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A mild and efficient procedure for the oxidation of epoxides and aziridines using cerium(IV) ammonium nitrate and NBS☆

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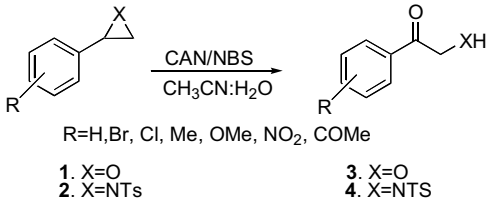
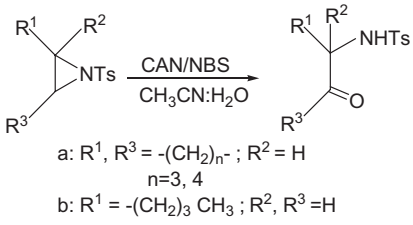
Abstract—The CAN and NBS combination has been used for the first time for the synthesis of versatile α-hydroxy ketones and α-amino ketones from oxiranes/aziridines, respectively, in excellent yields. This method is a direct, one-pot, synthesis under mild conditions using acetonitrile–water (9:1) as solvent.

Cerium(IV) ammonium nitrate (CAN) is a powerful one-electron oxidant useful for a variety of synthetic transformations.[1,2] CAN has become attractive in organic synthesis due to its ease of handling, non-toxicity and solubility in organic solvents such as MeOH, MeCN, etc. We have studied the use of CAN for the direct synthesis of α-hydroxy ketones and α-amino ketones from easily accessible epoxides and aziridines, respectively. However, these reactions resulted in the formation of diols and hydroxy amines only. Therefore, to access keto alcohols and amino ketones, we studied the combination of CAN with NBS, another oxidizing agent.[3] This yielded excellent results. A number of methods are reported for the synthesis of α-hydroxy ketones,[4–7] but only few methods are available for the preparation of α-amino arylketones although they are important in providing an alternative route to biologically active β-aminoalcohols.[8]

We report the oxidation of oxiranes/aziridines using ceric ammonium nitrate and NBS to give the corresponding α-hydroxy ketones and α-amino ketones, respectively, in good yields[9] (Schemes 1 and 2).



Scheme 1.



Scheme 2.

Initially, our efforts began with styrene oxide (Table 2, entry 1), which was treated with CAN (0.2 equiv) and NBS (1.0 equiv) in acetonitrile–water (9:1) to give the α-hydroxy ketone after simple workup in 94% yield. However, with phenoxy epoxide the desired keto alcohol was obtained in very poor yields (~15%) along with the corresponding 3-phenoxy-1,2-propanediol (~45%) and 1-bromo-3-phenoxy-2-propanol (~30%), whereas with cycloalkyl epoxides and alkyl epoxides a complex mixture of products was obtained, which could not be analyzed. To explore further the utility of this transformation, phenyl-*N*-tosylaziridine (Table 3, entry 1) was treated with a CAN and NBS combination to yield the α-amino ketones in 92% yield. Encouraged by this

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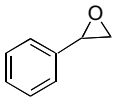
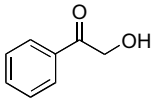
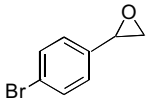
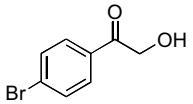
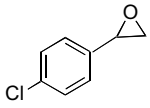
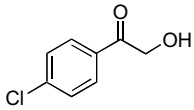
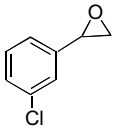
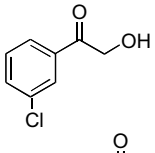
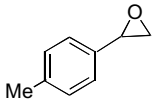
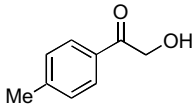
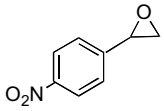
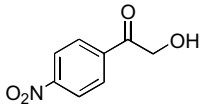
Table 1. Oxidation of oxirane/aziridine under various conditions[a]

Entry	Substrate	CAN (equiv)	NBS (equiv)	Time (h)	Yield (%)[b]
1	Styrene oxide	0.2	—	10	—[c]
2	Styrene oxide	—	1.0	10	15[d]
3	Styrene oxide	0.2	1.0	4	94
4	Phenyl-*N*-tosylaziridine	0.2	—	12	—[e]
5	Phenyl-*N*-tosylaziridine	—	1.0	12	—[f]
6	Phenyl-*N*-tosylaziridine	0.2	1.0	8	92

[a] All reactions were carried out at rt.
[b] All reactions were analyzed by HPLC and compared with authentic samples.
[c] Only 1-phenyl-1,2-ethanediol was formed.
[d] Yielded 2-bromo-1-phenyl-1-ethanol, 2-bromo-2-phenyl-1-ethanol (50% 1:1) and 1-phenyl-1,2-ethanediol (30%) along with keto alcohol.
[e] Only *N*-(2-hydroxy-2-phenylethyl)-4-methyl-1-benzene sulfonamide was formed.[2d]
[f] Yielded *N*-(2-bromo-2-phenylethyl)-4-methyl-1-benzene (35%) and *N*-(2-hydroxy-2-phenylethyl)-4-methyl-1-benzene sulfonamide (65%).

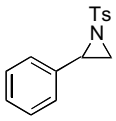
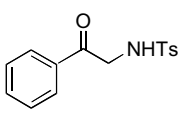
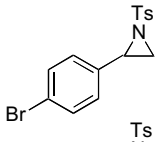
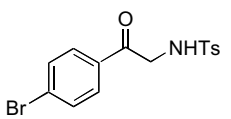
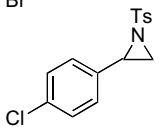
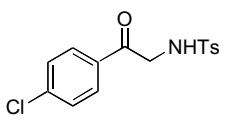
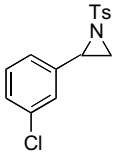
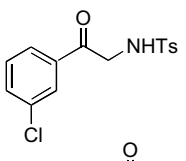
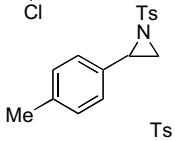
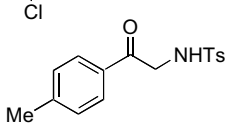
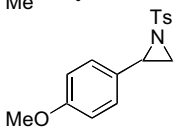
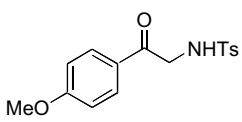
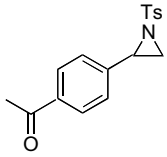
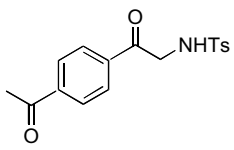
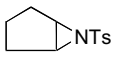
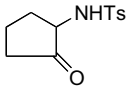
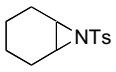
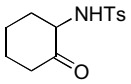
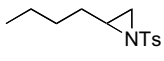
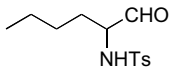
Table 2. Oxidation of epoxides with CAN/NBS

Entry	Epoxide	Product[a]	Time (h)	Yield (%)[b]
1			4	94
2			4	92
3			4	92
4			5	88
5			8	90
6			8	86

[a] All the compounds were characterized by ^{1}H NMR, IR and mass spectroscopy.
[b] Isolated yields.

finding cyclopentyl/cyclohexyl-*N*-tosylaziridines were oxidized to yield 1-(*N*-(*p*-tolylsulfonyl)amino-2-cylcopentanone (Table 3, entry 8) and 1-(*N*-(*p*-tolylsulfonyl)amino-2-cylcohexanone (Table 3, entry 9), respectively. In the case of an acyclic terminal aziridine (Table 3, entry 10), the reaction was highly regioselective with the formation of only one product oxidized at the less hindered terminal carbon.

Table 3. Oxidation of aziridines with CAN/NBS

Entry	Substrate	Product[a]	Time (h)	Yield[b] (%)
1			8	92
2			8	90
3			8	90
4			10	86
5			10	89
6			10	88
7			10	90
8			12	86
9			12	88
10			12	84

[a] All the products were characterized by IR, ^{1}H NMR and mass spectroscopy.
[b] Isolated yields.

Some of the functionalities, which were stable to CAN and NBS included the bromo, methoxy, methyl, chloro and acetoxy groups. The α-hydroxy ketones and α-amino ketones synthesized are being explored as building blocks for new chemical entities. The compounds were characterized by ^{1}H NMR, mass spectra, IR and compared with known compounds.[5,8]

Phenyl oxirane and phenyl-*N*-tosylaziridine were chosen for several control experiments to determine the role of each reagent (Table 1). CAN and NBS are both impor-

tant since no reaction occurs or oxidation takes place if either is omitted.

The oxidation mechanism may be postulated as follows: CAN first hydrolyses the substrate, which is further oxidized with NBS to give the corresponding keto products.[10]

Thus, we have demonstrated that α-hydroxy ketones and α-amino ketones can be generated directly from epoxides/aziridines in the presence of CAN and NBS.

Acknowledgements

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9. General procedure: To epoxide **1**/aziridine **2** (1 equiv) in 5 ml of acetonitrile: water (9:1) was added CAN (0.2 equiv) followed by NBS (1 equiv) and the mixture was left stirring at room temperature (Table 1 and 2). After completion of the reaction, the solvent was removed, the reaction mixture was diluted with water and extracted with ether (3×10 ml). The combined organic extract was dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by column chromatography on silica gel using *n*-hexane/ethyl acetate as eluent.
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