Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. *82* (6) 627–640 (2017)
JSCS–4992
UDC 546.96–31+542.943:547.239.2–304.2:547.415.3+542.96
Original scientific paper

RuO_4-mediated oxidation of secondary amines. 2. Imines as main reaction intermediates

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(Received 14 September 2016, revised 4 April, accepted 24 April 2017)

Abstract: Oxidation by RuO_4 (generated *in situ* from RuO_2 and $NaIO_4$) of secondary amines such as Bn–NH–CH_2R (**1**; R=H, Me) gave complex reaction mixtures, but mainly amides. In the presence of cyanide, the leading products were α-aminonitriles. Comparison of the oxidation products of **1** with those from the corresponding imines PhCH=N–CH_2R and Bn–N=CH–R showed that formation of the indicated imines is the first main step in the oxidation of **1**. A detailed mechanism is proposed.

Keywords: oxidation; secondary amines; ruthenium tetraoxide; imines; *α*-aminonitriles.

INTRODUCTION

Several mechanisms for the oxidation of alkanes,[1] arenes,[1] olefins,[2] alcohols[3] and amines[3–6] using various ruthenium-containing catalysts are known, but they refer to totally different substrates and/or oxidants than those used in the present study. Mechanisms for the oxidation of alkanes,[7,8] alkenes,[9] alcohols,[10] ethers[7] and tertiary amines[11–15] with RuO_4 as an oxidant[16] were previously proposed. For instance, it was advanced that *N*,*N*-dialkylanilines are oxidized by $RuCl_3/O_2$/NaCN (*i.e.*, *in situ* generated RuO_4) *via* iminium cations, formed through single electron transfer (SET) steps.[11] Independently, iminium ions were also proposed as key intermediates for the RuO_4-oxidation of tertiary aliphatic amines.[13–15] In all these cases,[11–15] the transient existence of iminium ions was proved by cyanide-trapping to give *α*-aminonitriles (Strecker reaction).

Information on the corresponding oxidation of secondary amines refers to lower-than-eight-valent ruthenium catalysts, from Ru^0 to Ru^{VII}.[17–23] The formation of imines seems to be favoured in all these cases. Imines are presumed to

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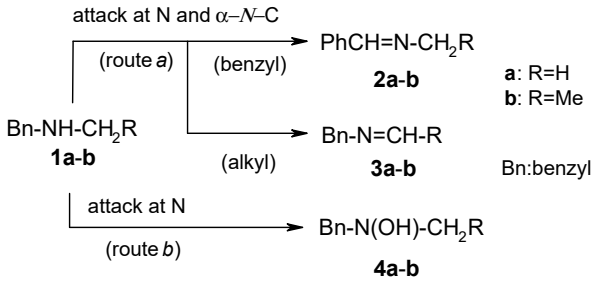
https://doi.org/10.2298/JSC160914055F

result also from secondary amines and RuO_4, a hypothesis[16] advanced in 2005, but still not experimentally demonstrated. It must be added here that imines are versatile intermediates, widely used in well-known reactions, such as aza-Baylis–Hillman,[24] aza-Diels–Alder,[25] Mannich[26] and Strecker reactions.[11,12]

As presented in a preceding paper,[27] the RuO_4-mediated oxidation of secondary aliphatic amines, such *N*-methyl- (**1a**) or *N*-ethylbenzylamine (**1b**) might start with the formation of imines **2a** and **b** plus **3a** and **b** (route a, Scheme 1) and/or *N*-hydroxylamines **4a** and **b** (route b). Imines would result *via* a formal dehydrogenation from the *N* atom and the adjacent *C* atom (benzyl for **2**, alkyl for **3**), but hydroxylamines would derive from an oxidative attack on the *N* atom. Comparison of the reaction products formed from **1** with those derived from **4** allowed the elimination route b as a main pathway.[27] Consequently, this paper analyzes route a as the mechanistic choice. By analogy with the previously discussed case of tertiary amines,[11–15] the intermediacy of imines will be proved by cyano-trapping reactions.



Scheme 1. Oxidative routes for **1a** and **b**.

EXPERIMENTAL

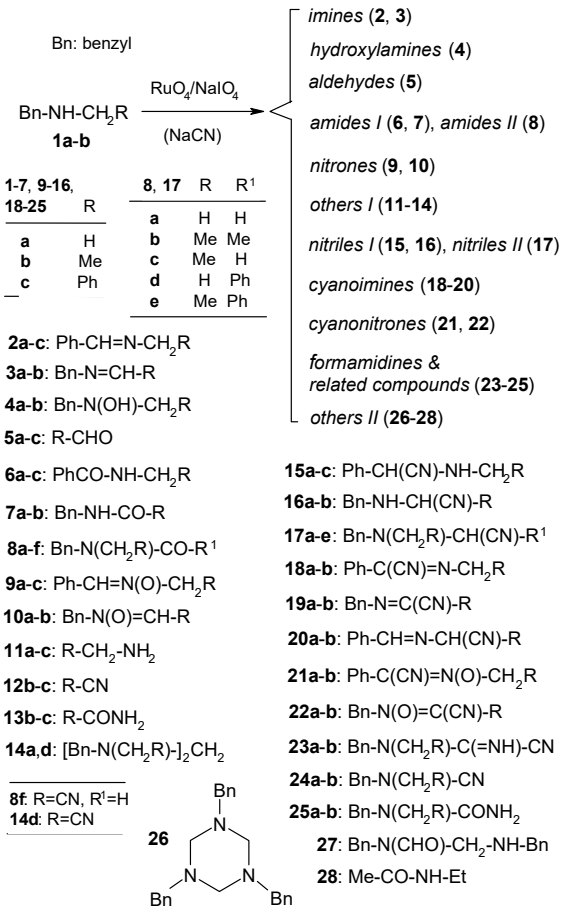
Instrumentation

Melting points were taken with a Boetius hot plate and are uncorrected. FT-IR spectra were registered on a Bruker Vertex 70 instrument, equipped with a diamond crystal ATR accessory. NMR spectra were recorded with a Varian Unity INOVA 400 spectrometer, operating at 400 MHz (^{1}H) and 100 MHz (^{13}C). Mass spectra were obtained with a GC 6890 Agilent Technologies gas chromatograph coupled with a MS 5975 B quadrupole mass spectrometer, using standard 70 eV ionization energy.

Materials

Hydrated RuO_2 (Aldrich), $NaIO_4$ (Merck), and the organic solvents (Chemical Co., Iaşi, Romania) were used as purchased, except for $CHCl_3$, which was stored over anhydrous Na_2CO_3 and filtered prior to use.

The formulae of all substrates and identified reaction products (**1**–**28**) are given in Scheme 2. Compounds **1**–**25** were practically identical to those with the same numbers in Part 1 of this work,[27] except for the newly added compounds **8f** and **14d**. The origin and spectral characteristics (^{1}H-NMR, ^{13}C-NMR and MS) of compounds **1**, **2** and **4**–**25** (except those of **8f** and **14d**) were previously presented.[27]



Scheme 2. Oxidation products of **1a**–**b**.

Derivatives **3b**,[28] **8f**,[29] **26**[30,31] and **27**[32] are all known from the literature and were prepared according to the indicated procedures. Compound **28** was purchased from Aldrich. The NMR and MS data for **3b**, **8f**, **14d** and **26**–**28** are presented as Supplementary material to this paper. Compound **14d** was described either as a solid (m.p., 62–64 °C)[33] or as an oil,[34] but the reported NMR characteristics were quite similar. A new, simpler method of preparation of **14d** (obtained as a solid) is proposed in the Supplementary material.

Oxidations by RuO_4/$NaIO_4$ (with or without NaCN)

All oxidations were performed as described in Part 1, including the identification and quantification of reaction products by NMR and GC–MS analyses of the various reaction mixtures.[27]

RESULTS AND DISCUSSION

The oxidations were performed either in the absence of cyanide (A-conditions) or in its presence (B-conditions); the respective results are presented in

Table I. To gain in simplicity, the desired entries (*x* and *y*) of Table I are cited as T-*x*,*y*. The yield of benzaldehyde (**5c**) from Table I actually refers to that of the sum **5c**+benzoic acid, since benzoic acid is always derived from **5c**.[27]

TABLE I. Oxidation of selected compounds

Entry No.	Compound (conversion, %)[a]	Reaction products[b] (yield[c], %)
	A) Oxidations in the absence of cyanide[d]	
1.	**1a** (55)[e]	**2a** (2.2), **2c** (8.6), **4a** (0.2), **5c** (8.0), **6a** (2.2), **6c** (1.8), **7a** (3.8), **8a** (30.0), **8d** (7.4), **9a** (2.4), **12c** (2.0), **13c** (0.6), **14a** (1.3)
2.	**1b** (81)[e]	**2b** (2.1), **2c** (4.1), **5c** (34.3), **6b** (3.9), **6c** (3.1), **7a** (1.7), **7b** (4.1), **8b** (3.5), **8c** (15.2), **8e** (3.8), **9b** (0.3), **12c** (7.4), **13c** (0.5)
3.	**11c** (100)	**2c** (36.1), **5c** (9.8), **6c** (0.2), **12c** (11.7), **13c** (4.7)
4.	**2a** (100)	**5c** (80.0), **6a** (18.5)
5.	**2b** (98)	**5c** (88.4), **6b** (9.7)
6.	**26** (80)	**2c** (8.7), **5c** (2.4), **7a** (3.5), **12c** (0.9), **13c** (1.5), **27** (65.5)
7.	**3b** (100)	**5c** (16.6), **6c** (1.2), **7a** (34.1), **7b** (5.9), **12c** (16.1), **13c** (0.3)
8.	**11c**+**11b**[f] (99)	**2b** (4.9), **2c** (9.4), **3b** (2.5), **5c** (1.8), **6b** (1.8), **6c** (0.7), **7a** (7.6), **7b** (9.1), **12c** (38.0), **13c** (8.0), **28** (2.1)
9.	**1b**+**11b**[g] (87)	**2b** (2.2), **2c** (3.2), **5c** (23.2), **6b** (3.8), **6c** (2.2), **7a** (1.0), **7b** (2.5), **8b** (6.1), **8c** (32.5), **8e** (2.6), **9b** (0.2), **12c** (5.4), **13c** (0.3)
	B) Oxidations in the presence of cyanide[d]	
10.	**1a** (13)[e]	**2c** (1.2), **5c** (0.9), **6a** (0.4), **7a** (0.7), **8a** (1.8), **8d** (8.9), **11c** (2.5), **12c** (0.9), **15a** (6.3), **16a** (2.2), **17a** (18.2), **17d** (15.3), **18a** (0.6), **20a** (0.3), **21a** (0.4), **22a** (0.8), **23a** (2.9), **24a** (1.0), **25a** (4.5)
11.	**1b** (37)[e]	**2b** (5.2), **2c** (1.8), **5c** (0.5), **6b** (0.5), **7b** (0.6), **8b** (1.0), **8c** (0.6), **8e** (2.7), **9b** (7.8), **12c** (1.5), **15b** (15.6), **16b** (10.9), **17b** (9.9), **17c** (1.0), **17e** (8.1), **18b** (0.8), **20b** (0.5), **21b** (0.5), **22b** (0.9), **23b** (4.2), **24b** (0.9), **25b** (8.0)
12.	**11c** (100)	**2c** (6.5), **6c** (0.4), **12c** (11.2), **15c** (36.5)
13.	**2a** (97)	**5c** (4.3), **6a** (0.5), **15a** (84.9), **18a** (0.4), **21a** (1.5)
14.	**2b** (98)	**5c** (2.3), **6b** (0.6), **15b** (84.5), **18b** (1.8), **21b** (1.1)
15.	**3b** (100)	**7b** (0.7), **12c** (1.2), **15c** (5.0), **16b** (75.3), **20b** (0.8), **22b** (1.2)
16.	**15b** (10)	**2b** (14.3), **5c** (21.3), **18b** (34.2), **21b** (18.0)
17.	**16a** (23)	**5c** (3.6), **6c** (2.2), **8f** (1.5), **12c** (1.5), **14d** (7.6), **15c** (26.2), **20a** (3.9), **22a** (9.6)
18.	**16b** (25)	**5c** (5.2), **6c** (1.9), **12c** (1.3), **13c** (0.5), **15c** (19.0), **19b** (4.2), **20b** (8.5), **22b** (15.3)

[a]Calculated against the reacted substrate; [b]formulae in Scheme 2; [c]yields (mole ratios of product/reacted substrate) are calculated regardless of the stoichiometry (excepting those of entry 7); [d]reaction conditions (for 1 mmol of substrate): A – $RuO_2 \cdot xH_2O$ (10–15 mg), co-oxidant $NaIO_4$ (4 mmol), 20 mL $CHCl_3$/water = 1/1 volume ratio, room temperature, 3–5 h; B – as in A, but NaCN (4 mmol) in water (10 mL) was also added; [e] data from ref. 1; [f]**11c**/**11b** = 1/1 mole ratio. Conversion and yields are referred to **11c**; [g]**1b**/**11b** = 1/0.4 mole ratio. Conversion and yields are referred to **1b**

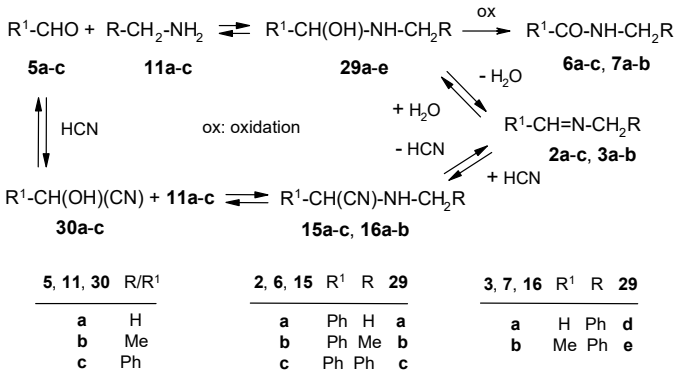
*Oxidation of amines **1a** and **b**. Reaction products*

The oxidation mixtures derived from **1a** and **b** under A-conditions (T-1,2) were quite complex and contained imines (**2**), hydroxylamines (only **4a** was det-

ected), aldehydes (**5c**), amides (**6**–**8**), nitrones (**9**), benzonitrile (**12c**), benzamide (**13c**), and diamine **14a** (from **1a** only). When performed under B-conditions (T-10,11), besides some of the previously cited compounds, benzylamine (**11c**, from **1a** only), *α*-aminonitriles (**15**–**17**), cyanoimines (**18**–**20**), cyanonitrones (**21** and **22**), and derivatives **23**–**25** were also obtained. As already presented,[35] the formamidines **23** and their hydrolysis products **24** and **25** prevail in more acid conditions, but their formation does not involve the oxidation of **1**. Consequently, they do not belong in the present discussion.

The steps in Scheme 3 can be invoked to show how amides I (**6** and **7**) and nitriles I (**15** and **16**) of Scheme 2 are formed. For instance, the condensation of benzaldehyde (**5c**) with benzylamine (**11c**) affords the hemi-aminal **29c**. This intermediate can give benzamide **6c** (by oxidation) and/or imine **2c** (by dehydration). Under B-conditions, most of the benzaldehyde should exist as its cyanohydrin **30c**. Condensation between **30c** and **11c** yields the cyanoderivative **15c**. Some of **15c** could give imine **2c**, by dehydrocyanation.

The origins of **8a**–**e**, **9a** and **b**, **10a** and **b**, as well as those of **17a**–**e** were discussed in Part 1.[27] Briefly, the oxidation of hydroxylamines **4a** and **4b** give nitrones **9a**+**10a** and **9b**+**10b**, respectively. Compounds **10** are less stable than **9** and this could explain the absence of **10a** and **b** in T-10,11. At the same time, amides **8** and nitriles **17** (amides II and nitriles II in Scheme 2, respectively) come from a two-step sequence, similar to that presented in Scheme 3: *i*) the condensation of **1a** and **b** with aldehydes **5a**–**c** affords hemi-aminals, which *ii*) are oxidized towards **8**. Analogously, nitriles **17** result from **1a** and **b** and cyanohydrins **30a**–**c**. Since hemi-aminals and **17a**–**e** do not contain a NH group, the formation of imines by dehydration/dehydrocyanation is no longer possible in these cases.



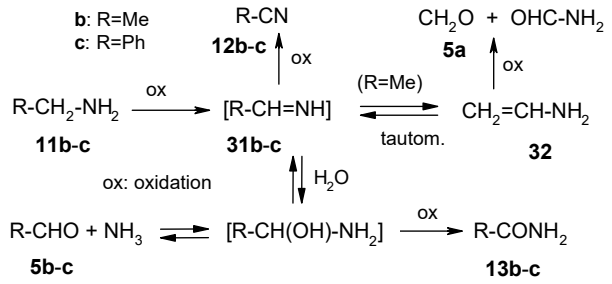
Scheme 3. Formation of amides I (**6** and **7**) and nitriles I (**15** and **16**).

Benzylamine (**11c**) was detected in one reaction mixture (T-10), but its transient formation should occur in all oxidations of **1a** and **b**, in order to explain

the formation of **2c** and **6c**. The existence of **12c**, **13c**, and **5c** (partially) in the oxidation mixtures derived from **1a** and **b** can be explained by the oxidation of **11c** itself, as detailed below.

*Oxidation of benzylamine (**11c**)*

It is well established[18,36–39] that a primary amine, such as **11c**, undergoes oxidation with ruthenium catalysts towards the corresponding nitrile and amide. This was verified with RuO_4 and the respective results (T-3,12) were interpreted as shown in Scheme 4.



Scheme 4. Oxidation of primary amines **11b** and **c**.

The first oxidation step gives the aldimine **31c**, which can be dehydrogenated further to **12c**, but which can also be trapped by water to yield the corresponding hemi-aminal. In turn, this last intermediate can undergo both oxidation to benzamide (**13c**) and splitting to a mixture of benzaldehyde (**5c**) and ammonia.

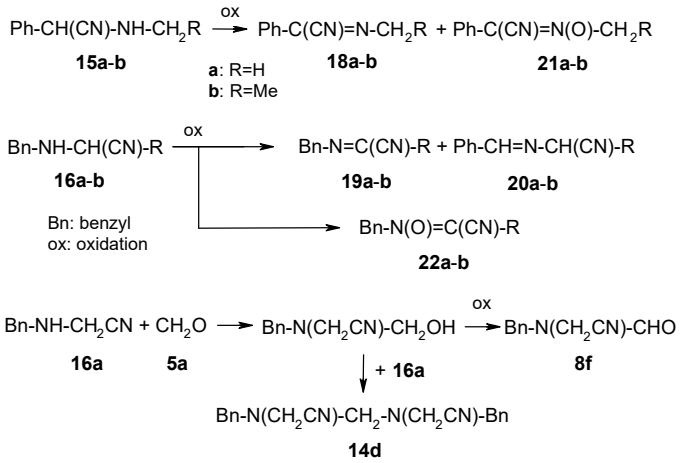
Formation of **2c**, **6c** and **15c** was outlined in the preceding paragraph (Scheme 3).

*Oxidation of imines **2** and **3***

In the absence of cyanide, imines **2a** and **2b** underwent clean transformation into mixtures of **5c**+**6a** and **5c**+**6b**, respectively (T-4,5), where benzaldehyde (**5c**) represented at least 80% of the reacted substrate. Clearly, as depicted in Scheme 3, hemi-aminals **29a** and **b**, transiently formed from water and the respective imine, are oxidized towards the corresponding benzamides **6a** and **b**, but largely split into equimolar mixtures of **5c** and **11a** and **b**. All these reactions are nucleophilic in nature, except for the oxidation step leading to **6a** and **b**.

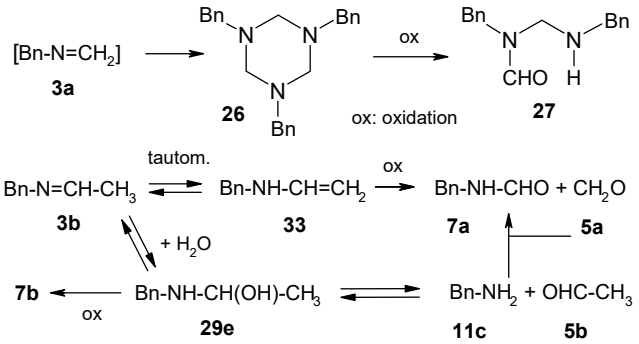
In the presence of cyanide, about 85 % of reacted **2a** and **b** were found as the corresponding nitriles **15a** and **b** (T-13,14), formed by a non-oxidative step, the nucleophilic addition of HCN to the C=N double bond (Scheme 3); the equilibria are largely shifted towards **15**, despite the presumably low amount of available HCN in the reaction at pH around 9. The oxidation of **15a** and **15b** can be invoked instead to explain the formation of **18a**+**21a** and **18b**+**21b**, respectively

(Scheme 5). This is supported by the oxidation of **15b** alone (T-16), where **18b**+**21b** account for about 50 % of the reacted substrate. Aminonitrile **15a** behaved similarly.



Scheme 5. Some oxidation products of α-aminonitriles **15** and **16**.

Unfortunately, imine **3a** is only known as its cyclic "trimer", the *sym*-triazacyclohexane derivative **26** (Scheme 6).30,31 When submitted to A-oxidation, its major reaction product was **27** (corrected yield 65 % in T-6). Although **26** and/or **27** were not observed in the oxidation mixture of **1a** (T-1), the transient formation of **3a** could not be excluded (see below).



Scheme 6. Different behaviour of imines **3a** and **3b**.

Unlike **3a**, the analogous imine **3b** could be isolated.[28] Despite its poor stability, it was possible to study its oxidation reaction (T-7; Scheme 6). With one notable exception (**7a**), the steps of Scheme 3 (re-written in Scheme 6, for clarity) are followed. For instance, the hemi-aminal **29e**, the water adduct of **3b**,

undergoes oxidation to acetamide **7b**, but also breaks into a **11c**+**5b** mixture.[14,15] Subsequent reactions of benzylamine (**11c**) are responsible for the presence of **5c**, **6c**, **12c** and **13c**, as presented before.

A possible explanation for the formation of **7a**, the major oxidation product of **3b**, is shown in Scheme 6. Imine **3b** has *β-N*–H protons and, by analogy with some preceding papers,[14–16] this enables tautomerization to enamine **33**. Oxidation of the C=C bond[14,15,34–43] in **33** should give a **7a**+**5a** equimolar mixture. When formed, **5a** could give additional **7a** through the sequence **5a** + **11c** → **29d** → **7a** (Scheme 3).

Under B-conditions (T-15), imine **3b** (and/or its tautomer **33**) gave the expected HCN-adduct **16b** (Scheme 3; Strecker reaction), accompanied by small amounts of **20b** and **22b**. Nitrile **15c** was also present, indicating that the following consecutive steps occurred: *i*) hydrolysis of **3b** to **11c**, *ii*) formation of **5c** by oxidation of **11c**, *iii*) transformation of **5c** into cyanohydrin **30c** in the presence of cyanide and *iv*) condensation of **30c** with **11c** to yield **15c** (Scheme 3). Cyano compounds **19b**, **20b** and **22b** are all oxidation products of **16b** (T-18; Scheme 5). The lack of **19b** in entry 15 might be due to its relatively low amount.

Nitrile **16a** (T-17) behaved similarly to **16b** (T-18), but with a few exceptions. Thus, cyanoimine **19a** is absent in T-17 probably because of increased instability or of its insufficient amount, below the detectable limit, while compounds **8f** and **14d**, formed from **16a**, have no analogues in the oxidation of **16b**. Their formation is elucidated in Scheme 5: condensation of **16a** with formaldehyde (**5a**; formed from the oxidation of **16a** itself) gives a hemi-aminal, which can not only undergo oxidation to **8f**, but can also react with **16a** to give **14d**. All these steps are identical to those forming **14a** during the oxidation of **1a** (T-1).[27]

*Oxidation of **1a** and **b**. Mechanistic considerations*

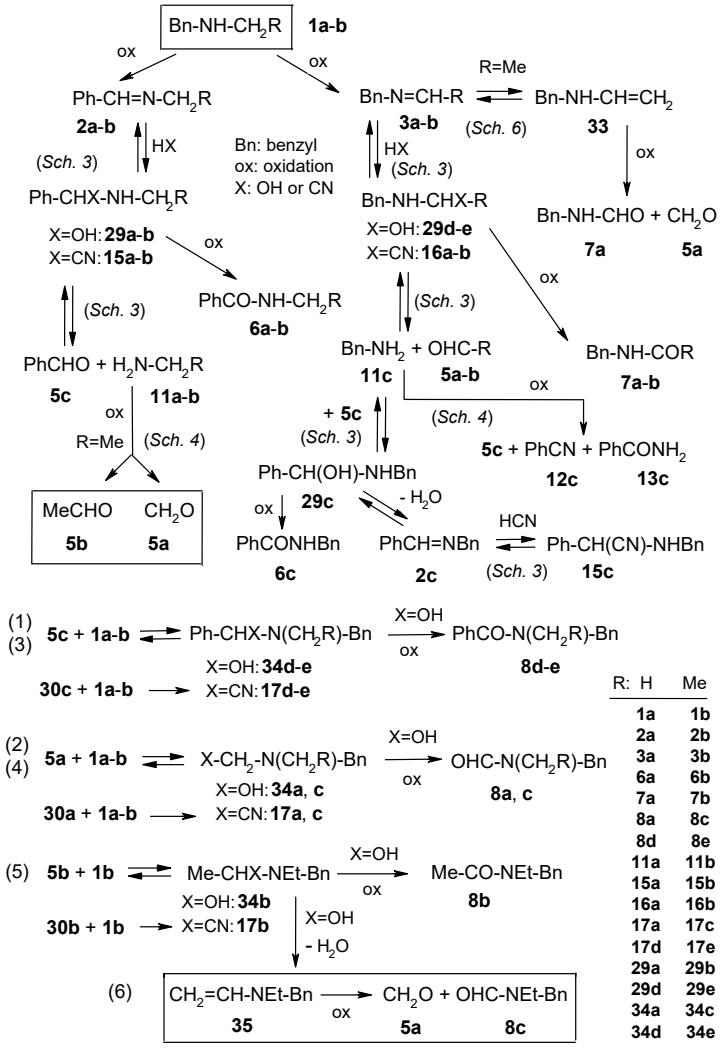
It is now possible to compare the oxidative results of **1** with those of **2**+**3**. Similarly to the comparison made above with the outputs derived from **4a**+**4b**,[27] no attention will be paid this time to the presence of amides **8a**–**e** and nitriles **17a**–**e**. Their formation requires the presence of **1a** and **b**, but these amines are absent when the reaction starts from imines **2** or **3**.

Comparing the results of the oxidation of **1b** (T-2,11) with those of **2b**+**3b** (T-5,14 + T-7,15), it could be observed that all compounds formed in the first case exist within the reaction products of one or the other imine. Unfortunately, a similar comparison cannot be made for **1a** *vs.* **2a**+**3a**, because of the lack of the data for **3a**. However, the transient existence of **3a** could be assumed. For example, the formation of **16a** under B-conditions (T-10) implies reaction **3a** + + HCN → **16a** (Scheme 3).

These considerations suggest that the main route followed during the RuO_4--mediated oxidation of amines **1a** and **1b** implies the initial formation of the cor-

responding imines **2a**+**3a** and **2b**+**3b**, respectively (Scheme 1, route a). The alternative route b involving the hydroxylamines **4a** and **4b** has only a minor contribution to the final results.[27]

All information presented before (Schemes 1–6) is summarized in Scheme 7, but some reactions and/or compounds have been omitted, for the sake of clarity. This is the case of the transformations **1a**→**14a**[27] and **1**+$(CN)_2$→**23**→**24**+**25**,[35] as well as of the subsequent oxidations of **15** (→**18**+**21**; T-16) and **16** (→**15**+**19**+**20**+**22**; T-17,18). At the same time, the sequence **1**→**4**→**9**+**10** is also missing, because it plays a minor role in the global picture.[27]



Scheme 7. Mechanism of the oxidation of secondary amines **1a** and **b**.

Oxidation of secondary amines **1a** and **1b** starts with the formation of imines **2a**+**3a** and **2b**+**3b**, respectively, by a formal dehydrogenation from the nitrogen atom and its adjacent C atom. Every imine can suffer nucleophilic addition at the C=N double bond, as detailed in Scheme 3. In the absence of cyanide, the addition of water yields the corresponding pairs of hemi-aminals **29a**+**29d** and **29b**+**29e**. In the presence of cyanide, both water and hydrocyanic acid act as nucleophiles. In this case, together with the cited hemi-aminals, the corresponding α-aminonitriles **15a**+**16a** and **15b**+**16b** are formed (Strecker reaction).

Hemi-aminals can be either oxidized to yield amides (**6a**+**7a** or **6b**+**7b**) or split into aldehyde + primary amine mixtures. In the later case, **29a** gives benzaldehyde + methylamine (**5c**+**11a**) and **29d** yields formaldehyde + benzylamine (**5a**+**11c**). Analogously, **5c** and ethylamine (**11b**) result from **29b**, while acetaldehyde (**5b**) and **11c** are obtained from **29e**.

Imine **3b**, through its tautomer **33**, could be the source of the benzylformamide (**7a**)+**5a** equimolar mixture (Scheme 6). Under A-conditions, this is the main reaction if the oxidation starts from **3b** (T-7). Starting from **1b**, this route to **5a** plays a minor role, as indicated by the relatively small amount of **7a** (1.7 % in T-2).

Except for amides **6** and **7** (**6a**+**7a** from **1a** and **6b**+**7a**+**7b** from **1b**), all other compounds formed until now are involved in subsequent reactions. On one hand, the resulting aldehydes can react with the available amines (primary or secondary) and, on the other hand, the primary amines themselves can be further oxidized. For example, benzylamine (**11c**) is oxidized to benzonitrile (**12c**), benzamide (**13c**) and benzaldehyde (**5c**) (Scheme 4). It reacts easily with **5c** to yield benzamide **6c** and imine **2c** through the intermediacy of **29c**. If hydrocyanic acid is present, the nitrile **15c** also results.

As aforementioned for **5c**+**11c**, aldehydes **5a**–**c** can react, at least in principle, with all available primary (**11a**–**c**) and secondary amines (especially **1a** and **b**). Actually, as indicated by the presence of compounds such as **8a**–**e** or **17a**–**e** in Table I, the condensations with **1a** and **b** seem to be more fruitful, probably because **1a** and **b** are always in excess with respect to **11a**–**c**. Consequently, the sequences 1–5 could be written (see the lower part of Scheme 7). More specifically, under A-conditions, the sequences 1 (**5c**+**1a**→**34d**→**8d**) and 2 (**5a**+**1a**→ →**34a**→**8a**) are active during the oxidation of **1a**, but 3 (**5c**+**1b**→**34e**→**8e**), 4 (**5a**+**1b**→**34c**→**8c**) and 5 (**5b**+**1b**→**34b**→**8b**) in the case of **1b**. Under B-conditions, all aldehydes **5a**–**c** are present as their cyanohydrins **30a**–**c** and the sequences 1–5 must be re-written with nitriles **17a**–**e** (as the final products) instead of hemi-aminals **34a**–**e**.

Some contradictions arise in the case of **1b**. According to the steps of Scheme 7 hitherto discussed, **5a** is generated from **33** and used (totally or partially) in sequence 4 to give formamide **8c**; at the same time, **5b** results from **29e**

and it is used (totally or partially) in sequence 5 to obtain acetamide **8b**. However, the relatively high amount of **8c** (15.2 % in T-2) cannot originate only from the small amount of **5a** (1.7 %, identical to **7a**) generated from **33**. Moreover, when derived from **29e**, the amount of **5b** should be the same as that of the initially formed **11c** (written as $\mathbf{11c_i}$). Taking into account that $\mathbf{11c_i}$ = **2c**+**6c**+ +**12c**+**13c**+$\mathbf{5c_{11c}}$, where $\mathbf{5c_{11c}}$ means that **5c** was generated from **11c** (Scheme 4) and using the values listed in T-2, it can be calculated that **5b** = $\mathbf{11c_i}$ = 15.1+ +$\mathbf{5c_{11c}}$. Unfortunately, the amount of $\mathbf{5c_{11c}}$ cannot be known because benzaldehyde (**5c**) results not only from **11c**, but also from imine **2b**. However, even the lower limit of **5b** (15.1 %) seems to be higher than that required in sequence 5 to produce **8b** (3.5 %). These considerations suggest that the aforementioned steps of Scheme 7 are incomplete: the apparent deficit of **5a** and excess of **5b** deserve an explanation.

To solve this problem, the sequence 5 was completed with the new sequence 6 (presented as a frame in the lower part of Scheme 7). Unlike **34c** or **34e**, hemi--aminal **34b** has a (*β*-O–)C–H bond and this renders possible the dehydration to **35**. Oxidation of the C=C bond in **35** should give an equimolar mixture of formaldehyde (**5a**) and formamide **8c**. Since this extra amount of **5a** will generate more **8c** through sequence 4, the total amount of **8c** becomes even higher.

It is conceivable that **5a** and **5b** could also be supplied by an auxiliary source, namely the oxidation of ethylamine (**11b**, frame in Scheme 7). It is necessary to remember that, during the oxidation of **1b**, amine **11b** results from **29b**→**5c**+**11b**. Analogously to the described behaviour of **11c**, the primary amine **11b** could be oxidized into acetonitrile (**12b**), acetamide (**13b**), and acetaldehyde (**5b**) (Scheme 4). Moreover, since the intermediate **31b** has *β*-*N*-protons, tautomerization to **32** is possible, just as in the aforementioned sequence **3b**→**33**. Oxidation of **32** leaves **5a**. Therefore, both aldehydes **5a** and **5b** are generated from **11b**. Experimental proof of these suppositions came from the oxidation of an equimolar mixture of **11c** and **11b** (T-8). Unlike the oxidation of **11c** alone (T-3), compounds **2b** and **6b**, as well as **3b**, **7a**, **7b** and **28** were detected in this case. Derivatives **2b** and **6b** resulted from the sequence **5c**+**11b**→**29b**→**2b**+**6b** (Scheme 3), where here **5c** came from the oxidation of **11c**. At the same time, it is clear that formaldehyde (**5a**) was trapped as **7a** (**11c**+**5a**→**7a**) and acetaldehyde (**5b**) as **3b**+**7b**+**28** (**11c**+**5b**→**3b**+**7b**; **11b**+**5b**→**28**).

The influence of the reaction **11b**→**5a**+**5b** on the oxidation of **1b** was tested by oxidizing a **1b**+**11b** mixture (T-9). With respect to the values in T-2, all yields in T-9 were smaller by a factor of 0.6–0.8 (mean value of 0.7), except for: *i*) those of **2b** and **6b**, which apparently remained constant and *ii*) the yields of **8b** and **8c**, which were about double. In reality, the values in T-9 are the sum of those derived from the oxidation of **1b** alone (the yields of T-2 multiplied by 0.7) and those attributable to the intervention of extra **11b** and its oxidation products.

Accordingly, the aforementioned two exceptions are actually enhancements due to the presence and oxidation of **11b**. The first cited exception is attributable to the sequence **5c**+**11b**→**29b**→**2b**+**6b**, where **11b** is that initially added and **5c** is an oxidation product of **1b**. This means that **2b** and **6b** came from two sources: the oxidation of **1b** and the aforementioned sequence. The second exception is due to the extra amounts of **5a** and **5b**, generated from the added **11b**, which give additional **8c** and **8b**, respectively, through the sequences 4–6 of Scheme 7.

Some comments are required for the reaction under B-conditions (T-11). All aldehydes are present only as their cyanohydrins and this favours nitrile formation. The new sequences 4 and 5 will be largely **30a**+**1b**→**17c** and **30b**+**1b**→ **17b**, respectively, and sequence 6 will have only a minor influence. For this reason, **8c** and **8b** are now present in such small amounts and **8c**/**8b** = 0.6 in T-11. When sequence 6 is active, **8c**/**8b** = 4.3 (T-2).

In preceding papers,[13–15] the oxidation regioselectivity (alkyl/benzyl) was calculated. Unfortunately, this was no longer possible for **1a** and **b**, because many reaction products originated from both types of initially formed imines (**2** and **3**). As outlined before, this is the case of **5a**–**c** and of all amides or nitriles resulting from them.

CONCLUSIONS

The RuO_4-mediated oxidation of secondary amines **1** generates in the first step imines as the main intermediates, by attack at both benzylic and alkylic *N*-α--sites. Reactions of imines with the available nucleophiles (water or hydrocyanic acid) explain the formation of *N*-monosubstituted amides (amides I) or *N*-monosubstituted α-aminonitriles (nitriles I), respectively. The oxidation output is complicated by subsequent reactions of these prime products giving, for example, *N*,*N*-disubstituted amides (amides II), *N*,*N*-disubstituted α-aminonitriles (nitriles II), and oxidation products of nitriles I. Since many reaction products result from two or more sources, it is impossible to calculate the reaction regioselectivity. Formation of all these compounds was rationalized and a complete reaction scheme was proposed and discussed.

SUPPLEMENTARY MATERIAL

Details on the preparation of **14d**, ^{1}H- and ^{13}C-NMR characteristics of **3b**, **8f**, **14d**, **26**–**28**, as well as MS data of **3b**, **8f** and **28** are available electronically at the pages of journal website: http://www.shd.org.rs/JSCS/, or from the corresponding author on request.

ИЗВОД

ОКСИДАЦИЈА СЕКУНДАРНИХ АМИНА ПОМОЋУ RuO_4. ДЕО 2. ИМИНИ КАО ГЛАВНИ РЕАКЦИОНИ ИНТЕРМЕДИЈЕРИ

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Оксидацијом секундарних амина, као што су Bn–NH–CH_2R (1; R=H, Me), помоћу RuO_4 (добијеном *in situ* из RuO_2 и $NaIO_4$) настаје сложена смеша производа коју углавном чине амиди. У присуству цијанида, главни производи реакције су α-аминонитрили. Поређењем структура производа оксидације **1** са производима оксидације одговарајућих имина PhCH=N–CH_2R и Bn–N=CH–R утврђено је да је формирање назначених имина први корак у оксидацији **1**. Предложен је детаљан механизам реакције.

(Примљено 14. септембра 2016, ревидирано 4. априла, прихваћено 24. априла 2017)

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