observed for the less reactive terminal double bond of the undecylenic methyl ester **17** (entry 9). As expected,[2] the conjugated double bond of L-(−)-carvone **15** (entry 7) was not affected and the epoxidation occurred selectively on the exocyclic double bond (affording a 1:1 mixture of diastereoisomers).[17] The epoxidation of olefin **12** (entry 4) produced a mixture of *syn*- and *anti*-epoxides in the molar ratio *syn*:*anti* 1:3.5.[18] Similar *anti*-selectivity, arising from preferential oxygen approach from the less hindered face, also occurred in the peracidic epoxidation of the analogous methyl ester.[19] Finally, in the epoxidation of cholesterol (entry 8) a mixture of α- and β-epoxides in the molar ratio α:β 1:3.5[20] was produced. Interestingly, the oxaziridinium **7**-mediated epoxidation of cholesterol displays β-selectivity in contrast to the well-known α-selectivity of the usual peracidic epoxidation of this Δ^5-steroid.[21]

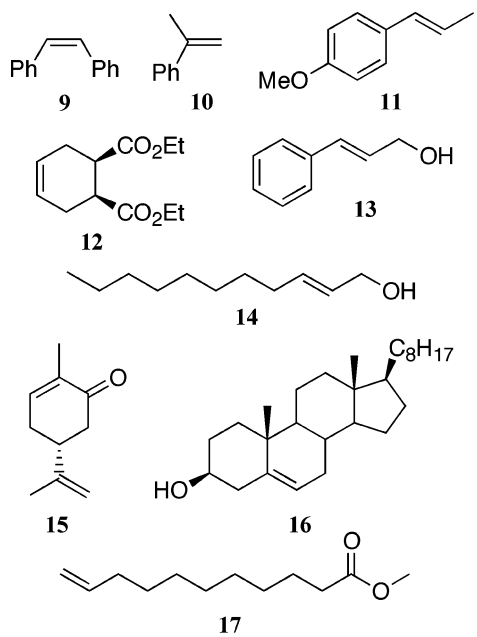


Figure 1.

Table 1. Epoxidation of olefins using iminium salt **6** as catalyst[a]

Entry	Olefin	Time (h)[b]	Yield (%)[c]
1	9	12	81
2	10	12	72
3	11	8	82
4	12	24	74[d]
5	13	9	79
6	14	10	76
7	15	12	80[e]
8	16	8	92[f]
9	17	24	28[g]

[a] Molar ratio olefin:iminium **6**:$KHSO_5$:CO_3HNa = 1:0.1:2:4, CH_3CN–H_2O (3%), rt.

[b] Reactions monitored by TLC.

[c] Epoxides were purified by C.C. on silicagel (the yields are not optimized) and gave satisfactory spectroscopic characterization.

[d] Molar ratio *syn*:*anti* = 2.5:7.5 determined by ^{1}H NMR analysis of the crude product.

[e] Exclusively exocyclic epoxide, 1:1 mixture of diastereoisomers (ratio determined by ^{1}H NMR analysis of the crude product).

[f] Epoxidation performed using CH_3CN/dioxane (1:1)-H_2O (3%) as solvent, molar ratio α:β = 2.2:7.8 determined by ^{1}H NMR analysis of the crude product.

[g] Conversion olefin→epoxide (40%) determined by ^{1}H NMR analysis of the crude product (60% of the substrate was unchanged).

In conclusion, we have prepared the new 3,3-dimethyl-3,4-dihydroisoquinolinium salt **6**, a nicely crystalline and easily handled iminium salt. Improved catalyst turnover and consequently enhanced efficiency resulted using this *gem*-disubstituted iminium salt as a convenient alternative to the parent unsubstituted iminium **1** in the catalytic oxidation of olefins by Oxone®.

Acknowledgements

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References

1. (a) Picot, A.; Milliet, P.; Lusinchi, X. *Tetrahedron Lett*. **1976**, *17*, 1573–1576; (b) Picot, A.; Milliet, P.; Lusinchi, X. *Tetrahedron Lett*. **1976**, *17*, 1577–1580; (c) Picot, A.; Milliet, P.; Lusinchi, X. *Tetrahedron* **1981**, *37*, 4201–4208.
2. (a) Hanquet, G.; Lusinchi, X.; Milliet, P. *Tetrahedron Lett*. **1988**, *29*, 3941–3944; (b) Hanquet, G.; Lusinchi, X. *Tetrahedron* **1997**, *53*, 13727–13738.
3. (a) Hanquet, G.; Lusinchi, X. *Tetrahedron Lett*. **1993**, *34*, 5299–5302; (b) Bohé, L.; Lusinchi, M.; Lusinchi, X. *Tetrahedron* **1999**, *55*, 155–166.
4. Hanquet, G.; Lusinchi, X. *Tetrahedron* **1994**, *50*, 12185–12200.
5. (a) Hanquet, G.; Lusinchi, X.; Milliet, P. *Tetrahedron Lett*. **1987**, *28*, 6061–6064; (b) Hanquet, G.; Lusinchi, X.; Milliet, P. *Tetrahedron* **1993**, *49*, 423–438.
6. Hanquet, G.; Lusinchi, X.; Milliet, P. *C.R. Acad. Sci. Paris*, *(II)* **1991**, *313*, 625–628.
7. (a) Bohé, L.; Hanquet, G.; Lusinchi, M.; Lusinchi, X. *Tetrahedron Lett*. **1993**, *34*, 7271–7274; (b) Bohé, L.; Lusinchi, M.; Lusinchi, X. *Tetrahedron* **1999**, *55*, 141–154.
8. Aggarwal, V. K.; Wang, H. F. *J. Chem. Soc., Chem. Commun*. **1996**, 191–192.
9. (a) Page, P. C. B.; Rassias, G. A.; Bethell, D.; Schilling, M. B. *J. Org. Chem*. **1998**, *63*, 2774–2777; (b) Page, P. C. B.; Rassias, G. A.; Barros, D.; Bethell, D.; Schilling, M. B. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3325–3334.
10. (a) Armstrong, A.; Ahmed, G.; Garnett, I.; Goacolou, K. *Synlett* **1997**, 1075–1076; (b) Armstrong, A.; Ahmed, G.; Garnett, I.; Goacolou, K.; Wailes, J. S. *Tetrahedron* **1999**, *55*, 2341–2352.
11. Minakata, S.; Takemiya, A.; Nakamura, K.; Ryu, I.; Komatsu, M. *Synlett* **2000**, 1810–1812.
12. Wong, M.-K.; Ho, L.-M.; Zheng, Y.-S.; Ho, C.-Y.; Yang, D. *Org. Lett*. **2001**, *3*, 2587–2590.
13. *N*,3,3-Trimethyl-3,4-dihydroisoquinolinium tetrafluoroborate (**6**). mp: 89–90°C (Cl_2CH_2–Et_2O); ^{1}H NMR ($CDCl_3$, 300 MHz): 1.50 (s, 6H); 2.71 (s, 2H); 3.76 (s, 3H); 7.34 (m, 1H); 7.44 (m, 1H); 7.69 (m, 1H); 7.88 (m, 1H); 8.98 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): 23.82; 39.51; 42.51; 62.47; 128.31; 128.56; 134.31; 137.98; 124.28; 136.17; 167.82. MS (FAB): 174 [($M^{+\bullet}$–tetrafluoroborate), base peak]. Anal. calcd for $C_{12}H_{16}NBF_4$: C, 55.21; H, 6.18; N, 5.37%. Found: C, 55.08; H, 6.12; N, 5.35%.
14. Ritter, J.; Kalish, J. *Org. Synth*. **1964**, *44*, 44–47.
15. Larsen, R. D.; Reamer, R. A.; Corley, E. G.; Davis, P.; Grabowski, E. J. J.; Reider, P. J.; Shinkai, I. *J. Org. Chem*. **1991**, *56*, 6034–6038.
16. Seeger, E.; Engel, W.; Teufel, H.; Machleidt, H. *Chem. Ber*. **1970**, *103*, 1674–1691.
17. Diastereoisomer ratio determined by ^{1}H NMR (Cl_3CD) analysis of the crude product, integrating the C9 methyls at δ 1.31 ppm (s, 3H) and δ 1.33 ppm (m, 3H)
18. Kuhn, T.; Tamm, C.; Reisen, A.; Zedner, M. *Tetrahedron Lett*. **1989**, *30*, 693–696.
19. *syn*:*anti* Molar ratio determined by ^{1}H NMR (Cl_3CD) analysis of the crude product, integrating the oxiranic protons at δ 3.18 ppm (m, 2H, *anti*-epoxide) and δ 3.23 ppm (m, 2H, *syn*-epoxide).
20. Molar ratio α:β determined by ^{1}H NMR (Cl_3CD) analysis of the crude product, integrating the oxiranic protons (C6-H) signals at δ 3.05 ppm (d, *J* 1.7 Hz, 1H, β-epoxide) and δ 2.86 ppm (d, *J* 4.4 Hz, 1H, α-epoxide).
21. Kirk, D. N.; Hartshorn, M. P. *Steroid Reaction Mechanisms*; Elsevier: Amsterdam, 1968; pp. 69–77.