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N-Isopropenylazoles: III.* Quantum-Chemical Analysis of the Reaction of Azoles with Allene and Propyne in the Gas Phase

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Abstract—Reactions of pyrrole, imidazole, pyrazole, and 1,2,4-triazole with allene and propyne in the gas phase with formation of the corresponding *N*-isopropenylazoles were simulated at the RHF/6-31G**, B3LYP/6-31G**, and MP2(full)/6-31G** levels. Dissociation of the N–H bond to give azolate ion is the main constituent of the reaction coordinate. All the examined azoles react preferentially with allene rather than with propyne; their reactivity decreases in the series pyrrole > imidazole > pyrazole > 1,2,4-triazole due to participation of the pyridine type nitrogen atoms in the prototropic propyne–allene rearrangement.

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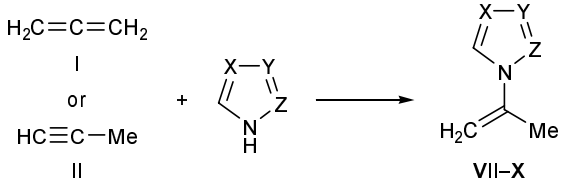
We were the first to effect direct N-isopropenylation of azoles with a propyne–allene mixture in a superbasic system (a suspension of KOH in DMSO) using pyrrole as substrate [2]. Detailed studies on this reaction with various azole systems, such as 2-, 2,3-, and 2,3,5-substituted pyrroles, indole, imidazole, 2-methylimidazole, pyrazole, and 1,2,4-triazole showed that it occurs at 125–145°C in a regioselective fashion, regardless of the nature of propenylating agent (propyne or allene) and substrate, leading to the formation of *N*-isopropenylazoles in 20–86% yield (unoptimized), depending on the azole structure [3]. Judging by the yields of products obtained under comparable conditions, the reactivity of unsubstituted azoles decreases as the number of electronegative pyridine-type nitrogen atoms in the azole ring increases, i.e., in the series pyrrole > imidazole > pyrazole > 1,2,4-triazole (the yields of the corresponding *N*-isopropenylazoles are 73, 60, 46, and 20%, respectively) [3]. Insofar as the rate-determining stage in this reaction is attack by azolate ion on the electron-deficient carbon atom of propyne or allene (deprotonation of azoles in the system KOH–DMSO is accompanied by heat evolution even at room temperature [4]), the reactivity decreases in parallel with reduction of the nucleophilicity of the azolate ion, which is related to its basicity, polarity, polarizability, strength of solvation, and other factors.

In the present work we examined the formation of azolate ions by the action of allene (**I**) and propyne (**II**) on pyrrole (**III**), imidazole (**IV**), pyrazole (**V**), and 1,2,4-triazole (**VI**) in the gas phase (Scheme 1) and estimated the probability for N-isopropenylation of these azoles to occur in less basic or neutral medium where solvate shielding of azolate ions is not significant. The potential energy surface for the reactions of allene and propyne with azoles were constructed using Gaussian-98 software package [5]. In order to check the validity of the employed *ab initio* methods in the prediction of topological parameters of the examined systems in the configurational region of the reaction, the calculations were performed at different levels [6–8]: RHF/6-31G**, B3LYP/6-31G**, and

Scheme 1.



III, **VII**, X = Y = Z = CH; **IV**, **VIII**, X = Z = CH, Y = N; **V**, **IX**, X = Y = CH, Z = N; **VI**, **X**, Y = CH, X = Z = N.

* For communication II, see [1].

MP2(full)/6-31G**. We calculated structural and electronic parameters and relative stabilities of prereaction bimolecular complexes and reaction products, determined optimal gradient paths between the initial and final states, and localized transition state structures. Geometric parameters of the molecular systems corresponding to transition states (i.e., at those stationary points of the potential energy surface where the number of negative Hessian eigenvalues λ is equal to unity 1 [9]) and energy minima (λ = 0) were fully optimized to a value of 10^{-5} a.u./bohr. While analyzing flat areas of the potential energy surface, which correspond to configurationally labile states (prereaction complexes), the limiting values were set at a level of 10^{-6} a.u./bohr. Structures corresponding to energy minima were localized by moving along the gradient path from a saddle point to the nearest critical point with a small initial shear along the transition vector; we thus succeeded in correctly determining the gradient reaction path.

Table 1 contains the principal energy parameters of the initial molecules, calculated at different levels for the gas phase, as well as their electric dipole moments and least harmonic frequencies and the corresponding experimental data.

The calculated parameters showed a good agreement with the available experimental dipole moments and least vibrational frequencies. The error in the determination of the dipole moments of propyne, pyrrole, and imidazole did not exceed 5%; all methods overestimated the dipole moment of pyrazole by 0.09–0.32 D; and the dipole moment of 1,2,4-triazole was underestimated by 0.14–0.30 D. The results of calculations suggest higher thermodynamic stability of propyne relative to isomeric allene in the gas phase. The difference in the relative stabilities of propyne and allene (ΔE_{tot}) without taking into account the energy of zero-point harmonic vibrations (ZPE) is small, 7.1, 14.1, and 19.3 kJ/mol according to the RHF/6-31G**,

Table 1. Total energies (E_{tot}, a.u.),[a] energies of zero-point harmonic vibrations (ZPE, a.u.), dipole moments (μ, D), and least vibrational frequencies (ν, cm^{-1}), calculated by the RHF/6-31G**, B3LYP/6-31G** (in brackets), and MP2(full)/6-31G** methods (in parentheses) for allene (**I**), propyne (**II**), pyrrole (**III**), imidazole (**IV**), pyrazole (**V**), and 1,2,4-triazole (**VI**); the corresponding experimental data [10] are given in braces

Compound no. (symmetry)	E_{tot}	ZPE	μ	ν
I (C_2)	–115.86856 [–116.66406] (–116.28079)	0.05916 [0.05531] (0.05660)	0 [0] {0.20} (0)	410 [384] (368)
II (C_{3v})	–116.87125 [–116.66943] (–116.28816)	0.05978 [0.05557] (0.05630)	0.67 [0.72] {0.72} (0.70)	394 [349] {356} (287)
III (C_s)	–208.81971 [–210.17634] (–209.54680)	0.08862 [0.08266] (0.08386)	1.89 [1.90] {1.84} (1.91)	499 [461] {565} (480)
IV (C_s)	–224.82430 [–226.22309] (–225.57516)	0.08183 [0.07126] (0.07241)	3.86 [3.70] {3.80} (3.94)	522 [515] {456} (535)
V (C_s)	–224.80328 [–226.20703] (–225.55920)	0.08162 [0.07141] (0.07249)	2.42 [2.28] {2.19} (2.51)	540 [512] {465} (540)
VI (C_s)	–240.81197 [–242.25584] (–241.58945)	0.06519 [0.05996] (0.06092)	2.98 [2.86] {3.16} (3.02)	598 [550] (585)

[a] 1 a.u. = 2622.9897 kJ/mol.

Table 2. Total energies (E_{tot}, a.u.), relative energies (E, kJ/mol), numbers of negative Hessian eigenvalues (λ), and energies of zero-point harmonic vibrations (ZPE, a.u.), calculated by the RHF/6-31G**, B3LYP/6-31G** (in brackets), and MP2(full)/6-31G** methods (in parentheses) for prereaction complexes formed by allene (**I**) with azoles **III**–**VI**, *N*-isopropenylazoles **VII**–**X**, transition states TS_1–TS_4, and transition states for the degenerate reactions of allene (**I**) with pyrazole (**V**) (TS_5) and 1,2,4-triazole (**VI**) (TS_6)

Structure (symmetry)	E_{tot}	E	λ	ZPE	Structure (symmetry)	E_{tot}	E	λ	ZPE
I+**III** (C_1)	–324.69163 [–326.84496] (–325.83498)	0 [0] (0)	0 [0] (0)	0.14878 [0.13898] (0.14513)	TS_3 (C_1)	–340.54614 [–342.74826] (–341.71551)	338.8 [334.4] (346.1)	1 [1] (1)	0.13256 [0.12118] (0.12463)
TS_1 (C_1)	–324.54756 [–326.71269] (–325.70009)	377.3 [346.9] (353.8)	1 [1] (1)	0.14316 [0.13085] (0.13974)	**IX** (C_s)	–340.72202 [–342.92403] (–341.90586)	–122.6 [–126.7] (–153.2)	0 [0] (0)	0.14135 [0.13170] (0.13643)
VII (C_s)	–324.73270 [–326.88801] (–325.88779)	–107.7 [–112.9] (–138.5)	0 [0] (0)	0.15347 [0.14328] (0.14974)	**I**+**VI** (C_1)	–356.68481 [–358.92566] (–357.87792)	0 [0] (0)	0 [0] (0)	0.12531 [0.11628] (0.12054)
I+**IV** (C_1)	–340.69662 [–342.89137] (–341.86355)	0 [0] (0)	0 [0] (0)	0.14101 [0.13739] (0.13943)	TS_4 (C_S)	–356.58969 [–358.79013] (–357.73923)	384.8 [355.5] (363.8)	1 [1] (1)	0.11987 [0.11234] (0.11662)
TS_2 (C_1)	–340.56920 [–342.76623] (–341.73218)	334.2 [328.2] (344.6)	1 [1] (1)	0.12964 [0.12002] (0.12376)	**X** (C_s)	–356.72996 [–358.97178] (–357.93509)	–118.4 [–121.0] (–149.9)	0 [0] (0)	0.12970 [0.12038] (0.12456)
VIII (C_s)	–340.73800 [–342.93502] (–341.91632)	–108.5 [–114.4] (–138.4)	0 [0] (0)	0.14571 [0.14099] (0.14351)	TS_5 (C_1)	–340.59422 [–342.79916] (–341.76271)	212.6 [200.9] (222.3)	1 [1] (1)	0.11371 [0.10763] (0.11024)
I+**V** (C_1)	–340.67529 [–342.87574] (–341.84745)	0 [0] (0)	0 [0] (0)	0.14110 [0.12758] (0.13241)	TS_6 (C_s)	–356.60314 [–358.85634] (–357.80110)	214.2 [181.8] (201.5)	1 [1] (1)	0.10732 [0.09464] (0.09839)

B3LYP/6-31G**, and MP2(full)/6-31G** calculations, respectively. No inversion of the relative stabilities of these compounds was observed when a correction for ZPE was taken into consideration. The corresponding values are 5.4, 13.0, and 20.1 kJ/mol (the same sequence of methods). The results of RHF/6-31G** calculations are the closest to the available experimental [11] and theoretical data [12].

However, the examined azoles give the most stable prereaction complexes with allene rather than with propyne. For example, according to the RHF/6-31G** calculations, the gain in the relative stability of allene–azole prereaction complexes **I**+**III**, **I**+**IV**, **I**+**V**, and **I**+**VI**, as compared to the corresponding complexes with propyne is 11.9, 8.8, 9.4, and 7.1 kJ/mol, respectively (for pyrrole, imidazole, pyrazole, and 1,2,4-triazole). In keeping with the transition state energies, the kinetic parameters for the addition of allene to azoles are more favorable than those for the addition of propyne. The difference in the activation barriers is 24.7, 21.3, 22.7, and 19.5 kJ/mol (the order is the same as above). The results of B3LYP/6-31G** and MP2/6-31G** calculations demonstrate an analogous but enhanced tendency. Therefore, in the further treatment we examined only the reactions of azoles **III**–**VI** with allene (**I**).

The energy of stabilization of the prereaction bimolecular allene–azole complexes relative to the isolated components (without taking into account ZPE correction; Tables 1, 2) ranges from 9 to 20 kJ/mol and increases in the series **I**+**III** < **I**+**IV** ≈ **I**+**V** < **I**+**VI**. Introduction of ZPE corrections (regardless of the calculation procedure) insignificantly reduces the relative stability of the above complexes, the stability series remaining unchanged. The addition products, *N*-isopropenylazoles **VII**–**X**, depending on the azole structure and calculation method, are more stable than the initial bimolecular complexes by ~110–150 kJ/mol (Table 2). The gains in the energy of compounds **VII** and **VIII** relative to the initial prereaction bimolecular complexes are approximately similar: the difference does not exceed 1.5 kJ/mol (Table 2). The difference in

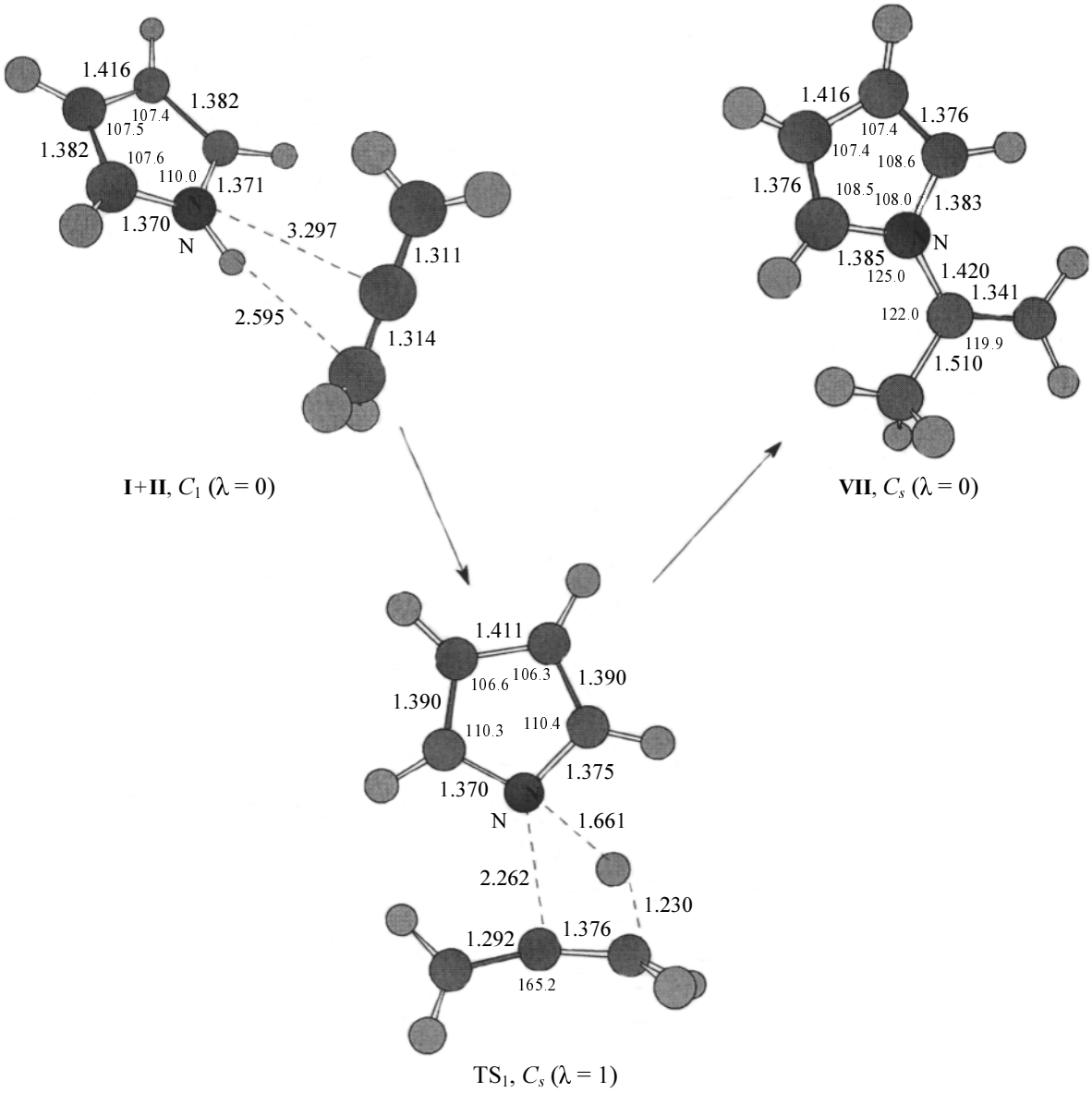


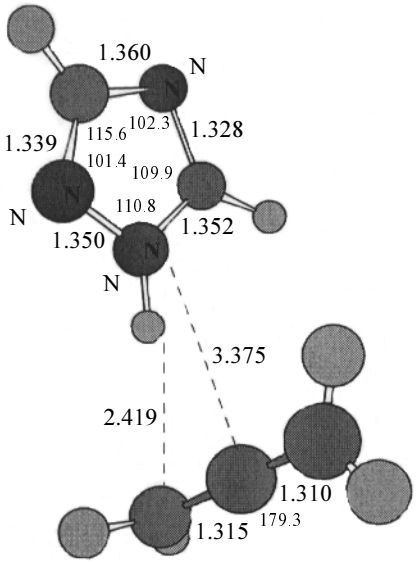
Fig. 1. Geometric parameters (bond lengths, Å, and bond angles, deg) of the prereaction complex formed by allene (**I**) with pyrrole (**III**), *N*-isopropenylpyrrole (**VII**) (minima on the potential energy surface), and transition state TS_1 (saddle point), calculated by the MP2(full)/6-31G** method.

the enthalpies of formation ΔH of compounds **IX** and **X** is slightly greater (<5.7 kJ/mol). On the whole, the heats of the reactions leading to *N*-isopropenylazoles **IX** and **X** are larger by ~10–15 kJ/mol than those calculated for compounds **VII** and **VIII**.

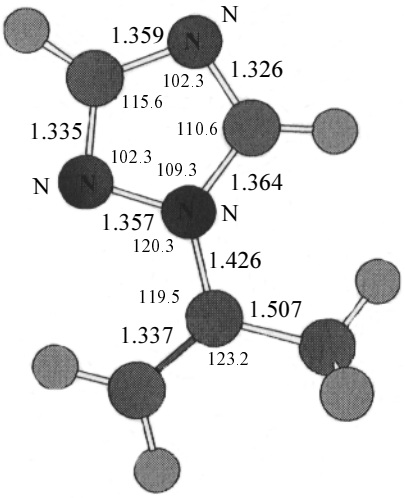
Thus the calculated gas-phase thermodynamic parameters do not agree with the experimentally found relations holding in the isopropenylation of azoles in the superbasic system KOH–DMSO with regard to the azole structure [3].

Analysis of the potential energy surface for the reactions of azoles **III**–**VI** with allene showed that the main constituent of the multifunctional reaction coordinate along the optimal gradient path connecting the prereaction complex and the product is dissociation of the N–H bond and that the transition state is a complex formed by the azolate ion, proton, and strongly polarized allene (Figs. 1, 2).

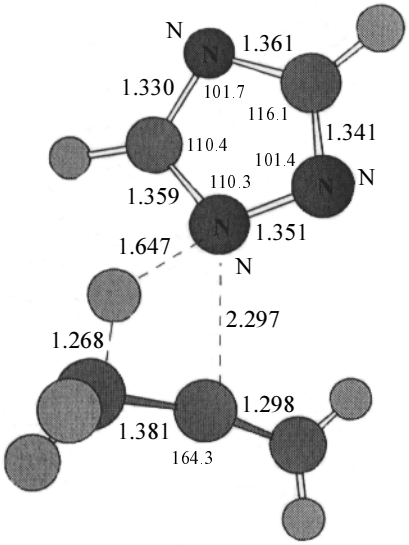
The largest difference (339–385 kJ/mol) in the activation energies of the transitions **III**–**VI**→**VII**–**X** (with no correction for ZPE) was obtained by the RHF calculations. The energies of activation may be arranged in the following series: TS_4(**VI**→**X**) ≈ TS_1(**III**→**VII**) > TS_2(**IV**→**VIII**) ≈ TS_3(**V**→**IX**). The



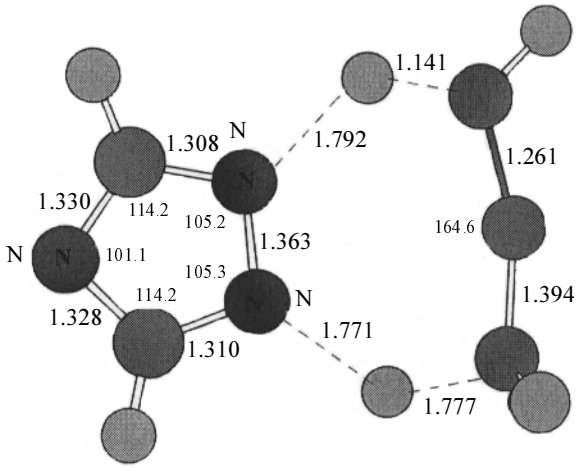
I+**VI**, C_1 ($\lambda = 0$)



X, C_s ($\lambda = 0$)



TS_4, C_s ($\lambda = 1$)

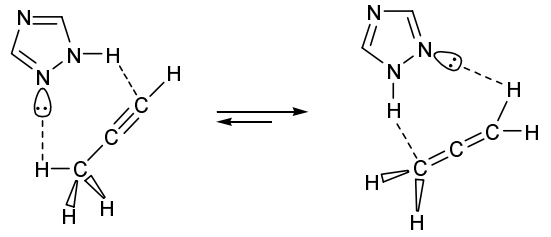


TS_6, C_s ($\lambda = 1$)

Fig. 2. Geometric parameters (bond lengths, Å, and bond angles, deg) of the prereaction complex formed by allene (**I**) with 1,2,4-triazole (**VI**) and *N*-isopropenyl-1,2,4-triazole (**X**) (minima on the potential energy surface), transition state TS_4, and transition state TS_6 for the pseudodegenerate rearrangement **II**+**VI** → **I**+**VI**, calculated by the MP2(full)/6-31G** method.

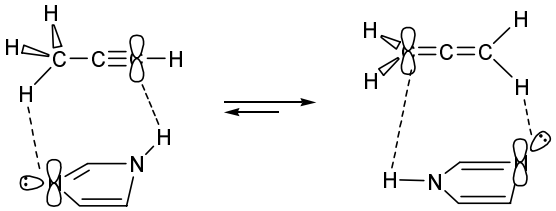
B3LYP and MP2 methods give smaller differences in the energies of activation of these reactions, 27 and 19 kJ/mol, respectively, while their sequence remains the same (Table 2). Introduction of ZPE correction reduces the activation barriers by 8–10 kJ/mol. The calculations revealed only one transition state (TS_1, Fig. 1) on the potential energy surface for the reaction of allene with pyrrole and the transformation of prereaction complex **I**+**III** into *N*-isopropenylpyrrole (**VII**) along the gradient path connecting these states, while no branching points were present. By contrast, the potential energy surfaces calculated for the reactions of pyrazole and 1,2,4-triazole with allene contained at least one more transition state leading to the initial azole and propyne, the latter being formed via propyne–allene prototropic rearrangement (Scheme 2). The energies of activation of these processes are lower by 120–170 kJ/mol than that for the direct addition reaction; this follows from comparison of TS_3 and TS_5 for pyrazole and TS_4 and TS_6 for 1,2,4-triazole

Scheme 2.



(Table 2, Fig. 2). The reaction of allene with imidazole may also involve side formation of prereaction sandwich-like associates, followed by pseudodegenerate rearrangement. According to the RHF/6-31G** calculations, the energy of activation of this process is lower by 83 kJ/mol than the energy of activation of the direct addition. However, taking into account that the sandwich associate is less stable (by 57 kJ/mol, RHF/6-31G** data) than prereaction complex **I**+**IV** (Table 2), this reaction channel seems to be less probable (Scheme 3).

Scheme 3.



The dipole moments of the structures corresponding to critical points on the potential energy surfaces of the above reactions (2.18, 4.49, 2.29, and 3.39 D for azoles **III**–**VI**; 1.36, 3.38, 1.41, and 3.11 D for *N*-isopropenylazoles **VII**–**X**; 4.06, 8.76, 5.02, and 6.17 D, for transition states TS_1–TS_4, respectively; RHF calculations) suggest reduction of the activation barriers and stabilization of prereaction complexes in going from the gas phase to a polar solvent.

To conclude, we can state the following. The kinetic and thermodynamic parameters of N-isopropenylation of azoles with allene, calculated for the gas phase, indicate that the probability for analogous process to occur in weakly basic or neutral (polar) media is fairly high for pyrrole. The presence in di- and triazole molecules of one or several alternative nitrogen centers capable of participating in concurrent processes involving prototropic rearrangements reduces the probability for the reaction to occur in the series imidazole > pyrazole > 1,2,4-triazole. Analogous processes are also possible in the superbasic system KOH–DMSO, and they could hamper *N*-isopropenylation of azoles.

REFERENCES

1. Klyba, L.V., Tarasova, O.A., Shemetova, M.A., Petrushenko, K.B., Mikhaleva, A.I., and Trofimov, B.A., *Russ. J. Org. Chem*., 2003, vol. 39, p. 1325.
2. Trofimov, B.A., Tarasova, O.A., Mikhaleva, A.I., Kalinina, N.A., Sinegovskaya, L.M., and Henkelmann, J., *Synthesis*, 2000, p. 1585.
3. Trofimov, B.A., Tarasova, O.A., Shemetova, M.A., Afonin, A.V., Klyba, L.V., Baikalova, L.V., and Mikhaleva, A.I., *Russ. J. Org. Chem*., 2003, vol. 39, p. 408.
4. Tarasova, O.A., Shmidt, E.Yu., Klyba, L.V., Sinegovskaya, L.M., Mikhaleva, A.I., Krivdin, L.B., and Trofimov, B.A., *Russ. J. Org. Chem*., 1998, vol. 34, p. 688.
5. Frisch, M.J., Trucks, G.W., Schlegel, H.B., Scuseria, G.E., Robb, M.A., Cheeseman, J.R., Zakrzewski, V.G., Montgomery, J.A., Stratmann, R.E., Burant, J.C., Dapprich, S., Millam, J.M., Daniels, A.D., Kudin, K.N., Strain, M.C., Farkas, O., Tomasi, J., Barone, V., Cossi, M., Mennucci, B., Pomelli, C., Adamo, C., Clifford, S., Ochterski, J., Petersson, G.A., Ayala, P.Y., Cui, Q., Morokuma, K., Malick, D.K., Rabuck, A.D., Raghavachari, K., Foresman, J.B., Cioslowski, J., Ortiz, J.V., Stefanov, B.B., Liu, G., Liashenko, A., Piskorz, P., Komaromi, I., Gomperts, R., Martin, R.L., Fox, D.J., Keith, T., Al-Laham, M.A., Peng, C.Y., Nanayakkara, A., Gonzalez, C., Challacombe, M., Gill, P.M.W., Jonson, B., Chen, W., Wong, M.W., Andres, J.L., Head-Gordon, M., Replogle, E.S., and Pople, J.A., *GAUSSIAN 98, Revision A.6*, Pittsburgh PA: Gaussian, 1998.
6. Foresman, J.B. and Frish, E., *Exploring Chemistry with Electronic Structure Methods*, Pittsburgh: Gaussian, 1996.
7. Schmidt, M.W., Baldridge, K.K., Boatz, J.A., Elbert, S.T., Gordon, M.S., Jensen, J.H., Koseki, S., Matsunaga, N., Nguyen, K.A., Su, S.J., Windus, T.L., Dupuis, M., and Montgomery, J.A., *J. Comput. Chem*., 1993, vol. 14, p. 1347.
8. Becke, A.D., *J. Chem. Phys*., 1993, vol. 98, p. 5648.
9. Minyaev, R.M., *Usp. Khim*., 1994, vol. 63, p. 939.
10. Osipov, O.A., Minkin, V.I., and Garnovskii, A.D., *Spravochnik po dipol'nym momentam* (Dipole Moment Handbook), Moscow: Vysshaya Shkola, 1971; *Physical Methods in Heterocyclic Chemistry*, Katritzky, A.R., Ed., New York: Academic, 1963; Sterin, Kh.E., Aleksanyan, V.T., and Zhizhin, G.N., *Katalog spektrov kombinatsionnogo rasseyaniya uglevodorodov* (Catalog of Raman Spectra of Hydrocarbons), Moscow: Nauka, 1976, p. 24; Movtovich, D.Ya., *Cand. Sci. (Chem.) Dissertation*, Rostov-on-Don, 1977.
11. Cox, J.D. and Pilcher, G., *Thermochemistry of Organic and Organometallic Compounds*, New York: Academic, 1970.
12. Kobychev, V.B., Vitkovskaya, N.M., Klyba, N.S., and Trofimov, B.A., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2002, p. 713.