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Regio- and Diastereoselective Ring-Opening Reaction of Epoxides with Nitric Oxide

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Abstract: Ring-opening reactions of epoxides with nitric oxide afforded *syn* or *anti* α-hydroxy nitrates in high regio- and diastereoselectivities in good yields.

Keywords: Epoxide, nitric oxide, ring opening

The three-membered ring of epoxides is an important kind of functional group.[1] Ring strain renders epoxides susceptible to ring-opening reactions. This ring-opening behavior makes epoxides useful synthetic intermediates, which fully deserve a prominent place in the arsenal of organic chemists. Epoxides are thereby widely employed in organic synthesis. New approaches have continuously emerged for the stereoselectivity of ring-opening reactions.[2] Among them, ring-opening reactions of epoxides by radicals

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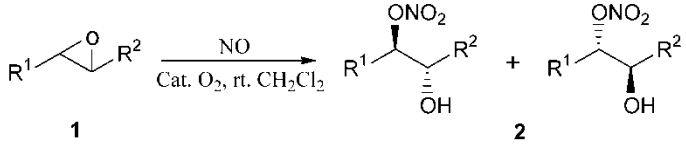
are particularly interesting.[3] We have found that the three-membered ring of aziridines and α,β-epoxy phenyl ketones can be efficiently cleaved by NO in high regio- and diastereoselectivities.[4] In particular, the ring-opening reaction of α,β-epoxy phenyl ketones with NO regioselectively afforded the C-3 ring-opened products in a highly *syn*-selective manner.[4c] As part of our ongoing research project on nitric oxide (NO), further study has been carried out to extend the substrate scope to other epoxides that have no neighboring carbonyl group. The ring-opening reaction occurred regioselectively at C-3, however, with an *anti*-selectivity to afford single *anti* α-hydroxy nitrates in good yield. It seems that the *syn*- or *anti*-selective ring-opening patterns of epoxides strongly depend on the substituent attached to the C-2 atom (Scheme 1).

When α-hydroxy epoxides were used as substrates, *anti* α-hydroxy nitrates were still obtained, in which the two neighboring hydroxy groups were on the *syn* position. In addition, ring-opened products of cyclic epoxides also led us to suggest that the two functional groups were newly formed at the opposite sides of the ring. It was clear that the ring-opening reaction of epoxides with NO gave *anti* α-hydroxy nitrates, which is different from those of α,β-epoxyketones with NO, which gave only *syn* products. The difference between α-carbonyl epoxides and noncarbonyl substituted epoxides with NO in the ring opening suggested that the carbonyl group was a key factor in the reaction and the mechanisms or intermediates of those were different.

EXPERIMENTAL

The reaction procedure was performed as previously described.[4] In a representative experiment, freshly prepared NO gas bubbled through the well-stirred 15-mL CH_2Cl_2 solution of **1a** (1 mmol). The reaction completed in ca. 10 h. Isolation and purification with column chromatography yielded the product **2a** (222.5 mg, 98%). The products were characterized by HRMS, fast atom bombardment mass spectrometer (FAB-MS), and ^1H and ^{13}C NMR spectroscopy. High-resolution mass spectrometer (HRMS): Bruker Daltonics Apex II FT-ICR; FAB: VG ZAB-HS; Bruker Apex II; NMR: ^{13}C: 100 MHz,



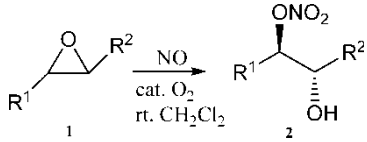
1 **2**

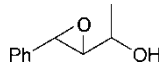
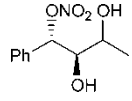
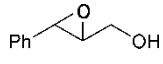
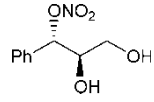
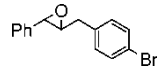
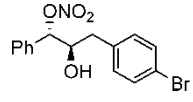
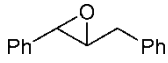
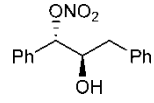
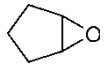
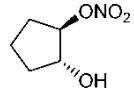
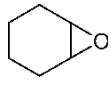
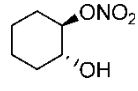
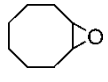
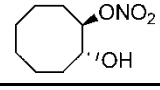
R^1, R^2= aryl, alkyl The isolated yield of trans-pairs up to 98%

Scheme 1.

^{1}H: 400 MHz, Varian Mecury 400 (TMS). **2a**: HRMS m/z 477.1495 (calcd. for $C_{10}H_{13}NO_5$ $[2M + Na]^+$, 477.1485, error = 2.0 ppm); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.425 (5H, s), 5.977 (1H, d, $J = 8.4$ Hz), 3.744 (1H, m, $J = 8.4$ Hz, $J = 5.2$ Hz, $J = 2.0$ Hz, $J = 1.6$ Hz), 3.507 (1H, t, $J = 6.4$ Hz), 2.657 (1H, d, $J = 4.8$ Hz), 1.909 (1H, d, $J = 8.0$ Hz), 1.224 (3H, d, $J = 6.4$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 134.7, 129.5, 129.0, 127.4,

Table 1. Ring-opening reaction of epoxides with NO in CH_2Cl_2 at ambient temperature



Entry		Epoxide[a]		Product[b]	RT (h)[c]	Yield (%)[d]
1	**1a**		**2a**		10	98
2	**1b**		**2b**		10	90
3	**1c**		**2c**		12	82
4	**1d**		**2d**		12	81
5	**1e**		**2e**		12	83
6	**1f**		**2f**		12	85
7	**1g**		**2g**		12	80

[a]Epoxides having a chiral center are racemic isomers.
[b]Products are the corresponding racemic isomers.
[c]Reaction time.
[d]Isolated yields after column chromatography.

86.8, 75.6, 66.0, 20.4; **2f**: FAB: m/z 162.1 $[M+1]^+$; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.809 (1H, m, $J = 12.8$ Hz, $J = 9.6$ Hz, $J = 4.4$ Hz), 3.675 (1H, m, $J = 10.8$ Hz, $J = 8.8$ Hz, $J = 4.8$ Hz, $J = 2.0$ Hz), 2.430 (1H, s), 2.190 (1H, m), 2.174 (1H, m), 1.830 (2H, m), 1.447 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 87.2, 70.5, 33.0, 28.7, 23.7, 23.4; **2g**: HRMS m/z 379.2084 (calcd. for $C_8H_{15}NO_4$ $[2M+H]^+$, 379.2075, error = 2.4 ppm); ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.190 (1H, m, $J = 8.8$ Hz, $J = 7.6$ Hz, $J = 7.2$ Hz), 3.903 (1H, m, $J = 9.2$ Hz, $J = 7.2$ Hz, $J = 6.8$ Hz, $J = 2.4$ Hz), 2.380 (1H, s), 1.919 (8H, m), 1.585 (4H, m); ^{13}C NMR (100 MHz, $CDCl_3$): δ 89.6, 71.4, 30.3, 29.0, 26.0, 25.2, 25.1, 22.5.

The reaction of the epoxide **1** with NO afforded the corresponding *anti* α-hydroxy nitrates compound **2** in good yields. The coupling constant of the vicinal hydrogen atoms is the distinct difference in the ring-opened products *anti* and *syn* α-hydroxy nitrates. In the former, the datum is ca. 8.4 ppm, whereas it is 3.6 Hz in the latter. The results are collected in Table 1.

In conclusion, this work reports a novel ring-opening method for epoxides. The ring-opening reaction of non-vicinal-carbonyl substituted epoxides with NO produced *anti* α-hydroxy nitrates in high regioselectivity in good to excellent yields.

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