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2-Amino ketones from osmium-catalysed oxidations of alkenes

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Abstract

The present article summarises imidoosmium-catalysed oxidations of alkenes to yield 2-amino ketones. Three different approaches are discussed. The first section describes the direct conversion of alkenes to yield racemic 2-amino ketone products in what represents a so-far unknown reactivity in osmium catalysis. It is followed by the description of a two-step procedure, which converts alkenes into enantiomerically pure vicinal amino alcohols followed by stereoselective oxidative conversion into 2-amino ketones. Both pathways derive from a common mechanistic background and constitute a novel side-reaction of the original aminohydroxylation chemistry. An alternative synthetic approach of osmium-catalysed aminohydroxylation of silyl enol ethers is discussed as well and is compared to the previous two procedures.

Keywords: Alkenes; Aminohydroxylation; Amino ketones; Oxidation; Osmium

1. Introduction

Carbonyl functionalities are usually of high synthetic importance due to their ease of further derivatisation, such as Aldol processes [1]. Among the wide number of carbonyl derivatives, 2-amino ketones represent an example of higher functionalisation, which is rather seldomly encountered. Their general synthesis is most conveniently accomplished from amino acid derivatisation [2] or from oxidations of enol ethers [3,4]. Alternative synthetic approaches rely on C–C [5–7] or C–N bond forming processes [8,9].

As an additional feature, the 2-amino ketone entity is present in some biologically relevant natural products such as the proteasome inhibitor epoxomicin, [10,11] the antitumor agent eponemycin, [11] the mersingins A and B [12] and cathinone, a powerful stimulants from *catha edulis* (Fig. 1) [13].

On the other hand, oxidative conversion of alkenes such as dihydroxylation [14] and aminohydroxylation [15] represents a powerful approach toward the introduction of heteroatoms into carbon skeletons. As such, direct access to carbonyl groups from alkenes constitutes an obviously desirable reaction. Within this area, Plietker has recently described direct conversion of alkenes into 2-hydroxy ketones under RuO_4 catalysis [16–19]. These reactions employ oxone as terminal oxidant and are characterised by excellent regioselectivities and pronounced functional group tolerance. In contrast, oxidations in the presence of osmium(VIII) reagents are generally of high chemoselectivity and thus give access to diols [14] or amino alcohols [15], respectively, without any significant amount of overoxidation. The synthesis of hydroxy ketones from unfunctionalised alkenes had only been encountered in initial protocols, which employ harsh oxidants [20,21]. 2-Hydroxy ketone formation under mild conditions was later conveniently accomplished by oxidation of silyl enol ethers under the usual dihydroxylation conditions [22–24].

2. Results and discussion

The direct synthesis of amino ketones from alkenes was discovered for the oxidation of (*E*)-stilbene under aminohydroxylation conditions [25]. In the presence of chloramine-T as both reoxidant to osmium and as nitrogen source and in the absence of any of the cinchona alkaloid standard ligands, no amino alcohols were produced. Instead, the final product mixture contained the 2-amino ketone **2a** as major product (Scheme 1). Application of

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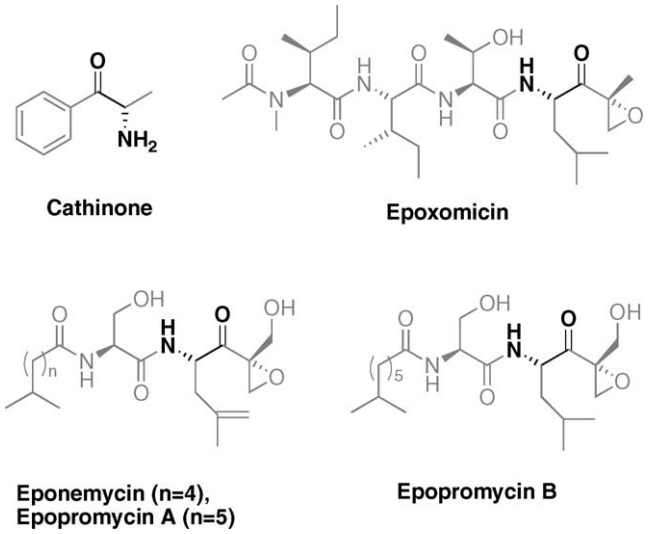
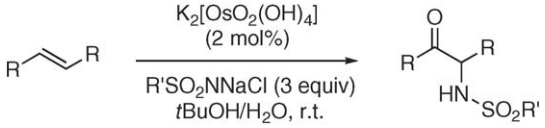


Fig. 1. Natural products incorporating the 2-amino ketone functional unit.

three equivalents of chloramine-T was found necessary in order to achieve full conversion to the ketone. In an early aminohydroxylation protocol under phase transfer conditions, Sharpless had detected a 9% yield for **2a** when 1.25 equivalents of oxidant with regard to the olefin had been used [26]. In addition to amino ketone **2a**, minor amounts of benzil were isolated. The latter compound is believed to originate from further oxidation, although it presently remains unknown at which stage of the reaction it is formed. The X-ray structure of **2a** was carried out and confirmed the expected overall constitution of the product.

The ketamination reaction proofed general for several chloramine salts (Table 1, entries 1–4) which all converted stilbene into the corresponding 2-amino ketones. Again, benzil formation took place as the side-reaction with yields in the range of 14–35%. The aliphatic substrate 5-decene could be transformed cleanly into the corresponding amino ketone **2e** employing chloramine-T as oxidant (entry 5). In this case, no diketone was detected, which suggests that the benzil formation in related

Table 1
Direct ketamination of symmetrical alkenes



1,3 2a-e

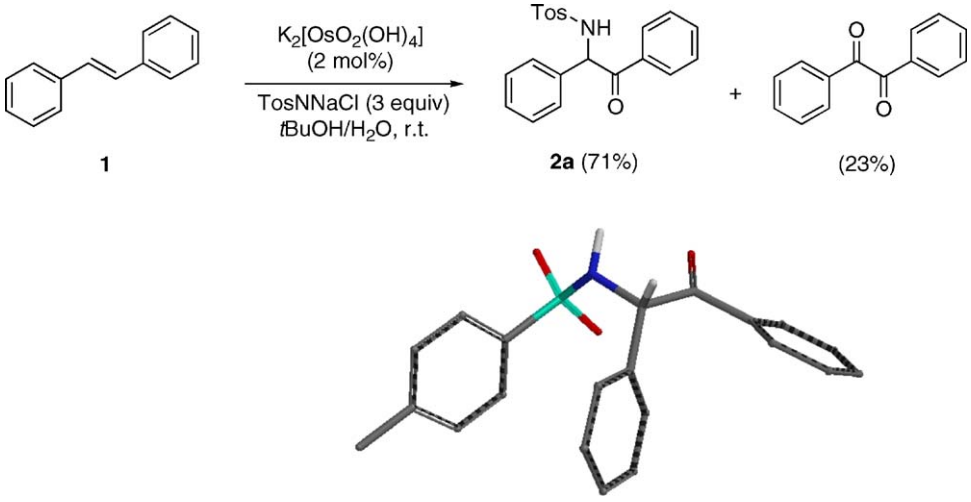
Entry	Substrate (R)	Oxidant (R')	Product	Yield (%)[a]
1	**1** (R = Ph)	Tol	**2a**	71 (23)[b]
2	**1** (R = Ph)	Ph	**2b**	77 (14)
3	**1** (R = Ph)	Me	**2c**	61 (35)
4	**1** (R = Ph)	*t*Bu	**2d**	70 (21)
5	**3** (R = *n*Bu)	Tol	**2e**	82

[a] Isolated yield at 100% alkene conversion.
[b] Values in brackets refer to the amount of benzil side product.

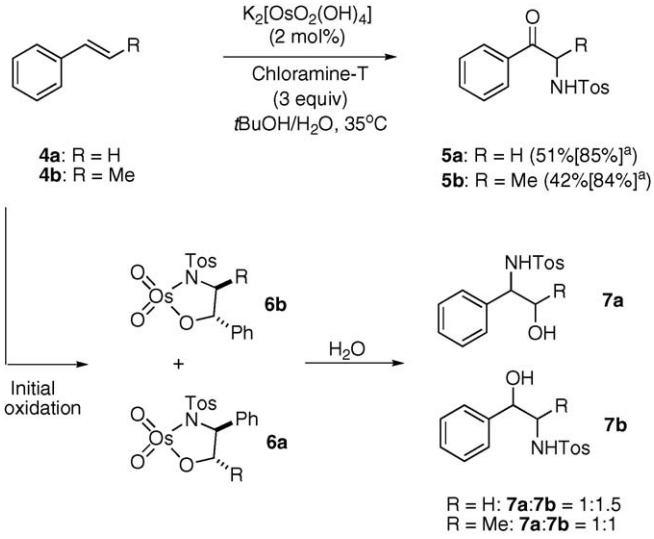
stilbene oxidation originates from a preferential oxidation in benzylic position.

Apart from symmetrical alkenes **1** and **3**, the unsymmetrically substitued alkenes styrene **4a** and β-methyl styrene **4b** underwent formation of 2-amino ketones as well. For these substrates, only the amino ketones **5a**,**b** with the amine in homobenzylic position could be obtained. As expected, the reaction suffers from the inherent regioselectivity problem [15] of the initial step of alkene functionalisation. Here, two intermediary regioisomers **6a**,**b** with the amino group in benzylic and homo-benzylic position will be formed. A regioselectivity of 1.5:1 and 1:1, repectively, had been established from the corresponding aminohydroxylation reactions that were investigated by Sharpless and co-worker [27]. These require overall yields of 60 and 50%, respectively, for **5a** and **5b**. The obtained yields (51 and 42%) are in good agreement and suggest that no or little competing reactions occur for those products with the amine in homo-benzylic position (Scheme 2).

The overall mechanistic rationale for the observed 2-amino ketone formation under imidoosmium catalysis is depicted in Fig. 2 and reveals this reaction as a side reaction in the second



Scheme 1. Direct ketamination of (*E*)-stilbene and solid state structure of 2-amino ketone product **2a** (below).



Scheme 2. Direct ketamination of alkenes: the regiochemistry issue. [a]Yield based on maximum yield according to the initial regioselectivity.

cycle of aminohydroxylation [15]. After the initial aminohydroxylation of the alkene, the resulting osma(VI)azaglycolate **A** undergoes re-oxidation to the osma(VIII)azaglycolate **B**. In the absence of a *Cinchona* alkaloid ligand, hydrolysis to the amino alcohol is slow, leading to concomitant oxidation of a second alkene, thereby generating the bisazaglycolate **C** and finally, upon further reoxidation, osma(VIII)bisazaglycolate **D**. Intramolecular oxidation of one amino alcohol ligand as depicted forms the mono-bound 2-amino ketone (intermediate **E**), which is hydrolysed off to regenerate complex **A** and closes the overall catalytic cycle (Fig. 2).

Upon inclusion of the cinchona alkaloid ligand to the reaction mixture, amino alcohols become the only detectable reaction products as known from Sharpless initial investigation on aminohydroxylation [28,29]. This difference in reaction outcome is readily explained by the enhanced hydrolysis rate of the intermediate osma(VIII)azaglycolate **B** under such conditions, which

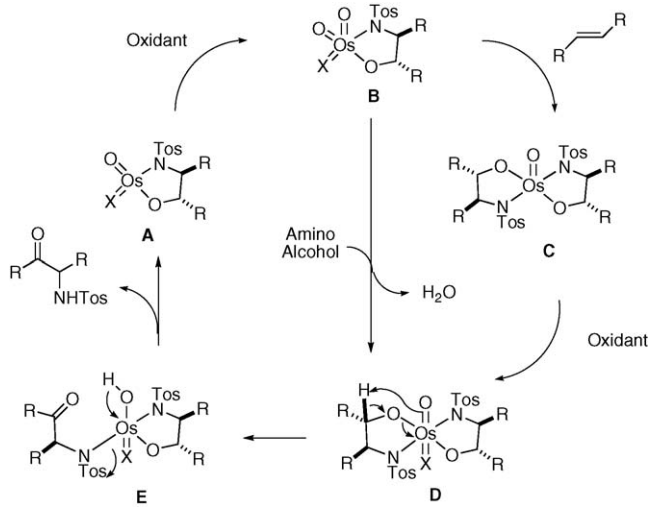


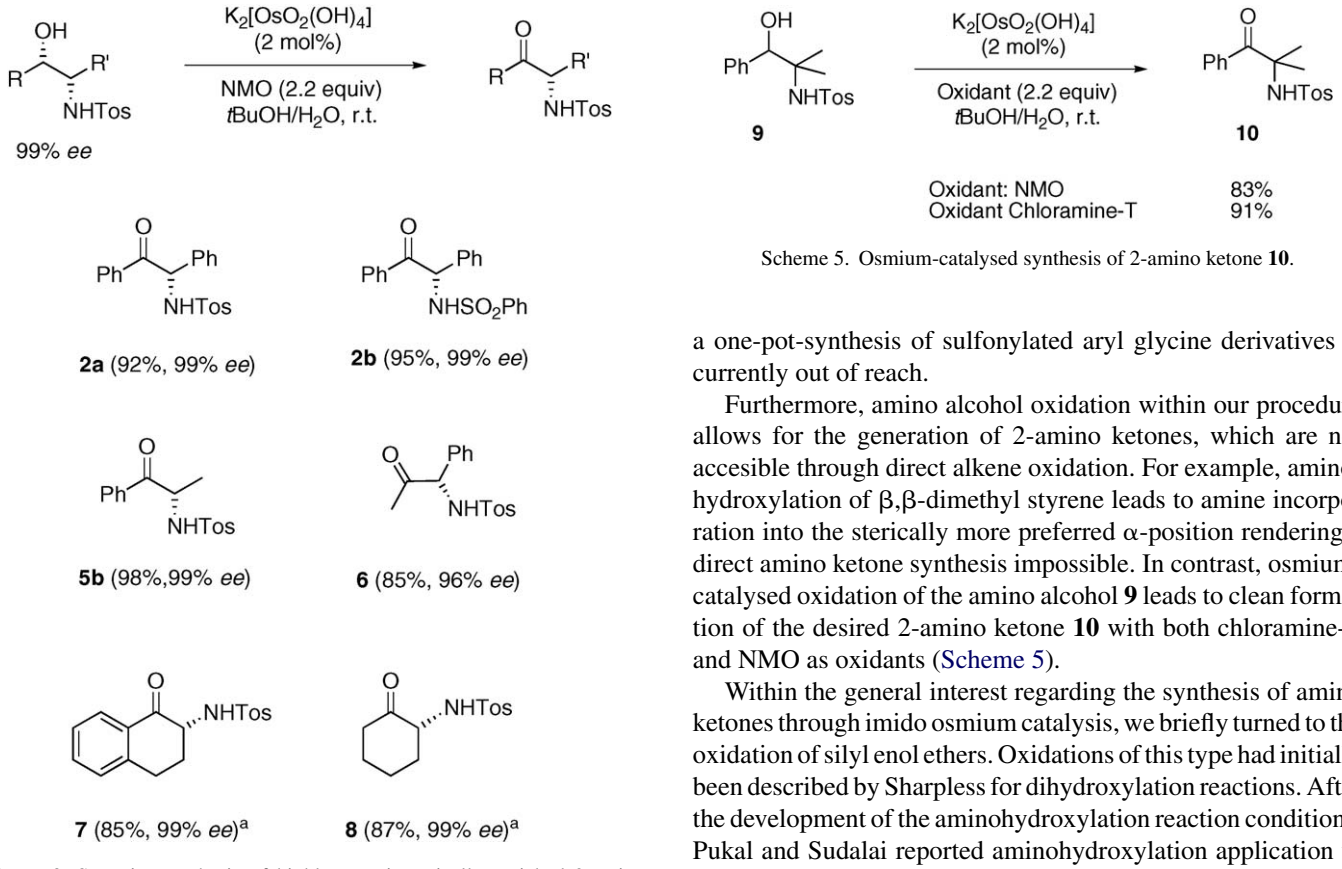
Fig. 2. Mechanistic rationale for 2-amino ketone formation from alkenes under imidoosmium catalysis. X═O, NTos

is induced by the ligand [30]. As a consequence, the absence of the ligand is crucial for the kinetic stability of intermediates **C** and **D** and thus for the overall ketamination course. A related mechanistic scenario had been proposed for the undesired formation of hydroxy ketones in early dihydroxylation protocols [31].

These mechanistic suggestions explain the preferential formation of 2-amino ketones under aminohydroxylation conditions in the absence of a cinchona alkaloid ligand. However, they do not explain the complete absence of amino alcohols from the reaction products, since hydrolysis at the stages of the azaglycolates **B** or **C** might well take place liberating free amino alcohol product. Apparently, there must be a correction mechanism involved, which allows for exclusive 2-amino ketone formation. Inspection of the catalytic cycle suggests that such a correction mechanism would best be achieved upon condensation of free amino alcohol with **B**, which directly furnishes **D** as the immediate precursor to amino ketone formation. The condensation reaction of an amino alcohol with the azaglycolate **B** to yield **D** is reminiscent of the related chemistry between an osmium ester and a free diol as revealed from the seminal work by Criegee [32–34].

All the oxidation products obtained so far are racemic in nature due to the required absence of the stereoinducing cinchona alkaloid ligands. However, the mechanistic insight that 2-amino ketones should be formed from a sequence of condensation between amino alcohols and azaglycolate osmium esters followed by oxidation of an azaglycolate ligand led to the development of an enantioselective synthesis of this class of compounds. For example, 1,2-diphenyl-2-tosylamino ethanol was cleanly converted to **2a** in the presence of 2 mol% potassium osmate and 2.2 equivalents of chloramine-T. As expected, oxidation of enantiopure vicinal amino alcohols in the presence of 2 mol% of potassium osmate led to clean formation of the desired 2-amino ketones. The degree of preservation of the initial enantiomeric excess was found to depend crucially on the nature of the oxidant in this transformation. Chloramine-T was encountered too basic and led to a decrease in enantiomeric excess in the range of 10–24%. Gratifyingly, the common *N*-methyl-morpholine-*N*-oxide (NMO) was found to represent the optimum solution and enabled the catalytic conversion of vicinal amino alcohols to the corresponding 2-amino ketones under conservation of the initial enantiomeric excess (Scheme 3).

Under optimised conditions, (*S*)-configured amino ketones **2a**,**b**, **5b** and **6** were obtained from the respective (*S*,*S*)-amino alcohols (Scheme 3). These derived from standard AA reaction [15,28,29] followed by ee enrichment through crystallisation (99% ee). In an analogous manner, (*R*,*R*)-1,2-diphenyl-2-tosylamino ethanol gave (*R*)-**2a** in 99% ee. In addition, NMO proofed an optimum oxidant regarding the chemoselectivity within the final oxidation. Thus, within the competing ketone vs imine oxidation at the stage of the intermediate **D**, no benzil formation was detected in the formation of **2a**,**b** and the compounds **5b** and **6** were equally formed with complete chemoselectivity and in high yields. Finally, enantiopure 2-amino ketones **7** and **8** were obtained from *trans*-configured amino alcohol



Scheme 3. Stepwise synthesis of highly enantiomerically enriched 2-amino ketones. [a]From the corresponding trans-configured amino alcohol.

precursors. These results demonstrate the high efficiency of the present process since the NMO-based (Scheme 3) leads to high chemoselectivity in the oxidation of the amino alcohols, generally without any detectable degree of racemisation nor overoxidation.

This latter process of two-step oxidation is particularly interesting when compared to a synthetic protocol by Reddy and Sharpless [35]. Owing to the problematic regioselectivity in aminohydroxylation, [15] oxidation of styrenes employing a carbamate-based nitrenoid led to formation of the regioisomeric amino alcohols which in the presence of TEMPO underwent a second addition to form aryl glycine and the, in this case undesired, 2-amino ketone with Cbz-protection (Scheme 4). Since our direct ketamination protocol requires sulfamide-based nitrenoids, a potential shortening of the Sharpless sequence to

Scheme 5. Osmium-catalysed synthesis of 2-amino ketone **10**.

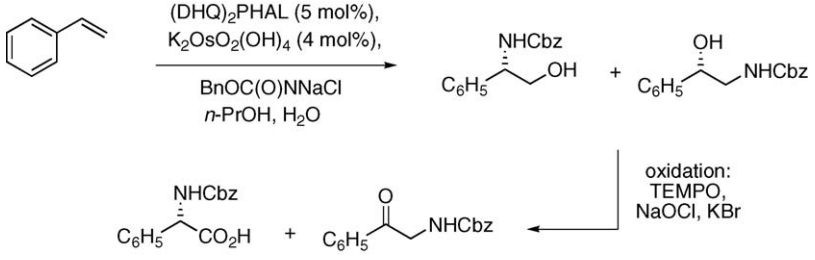
a one-pot-synthesis of sulfonylated aryl glycine derivatives is currently out of reach.

Furthermore, amino alcohol oxidation within our procedure allows for the generation of 2-amino ketones, which are not accesible through direct alkene oxidation. For example, aminohydroxylation of β,β-dimethyl styrene leads to amine incorporation into the sterically more preferred α-position rendering a direct amino ketone synthesis impossible. In contrast, osmium-catalysed oxidation of the amino alcohol **9** leads to clean formation of the desired 2-amino ketone **10** with both chloramine-T and NMO as oxidants (Scheme 5).

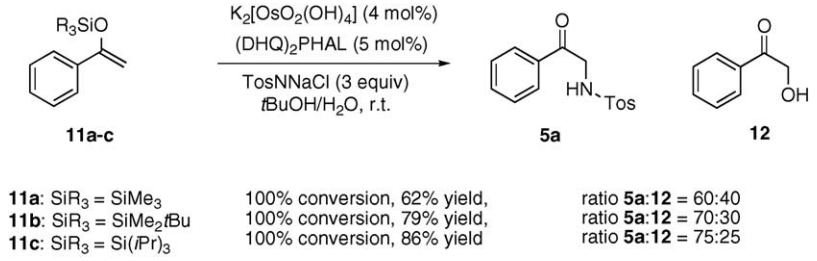
Within the general interest regarding the synthesis of amino ketones through imido osmium catalysis, we briefly turned to the oxidation of silyl enol ethers. Oxidations of this type had initially been described by Sharpless for dihydroxylation reactions. After the development of the aminohydroxylation reaction conditions, Pukal and Sudalai reported aminohydroxylation application to the oxidation of silylenol ethers to give 2-amino ketones in yields between and 28 and 56% and enantiomeric excesses of 70–97% after recrystallisation [36,37].

In our experiments with 1-phenyl-silylenol ether, we detected the formation both of the expected 2-amino ketone as well as the corresponding 2-hydroxy ketone (Scheme 6). It was also observed that the nature of the trialkylsilyl group has a significant influence on the overall reaction course.

The results can be summerised as follows: silyl enol ethers undergo unselective oxidative transformation into 2-amino and 2-hydroxy ketones, respectively. The overall yields of the reactions and the ratio between amino and hydroxy ketone increase in the order trimethylsilyl < dimethyl-*tert*-butylsilyl < tris(2-propyl)silyl. However, for $(DHQ)_2PHAL$ as ligand there is no influence of the nature of the silyl substituent on the overall reaction rates of these reactions which are usually completed within two hours. Apparently, the high reactivity of the enol ethers does not allow for an efficient domination of the transition state



Scheme 4. Two-step oxidation of styrenes: synthesis of aryl glycines and 2-aminoketones via a two-step oxidation with different catalysts.



Scheme 6. 2-Amino ketones from imidoosmium-catalysed oxidation of silylenol ethers.

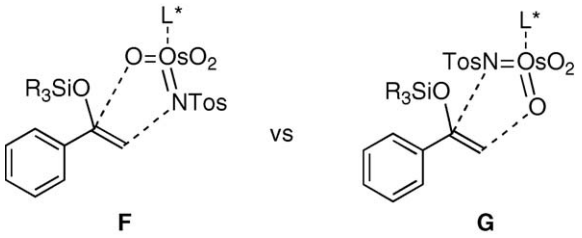
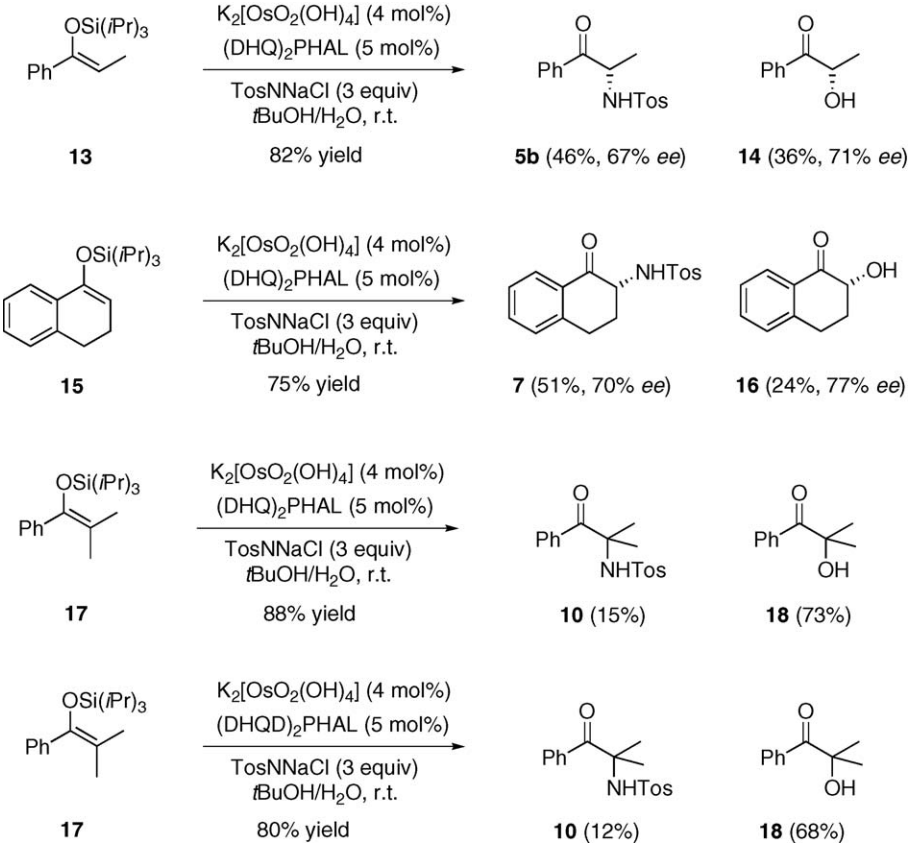


Fig. 3. Competing transitions states **F** and **G** in the aminohydroxylation of silyl enol ethers.

of the oxidation reaction through the ligand. As a consequence, transition states **F** and **G** are believed to be involved to equal extends which results in formation of both 2-amino ketone and 2-hydroxy ketone (Fig. 3).

Employing TIPS protected enol ether as starting materials, synthesis of 2-amino ketones via imidoosmium catalysed oxidation was briefly investigated (Scheme 7). For these cases, mixtures of amino ketone and hydroxy ketone were always encountered. Oxidation of substrates **13** and **15** led to the expected amino ketones **5b** and **7**, respectively, in moderate yields and good enantiomeric excesses. In addition, the hydroxy ketones **14** and **16** were isolated as by-products and with comparable inductions. Steric influences can be decisive in this type of transformation. For example, the β,β-dimethyl silylenol ether **17** gave the desired 2-amino ketone **10** in only very small amounts. Instead, the corresponding hydroxy ketone **18** constitutes the major product. Here, the pronounced sensitivity of the cinchona alkaloid ligated imidoosmium catalyst toward substituents at the alkene renders the amino ketone formation problematic, regardless whether the ligand with dihydroquinine or dihydroquinidine core is employed.

For the observed reasons of low regioselectivity, we conclude that the formation of 2-amino ketones from enolethers does not



Scheme 7. Imidoosmium-catalysed oxidation of silylenol ethers.

constitute a viable alternative over the direct ketamination or the stepwise ketamination procedure.

3. Conclusions

We have described the synthesis of 2-amino ketones from alkenes in an osmium-catalysed reaction, which can be carried out within two alternative pathways. The direct ketamination is an achiral process and allows for the isolation of the target compounds in good yields, although loss of material may arise from the inherent regioselectivity problems. The mechanistic similarities with the parent aminohydroxylation reaction characterise this transformation as a side process of the secondary aminohydroxylation cycle. A second approach consists of osmium-catalysed asymmetric aminohydroxylation to yield enantiomerically enriched vicinal amino alcohols, which can be submitted to osmium-catalysed oxidation. Such a two-step process yields 2-amino ketones with high chemoselectivity unter preservation of the initial enantiomeric excess. Finally, the latter process was found to be preferential over a direct aminohydroxylation of silylenol ethers.

In summary, we have established a new imidoosmium-catalysed process, which yields 2-amino ketones from alkenes.

4. Experimental

Potassium osmate $K_2[OsO_2(OH)_4]$ was purchased from Aldrich and stored under argon. $(DHQD)_2PHAL$ and $(DHQ)_2PHAL$ were purchased from Fluka. All commercially available alkenes were purchased from Aldrich. All solvents were reagent grade and used as received. Column chromatography was performed with silica gel (Merck, type 60, 0.063–0.2 mm and Machery Nagel, type 60, 0.015–0.025 mm). NMR spectra were recorded on a Bruker DPX 300 MHz and Bruker DRX 500 MHz spectrometer. All chemical shifts in NMR experiments are reported as ppm downfield from TMS. The following calibrations were used: $CDCl_3$ $\delta = 7.26$ and 77.00 ppm. Other solvents were calibrated against TMS as standard ($\delta = 0.0$ ppm). Multiplets are given by the common abbreviations (s, singlet; d, doublet; t, triplet, q, quartet; m, multiplet; ps for pseudo). MS and HRMS experiments were performed on a Kratos MS 50 within the service centres at the Kekulé-Department, Bonn. HPLC determinations were carried out on a Knauer Wellchrome (injection valve A0258, pump K-100, solvent organizer K-1500, UV-detector K-2600). The reported values refer to 254 nm detection wavelength.

5. General procedure A for ketamination of olefins

A portion of potassium osmate $K_2[OsO_2(OH)_4]$ (0.02 mmol) is added to 20 mL of a mixture of distilled water and *tert*-butanol (1/1, v/v) and stirring is applied until complete dissolution of the solid. The respective chloramine sodium salt (3.0 mmol) is added in one portion and the resulting solution is warmed to 30–35 °C with stirring. The respective olefin (1.0 mmol) is added to the reaction mixture and stirring is continued for 2d. The reaction mixture is cooled to room temperature, treated with an aqueous solution of sodium bissulphite and extracted three times with ethyl acetate. Drying of the organic phases over $MgSO_4$ and removal of the solvents under reduced pressure leaves an oily to solid residue, which is analysed by NMR. Purification by column chromatography (silica gel, hexanes/ethyl acetate, 4/1, v/v) gave the 2-amino ketones in analytically pure form.

6. General procedure B for osmium-catalysed oxidation of amino alcohols to amino ketones

A portion of potassium osmate $K_2[OsO_2(OH)_4]$ (0.02 mmol) is added to 10 mL of a mixture of distilled water and *tert*-butanol (1/1, v/v) and stirring is applied until complete dissolution of the solid. Chloramine-T or NMO (2.2 mmol) is added in one portion and the resulting solution is kept stirring at room temperature. The respective amino alcohol (1.0 mmol) is added to the reaction mixture and stirring is continued for a period between 8 and 48 h with TLC control. The reaction mixture is treated with an aqueous solution of sodium bissulphite and extracted three times with ethyl acetate. Drying of the organic phases over $MgSO_4$ and removal of the solvents under reduced pressure leaves an oily to solid residue, which is analysed by NMR. Purification by column chromatography (silica gel, hexanes/ethyl acetate, 4/1, v/v) gave the 2-amino ketones in analytically pure form.

7. General procedure C for osmium-catalysed oxidation of silyl enol ethers to amino ketones and hydroxy ketones

A portion of potassium osmate $K_2[OsO_2(OH)_4]$ (0.02 mmol) is added to 10 mL of a mixture of distilled water and *tert*-butanol (1/1, v/v) and stirring is applied until complete dissolution of the solid. Chloramine-T (3.0 mmol) is added in one portion and the resulting solution is kept stirring at room temperature. The respective silyl enol ether (1.0 mmol) is added to the reaction mixture and stirring is continued for a period between 1 and 2 h with TLC control. The reaction mixture is treated with an aqueous solution of sodium bissulphite and extracted three times with ethyl acetate. Drying of the organic phases over $MgSO_4$ and removal of the solvents under reduced pressure leaves an oily to solid residue, which is analysed by NMR. Purification by column chromatography (silica gel, hexanes/ethyl acetate, 5/1, v/v) gave the 2-amino ketones and 2-hydroxy ketones in analytically pure form.

8. 2-(*N*-Tosylamino)-1,2-diphenylethanone [27]

Synthesised from (*E*)-stilbene and chloramine-T according to the general procedure A.

Synthesised in enantiomerically pure form from (1*S*,2*S*)-1,2-diphenyl-2-tosylamino-ethanol and NMO according to the general procedure B.

^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 2.30$ (s, 3H), 5.99 (d, $J = 7.3$ Hz, 1H), 6.22 (d, $J = 7.3$ Hz, 1H), 7.06 (d, $J = 8.6$ Hz, 1H), 7.06 (d, $J = 8.5$ Hz, 1H), 7.14–7.19 (m, 5H), 7.30–7.39 (m, 2H), 7.47–7.55 (m, 3H), 7.79 (d, $J = 8.6$ Hz, 1H), 7.80 (d, $J = 8.5$ Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 21.35$, 61.70, 126.95, 128.12, 128.44, 128.66, 128.92, 129.06, 129.32, 133.86, 133.90,

135.71, 137.46, 143.09, 194.59. HRMS calcd for $C_{21}H_{19}NO_3S$: 365.1086. Found: 365.1088. HPLC: Chiralcel-OD, *n*-hexane/2-propanol, 95/5, 0.5 mL/min, retention times 49 and 64 min.

9. 2-(*N*-Phenylsulfonylamino)-1,2-diphenylethanone [38]

Synthesised from (*E*)-stilbene and chloramine-B according to the general procedure A. Synthesised in enantiomerically pure form from (1*S*,2*S*)-1,2-diphenyl-2-(phenylsulfonylamino)-ethanol and NMO according to the general procedure B.

^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 5.95$ (d, $J = 7.3$ Hz, 1H), 6.19 (d, $J = 7.3$ Hz, 1H), 7.07–7.09 (m, 5H), 7.15–7.22 (m, 2H), 7.24–7.32 (m, 3H), 7.38–7.45 (m, 1H), 7.54–7.58 (m, 2H), 7.71–7.75 (m, 2H). ^{1}H NMR (DMSO-d_6, 300 MHz): $\delta = 4.44$ (d, $J = 5.5$ Hz, 1H), 4.65 (d, $J = 5.5$ Hz, 1H), 6.99–7.14 (m, 10H), 7.21–7.36 (m, 2H), 7.42 (d, $J = 7.2$ Hz, 2H), 8.02 (d, $J = 8.7$ Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 61.79$, 126.85, 128.13, 128.70, 128.94, 129.08, 132.27, 133.95, 135.49, 140.51, 162.33, 194.38. ^{13}C NMR (CD_3OD, 75 MHz): $\delta = 65.98$, 78.11, 127.89, 128.00, 128.10, 128.48, 128.78, 128.87, 128.95, 129.58, 132.97, 139.99, 142.45, 142.58, 203.77. HRMS calcd for $C_{20}H_{17}NO_3S$: 351.0929. Found: 351.0940. HPLC: Chiralcel-OD, *n*-hexane/2-propanol, 95/5, 0.5 mL/min, retention times 56.3 and 72.7 min.

10. 2-(*N*-Mesylamino)-1,2-diphenylethanone

Synthesised from (*E*)-stilbene and chloramine-M according to the general procedure A.

^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 2.51$ (s, 3H), 5.93 (br d, $J = 6.1$ Hz, 1H), 6.05 (d, $J = 6.1$ Hz, 1H), 7.23-7.35 8 m, 7H), 7.44–7.48 (m, 1H), 7.85-7.87 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 42.29$, 62.14, 128.28, 128.82, 129.05, 129.16, 129.59, 133.68, 134.09, 136.23, 194.22. HRMS calcd for $C_{15}H_{15}NO_3S$: 289.0773. Found: 289.0778.

11. 2-(*N*-*tert*-Butylsulfonylamino)-1,2-diphenylethanone [39]

Synthesised from (*E*)-Stilbene and *N*-chloro *tert*-butylsulfonamide sodium salt [40] according to the general procedure A.

^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.24$ (s, 9H), 5.76 (br d, $J = 7.3$ Hz, 1H), 6.14 (d, $J = 7.3$ Hz, 1H), 7.28–7.37 (m, 8H), 7.90–7.93 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 23.89$, 59.83, 62.22, 127.60, 128.01, 128.53, 128.74, 128.97, 129.21, 133.85, 137.34, 195.64. HRMS calcd for $C_{18}H_{21}NO_3S$: 331.1242. Found: 331.1241.

12. 6-(*N*-Tosylamino)-decan-5-one [41,42]

Synthesised from (*E*)-5-decene and chloramine-T according to the general procedure A at 40 °C.

^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.79$ (*t*, $J = 7.1$ Hz, 3H), 0.83 (*t*, $J = 6.8$ hz, 3H), 1.05–1.11 (m, 1H), 1.18–1.33 (m, 8H), 1.70–1.73 (m, 1H), 2.14–2.19 (m, 1H), 2.28–2.30 (m, 1H), 2.40 (m, 3H), 3.82 (dd, $J = 7.3$, 4.3 Hz, 1H), 5.50 (d, $J = 7.6$ Hz, 1H), 2.27 (d, $J = 8.2$ Hz, 2H), 7.69 (d, $J = 8.2$ Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 13.55$, 13.68, 21.39, 21.94, 22.24, 25.37, 26.61, 32.03, 39.11, 61.25, 127.24, 129.57, 136.78, 143.46, 207.97. HRMS calcd for $C_{17}H_{27}NO_3S$: 325.1712. Found: 325.1724.

13. 1-Phenyl-2-(*N*-tosylamino)-propanone [43]

Synthesised from (*E*)-β-methyl styrene and chloramine-T according to the general procedure A. Synthesised in enantiomerically pure form from (1*S*,2*S*)-1-phenyl-2-tosylamino-propanol and NMO according to the general procedure B.

^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.32$ (d, $J = 7.2$ Hz, 3H), 2.24 (s, 3H), 4.86 (dq, $J = 7.2$, 7.5 Hz, 1H), 5.73 (d, $J = 7.5$ Hz, 1H), 7.09 (d, $J = 8.2$ Hz, 2H), 7.32–7.39 (m, 2H), 7.48–7.53 (m, 1H), 7.62 (d, $J = 8.2$ Hz, 2H), 7.66–7.71 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 21.02$, 21.36, 53.30, 127.02, 128.44, 128.80, 129.61, 133.41, 134.02, 137.12, 143.45, 198.07. HRMS calcd for $C_{16}H_{17}NO_3S$: 303.0929. Found: 303.0925. HPLC: Chiralcel-OD, *n*-hexane/2-propanol, 97/3, 0.5 mL/min, retention times 72 and 76.9 min.

14. 1-Phenyl-1-(tosylamino)-propan-2- one [43]

Synthesised in enantiomerically enriched form from (1*S*,2*S*)-1-phenyl-1-tosylamino-propan-2-ol and NMO according to the general procedure B. Purification of this compund was carried out by column chromatography on neutral alox under argon employing *n*-hexane/ethyl acette (1/1, v/v) as eluent.

^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 1.91$ (s, 3H), 2.27 (s, 3H), 4.97 (br s, 1H), 5.99 (d, $J = 5.4$Hz, 1H), 6.97–7.02 (m, 3H), 7.04–7.06 (m, 2H), 7.21 (d, $J = 8.2$ Hz, 2H), 7.74 (d, $J = 8.2$ Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 21.08$, 26.26, 66.34, 127.08, 128.36, 128.95, 135.37, 137.66, 143.57, 202.60. HPLC: Chiralcel-OD, *n*-hexane/2-propanol, 95/5, 0.5 mL/min, retention times 41.2 and 47.6 min.

15. 2-Methyl-1-phenyl-2-tosylamino-propanone [43]

Synthesised from 2-methyl-1-phenyl-2-tosylamino-propanol and chloramine-T according to the general procedure B.

^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.54$ (s, 6H), 2.33 (s, 3H), 5.60 (s, 1H), 7.17 (d, $J = 8.4$ Hz, 2H), 7.18–7.35 (m, 2H), 7.40–7.46 (m, 1H), 7.62 (d, $J = 8.4$ Hz, 2H), 7.74–7.77 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 21.46$, 26.67, 63.99, 126.95, 128.28, 128.95, 129.53, 132.09, 135.33, 139.81, 143.21, 201.60. HRMS calcd for $C_{17}H_{19}NO_3S$: 317.1086. Found: 317.1092.

16. 2-Tosylamino-acetophenone [44]

Synthesised from styrene and chloramine-T according to the general procedure A.

Synthesised from 1-phenyl-2-tosylamino-ethanol and chloramine-T according to the general procedure B.

^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 2.38$ (s, 3H), 4.46 (d, $J = 4.5$ Hz, 2H), 5.63 (br s, 1H), 7.27 (d, $J = 8.1$ Hz, 2H), 7.43–7.49 (m, 2H), 7.60–7.81 (m, 3H), 7.79 (d, $J = 8.1$ Hz, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz): $\delta = 21.50$, 48.64, 127.22, 128.89, 129.91, 133.76, 124.35, 136.24, 143.66, 192.48. HRMS calcd for $C_{15}H_{15}NO_3S$: 289.0773. Found: 289.0780.

17. 2-Tosylamino-α-tetralone [45]

Synthesised from *trans*-2-tosylamino-1,2,3,4-tetrahydronaphthol and chloramine-T according to the general procedure B. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.92$-2.08 (m, 1H), 2.32 (s, 3H), 2.66 (dddd, $J = 2.5$, 5.7, 8.3, 13.2 Hz, 1H), 2.86–3.02 (m, 2H), 3.78 (ddd, $J = 2.6$, 4.9, 13.8 Hz, 1H), 5.97 (d, $J = 2.6$ Hz, 1H), 7.12–7.24 (m, 2H), 7.28 (d, $J = 8.3$ Hz, 2H), 7.42 (dt, 1.5, 7.5 Hz, 1H), 7.72 (d, $J = 8.3$ Hz, 2H), 7.86 (dd, $J = 1.1$, 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 21.46$, 28.09, 31.84, 59.09, 126.87, 127.17, 127.83, 128.91, 129.79, 130.61, 134.40, 136.28, 143.66, 143.81, 193.78. HRMS calcd for $C_{17}H_{17}NO_3S$: 315.0929. Found: 315.0930.

18. 2-Tosylamino-cyclohexanone [44,46]

Synthesised from 2-tosylamino-cyclohexanol and chloramine-T according to the general procedure B. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.44$-1.73 (m, 3H), 1.83–1.88 (m, 1H), 2.05–2.09 (m, 1H), 2.21 (dt, $J = 1.1$, 10.4 Hz, 1H), 2.40 (s, 3H), 2.42–2.53 (m, 2H), 3.77 (m, 1H), 5.76 (br d, $J = 4.6$ Hz, 1H), 7.28 (d, $J = 8.3$ Hz, 2H), 7.70 (d, $J = 8.3$ Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 21.38$, 23.89, 27.44, 36.92, 40.55, 60.63, 127.1, 129.69, 137.04, 143.47, 205.58. HRMS calcd for $C_{13}H_{17}NO_3S$: 267.0929. Found: 267.0938.

19. 2-Hydroxy-acetophenon

Synthesised from silylenol ethers **11a–c** and chloramine-T according to the general procedure C. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 4.40$ (s, 2H), 7.33–7.64 (m, 3H), 7.87-8.01 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 56.44$, 128.66, 129.06, 129.27, 135.10, 192.18.

20. 2-Hydroxy-propiophenone [47]

Synthesised from silylenol ether **13** and chloramine-T according to the general procedure C. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.41$ (d, J = 6.0 Hz, 3H), 3.82 (br s, 1H), 5.01 (q, J = 6.0 Hz, 1H), 7.36–7.62 (m, 3H), 7.85-7.93 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 22.01$, 69.17, 128.31, 128.72, 129.22, 134.27, 201.63. HRMS calcd for $C_9H_{10}O_2$: 150.0681. Found: 150.0688.

21. 2-Hydroxy-α-tetralone [48]

Synthesised from silylenol ether **15** and chloramine-T according to the general procedure C. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.88$-2.09 (m, 2H), 2.79–3.02 (m, 2H), 4.22 (dd, $J = 6$, 13 Hz, 1H), 7.10–7.28 (m, 2H), 7.39-7.45 (m, 1H), 7.92–8.03 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 27.77$, 31.91, 73.90, 126.92, 127.60, 128.92, 134.16, 144.34, 199.61. HRMS calcd for $C_{10}H_{10}O_2$: 162.0681. Found: 162.0690.

22. 2-Hydroxy-2-methyl-1-phenylpropanone [49]

Synthesised from silylenol ether **17** and chloramine-T according to the general procedure C. ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.57$ (s, 6H), 3.99 (br s, 1H), 7.37-7.61 (m, 3H), 7.88–7.96 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 28.43$, 76.33, 128.46, 129.63, 132.93, 163.22, 204.98. HRMS calcd for $C_{10}H_{12}O_2$: 164.0837. Found: 164.0840.

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