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Heterocyclic Rearrangements in Constrained Media. A Zeolite-Directed Photorearrangement of 1,2,4-Oxadiazoles

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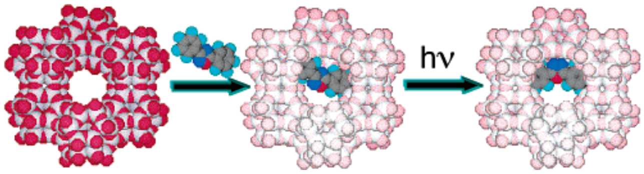
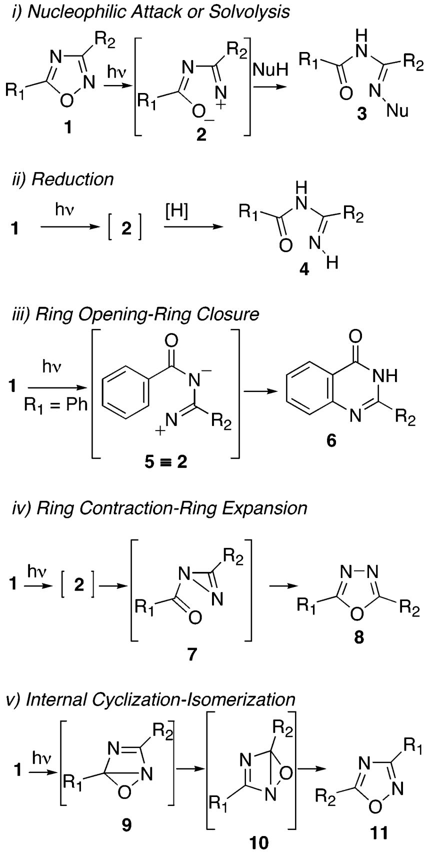


The first intrazeolite-photoinduced rearrangement of a five-membered heterocycle is reported. A completely different behavior compared to solution irradiations has been observed. The zeolite's role in directing the photoreaction of 3-phenyl-1,2,4-oxadiazoles toward the formation of the corresponding 1,3,4-oxadiazoles in a *ring contraction−ring expansion* route is discussed.

The study of organic transformations within constrained media is a research topic that has received considerable attention in recent years. In that regard zeolites represent ideal hosts with long-range order that can be used to perform chemical and photochemical[1] reactions. In fact, steric and electronic interactions between the reagents and the zeolite framework often influence the reaction pathways leading to new products or to different product distributions compared with the reaction in solution.[2]

We report here the first example of an intrazeolite photoinduced rearrangement of a five-membered heterocycle. This class of photoreaction in solution, embraces a large variety of ring-to-ring intramolecular transformations, involving several permutations[3] of the ring heteroatoms, which have been systematized as a function of the reaction patterns.[4]

SCHEME 1. Solution Photochemistry of 1,2,4-Oxadiazoles



Within the framework of our interest in heterocyclic rearrangements, we have previously studied the solution photochemistry of O−N bond containing azoles and demonstrated its dependence on the nature and position of substituents and on the identity of the photoreaction medium. Such azoles usually undergo photochemical cleavage of the O−N bond, producing intermediates that will subsequently develop into final products. In the case of 1,2,4-oxadiazoles this cleavage leads to well-established reaction pathways involving a zwitterion or nitrene-like photolytic species as depicted in Scheme 1.[5] In addition, for specific 1,2,4-oxadiazoles, under specific irradiation conditions, the *internal cyclization−isomerization* route has been also observed.[6]

The availability of these diverse pathways provide an exciting opportunity to investigate the effect of the zeolitic environment in directing the photochemical behavior of 1,2,4-oxadiazoles. In this paper we report a dramatic difference in the solution and intrazeolite photochemical behavior of 3-phenyl-1,2,4-oxadiazoles **12a**,**b**.

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(1) Dutta, P. K.; Kim, Y. *Curr. Opin. Solid State Mater. Sci.* **2003**, *7*, 483−490 and references therein.

(2) See among others: (a) Sen, S. E.; Smith, S. M.; Sullivan, K. A. *Tetrahedron* **1999**, *55*, 12657−12698. (b) Hashimoto, S. *J. Photochem. Photobiol. C* **2003**, *4*, 19−49.

(3) Pavlik, J. W.; Tongcharoensirikul, P. *J. Org. Chem.* **2000**, *65*, 3626−3632.

(4) Padwa, A. In *Rearrangements in Ground and Excited States*; P. De Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 3, pp 501−547.

(5) (a) Buscemi, S.; Cicero, M. G.; Vivona, N.; Caronna, T. *J. Heterocycl. Chem.* **1988**, *25*, 931−935. (b) Buscemi, S.; Pace, A.; Vivona, N.; Caronna, T. *J. Heterocycl. Chem.* **2001**, *38*, 777−780.

(6) (a) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N. *J. Org. Chem.* **2002**, *67*, 6253−6255. (b) Buscemi, S.; Pace, A.; Pibiri, I.; Vivona, N.; Caronna, T. *J. Fluorine Chem.* **2004**, *125*, 165−173.

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NaY was selected as the zeolite host for the reaction because its 7.4 Å pores and 13 Å diameter supercages can easily absorb and accommodate the nearly rod-shaped like **12** (long axis 12.5 Å; short axis 5 Å for representative **12a**).[7] Indeed, the zeolite samples **12**@NaY were readily prepared by intercalation of compounds **12** from petroleum ether into dry NaY to give a loading level of $\langle s \rangle = 1.0$ (molecules per supercage). The loading level of **12** was verified by UV analysis of the petroleum ether. The structural integrity of **12** in the interior of the zeolite was demonstrated by its successful extraction after being included in zeolite for 24 h in the dark. Moreover, fluorescence spectra of representative **12a** (indipendent from excitation and emission wavelengths) showed its characteristic 0−0 transition band which is bathochromically shifted by only 20 nm in comparison to methanol (see the Supporting Information).

Irradiation of a perfluorohexane slurry[8] of **12a**@NaY at 254 nm for 6 h followed by extractive removal of the products resulted in isolation of 2,5-diphenyl-1,3,4-oxadiazole (**16a**) (28%) together with *N*-benzoyl-*N′*-phenylurea (**17a**) (6%) and unreacted starting material (65%). In analogy, irradiation of **12b**@NaY produced **16b** (20%) and **17b** (2%), but no trace of the regioisomer **19** (Scheme 2) which could have been formed through an *internal cyclization−isomerization* route (not detectable with the symmetrically substituted **12a**, of course).

The formation of **16** and **17** is unprecedented in solution.[9] A previous photochemical study on **12a** in Et_2O resulted in formation of reduction product, **4** ($R_1 = R_2 =$ Ph) and 2-phenyl-4(3*H*)-quinazolinone (**6** $R_2 =$ Ph).[10] As a comparison, a new irradiation of **12a**,**b** (10 mg) in methanol (10 mL) for 1h at 254 nm resulted in the formation of the solvolysis products **18a**[9,11] (26%) and **18b** (9%) together with the unreacted **12a** (74%) and **12b** (88%). Moreover, irradiations of compounds **12** in an inert apolar solvent such as perfluorohexane left the substrate practically unchanged, confirming that a polar media is needed to favor the photoreactivity.

Potential mechanisms for the formation of the products are shown in Scheme 2, where the rearranged 1,3,4-oxadiazoles **16** are the result of a *ring contraction−ring expansion* pattern.

The possibility of a reversible intrazeolite ring-to-ring isomerization of **16** was ruled out by a control experiment that demonstrated its photostability under the reaction conditions. The formation of **17** by a 1,2-phenyl shift in **13** to give **15** followed by reaction with adventitious water is not observed in methanol. This probably reflects rapid formation of **18** by reaction with the nucleophilic solvent.

SCHEME 2. Comparison between the Intrazeolite and Solution Photochemistry of 3-Phenyl-1,2,4-oxadiazoles 12a,b

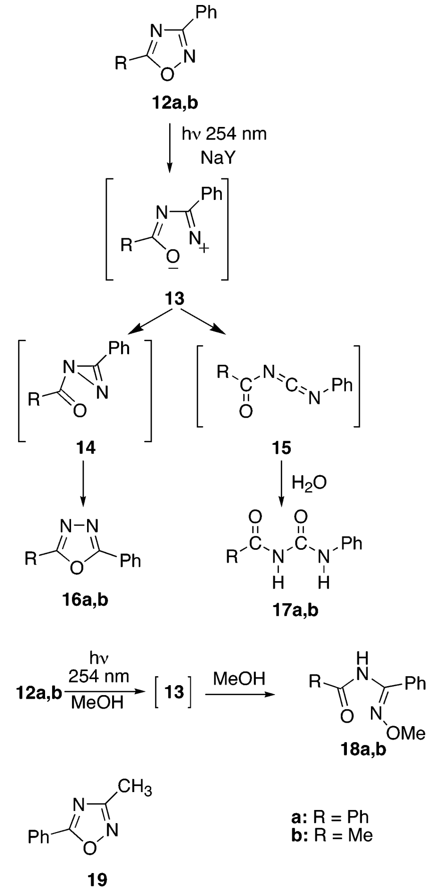

TABLE 1. Analytical Irradiations[a] of Oxadiazole 12a

medium	$\langle s \rangle$[b]	dilution[c]	yields (%) 12a	16a	17a
silica	0.14[d]	13	96	2	
LiY	⟨1.0⟩	13	60	4	
NaY	⟨1.0⟩	14	35	60	4
NaY (24 h)[e]	⟨1.0⟩	14	30	60	5
NaY (diluted)	⟨1.0⟩	4	32	60	5
NaY (less loaded)	⟨0.1⟩	14	5	90	
CsY[f]	⟨1.0⟩	17	85	11	
CsX	⟨0.6⟩	18	98		

[a] Irradiated under identical conditions for 6 h at 254 nm in a quartz tube. [b] Molecular occupancy (molecules per supercage). [c] Amount (mg) of powder sample suspended per milliliter of solvent. [d] Milligrams of substrate per milligram of silica. [e] Irradiated for 24 h. [f] The presence of 2-phenyl-4(3*H*)-quinazolinone (**6**; $R_2 =$ Ph) was also detected (3%).

To provide further insight into the effect of the zeolite in directing this photochemical behavior, we performed a series of analytical scale irradiations on representative **12a** on silica and in different cation exchanged zeolites (see Table 1).

Interestingly, prolonged irradiation times did not significantly affect the extent of conversion of the substrate. This is not due to a shielding effect of the zeolite particles since a lower zeolite/solvent ratio did not influence the percent conversion. However, irradiation of a sample of **12a**@NaY with a substantially reduced loading level of **12a** ($\langle s \rangle = 0.1$) resulted in a significantly enhanced conversion (Table 1). This is consistent with competitive absorption of light by the substrate **12a**

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(7) Calculated by using PCMODEL V 7.0. Serena Software, Bloomington, IN.

(8) Pace, A.; Clennan, E. L. *J. Am. Chem. Soc.* **2002**, *124*, 11236−11237.

(9) In a previous report, a trace amount of **16a** has been observed by HPLC during irradiation of **12a** in MeOH. (Buscemi, S.; Cicero, M. G.; Vivona, N.; Caronna, T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1313−1315).

(10) Newman, H. *Tetrahedron Lett.* **1968**, 2417−2420.

(11) A previous study in methanol, besides solvolysis **18a**, also reported formation of 2-phenyl-4(3*H*)-quinazolinone (**6** $R_2 =$ Ph). Newman, H. *Tetrahedron Lett.* **1968**, 2421−2424.

($\epsilon_{254} = 29\ 000$) and the photochemically inert product **16a** ($\epsilon_{254} = 17\ 000$).

To assess wether the role of zeolite in promoting the observed phototransposition was due to its highly polar environment or also to some steric interaction, we considered irradiations of the substrate on the polar silica surface. The irradiation of **12a** adsorbed on silica and suspended in perfluorohexane left the starting material for the most part unchanged with formation of only 2% of **16a** (Table 1). This indicates that the highly polar silica surface has only a slight effect in promoting the rearrangement and this supports the hypothesis that the observed reactivity of **12a**@NaY is a function of its residence inside the zeolite supercages and not on its silica-like surface.

Finally, since the formation of **16a** does not follow the order of acidity (LiY >NaY > CsY) or basicity (CsX > CsY > NaY > LiY) of the zeolite[2,12] the electronic effect of the cation or of the zeolite wall in promoting the reaction may be excluded [the only case where such effects could be claimed is during irradiation in CsY, where the formation of a few percent of the quinazolin-4-one (**6** R_2 = Ph) can be ascribed to a photoinduced electron transfer[13] between the zeolite framework and the oxadiazole]. Interestingly, irradiation in the better donor more basic CsX left the substrate practically unchanged.

There appears to be no correlation between the zeolite electronic properties and the reaction outcome. Although a complete study that considers steric and electronic substituent effects on this intrazeolitic transformation is needed, an interesting first-glance hypothesis considers what follows: (i) polar media favors the formation of photolytic species such as **13**, that in methanol will immediately undergo a nucleophilic attack by the solvent leading to the formation of solvolysis product; (ii) in the absence of a nucleophilic or hydrogen donor solvent, the photolytic intermediate **13** can choose between recombination to the original oxadiazole, recyclization into a quinazolin-4-one, or formation of a diazirine-like intermediate **14** evolving to 1,3,4-oxadiazole **16**; (iii) on the highly polar silica surface, the formation of **14** (and hence **16**) is observed only in a limited extent since it requires a large deformation of the spatial assembly of photolytic species **13**; (iv) in LiY, and in more extent in NaY, instead, species **13** can be forced (by steric constriction) to rearrange into **14** and give the final 1,3,4-oxadiazole **16** in good yields.

These observations, and in particular the lack of reactivity in CsX which has a significantly reduced supercage void volume in comparison to NaY,[14] suggests that *size and shape selectivity*[15] might be playing an important role in directing the intrazeolite photochemical behavior of **12** preventing or allowing the necessary spatial reorganizations of the intermediates. In particular, it is tempting to suggest that the preferential intrazeolite formation of **16** is a direct result of the spatially compact structure of intermediate **14** enforced by the ring-strain prohibition on a planar amide nitrogen. In contrast, the elongated structures of intermediates **5** and **15** spatially discriminate against formation of **6**, and **17**.

In summary, the polar solvent cage in methanol and supercage in the zeolite both support formation of zwitterionic intermediate **13**. In solution the high concentration of methanol promotes formation of the solvolysis product **18**. In the zeolite the lifetime of intermediate **13** could be extended and either slower formation of intermediates **14** and **15** allowed to compete or, more generally, the relative rate of the branch point for either are inhibited or accelerated by the supercage. In addition, the smaller molecular volume of intermediate **14** in comparison to **15** leads to **16** as the major and **17** as the minor product of this novel intrazeolite photorearrangement.

The possibility of *size and shape selectivity* in other heterocyclic photorearrangements is currently under investigation.

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Supporting Information Available: Plots of loading % of **12a**,**b** in zeolite, excitation and emission spectra of **12a** in methanol and in NaY, and full experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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[12] Ono, Y.; Baba, T. *Catal. Today* **1997**, *38*, 321−337.

[13] Formation of the quinazolin-4-one system from 5-aryl-1,2,4-oxadiazoles irradiated in the presence of sensitizers or electron-donor reagents has been systematized through an electron-transfer process. Buscemi, S.; Pace, A.; Vivona, N.; Caronna, T.; Galia, A. *J. Org. Chem.* **1999**, *64*, 7028−7033.

[14] The vacant space in the zeolite supercage is as follows: LiY, 834 Å^3; NaY, 827 Å^3; CsY, -781 Å^3; CsX, 732 Å^3. Ramamurthy, V.; Eaton, D. F.; Caspar, J. V. *Acc. Chem. Res.* **1992**, *25*, 299−307.

[15] Ramamurthy, V. *J. Photochem. Photobiol. C* **2000**, *1*, 145−166.