Letters to the Editor

Acid catalysis in the oxidative nucleophilic alkoxylation of 1,3,7-triazapyrenes

I. V. Borovlev, O. P. Demidov, and N. A. Saigakova*

Stavropol State University,
1a ul. Pushkina, 355009 Stavropol, Russian Federation.
Fax: +7 (865 2) 35 4033. E-mail: k-biochem-gcs@stavsu.ru

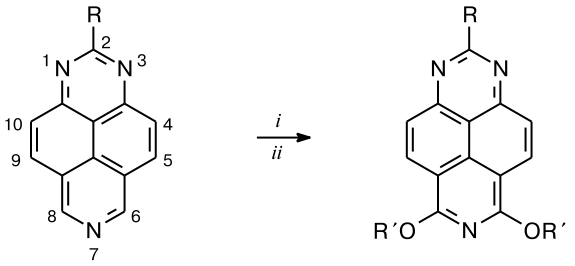
The classic approach to the synthesis of alkoxy derivatives of azaheterocycles is based on nucleophilic displacement of a good leaving group. In the case of electron-deficient nitrogen-containing hetarenes, direct oxidative nucleophilic substitution of an alkoxy group for hydrogen (ONSH)[1] may be a good alternative that avoids preliminary introduction of good nucleofuges into these substrates. However, only a few examples of successful ONSH-type alkoxylation of heterocycles have been documented.[2,3] For instance, we have recently discovered[3] that 1,3,7-triazapyrenes **1a**,**b** readily undergo dialkoxylation with primary alcohols in the system $ROH/H_2O/KOH/K_3Fe(CN)_6$ to give earlier unknown 6,8-dialkoxy-1,3,7-triazapyrenes **2a**—**d** (Scheme 1).

Our further investigations in this area unexpectedly revealed that 1,3,7-triazapyrenes **1a,b** can be easily alkoxylated with primary alcohols in acidic media as well. Room-temperature alkoxylation in anhydrous alcohol saturated with dry HCl in the presence of an excess of $K_3Fe(CN)_6$ yielded the same dialkoxy derivatives **2a**—**d**.

We are unaware of other examples of acid-catalyzed oxidative nucleophilic substitution of an alkoxy group for hydrogen.

Monoalkoxylation is not a final reaction step: even when the oxidant is deficient, the reaction gives products **2** with incomplete conversion of the starting triazapyrene (^{1}H NMR data).

Scheme 1



1a,b **2a—d**

1: R = H (**a**), Me (**b**)
2: R = H, R′ = Me (**a**); R = R′ = Me (**b**); R = H, R′ = Et (**c**); R = H, R′ = Pr (**d**)
i. R′OH, H_2O, KOH, $K_3Fe(CN)_6$ or *ii*. R′OH, HCl, $K_3Fe(CN)_6$

1,3,7-Triazapyrenes **1a**,**b** were prepared as described earlier.[4] The ^{1}H NMR spectra of compounds **2a**—**d** were recorded on a Bruker-250 spectrometer (250 MHz) in $CDCl_3$ with $SiMe_4$ as the internal standard and proved to be identical with the spectra of the samples obtained earlier[3] in a different way, the recording conditions being the same.

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Synthesis of 6,8-dialkoxy-1,3,7-triazapyrenes (general procedure). A mixture of compound **1a** or **1b** (1 mmol) and an appropriate anhydrous alcohol (40 mL) saturated with dry HCl was vigorously stirred at room temperature for 1 h. Throughout the reaction time, pulverized $K_3Fe(CN)_6$ (2 g, 6.1 mmol) was added in small portions. The reaction mixture was poured into water (50 mL) and alkalified with ammonia to a neutral reaction. The product was extracted with toluene (3×50 mL) and the extracts were concentrated. The yields of 6,8-dimethoxy-1,3,7-triazapyrene (**2a**), 6,8-dimethoxy-2-methyl-1,3,7-triazapyrene (**2b**), 6,8-diethoxy-1,3,7-triazapyrene (**2c**), and 6,8-dipropoxy-1,3,7-triazapyrene (**2d**) are 0.264 (90%), 0.246 (88%), 0.217 (74%), and 0.234 g (73%), respectively.

References

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