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Nucleophilic aromatic substitution of hydrogen and related reactions

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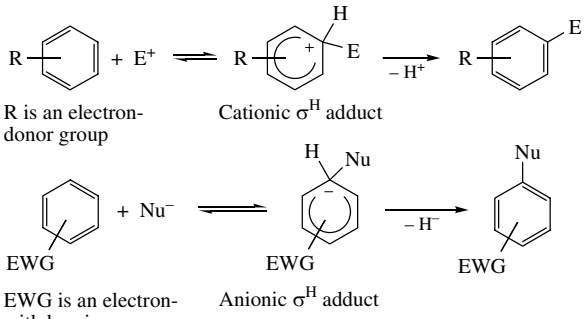
The classical concept of nucleophilic aromatic substitution (S_NAr^{ipso}) has been complemented with a new synthetic methodology (S_N^H), enabling one to build new carbon–carbon C(sp^2)–C(sp^3), C(sp^2)–C(sp^2) and C(sp^2)–C(sp) or carbon–heteroatom C(sp^2)–X (X is O, N, P, S, halogen) bonds through nucleophilic displacement of hydrogen in an aromatic ring.

In the formation of new chemical bonds through the nucleophilic aromatic displacement of hydrogen (S_N^H) in π-deficient aromatic compounds, the S_N^H reactions undoubtedly belong to key chemical processes.[1] Indeed, published data demonstrate a common character of the S_N^H reactions as a fundamental property of aromatic (heteroaromatic) compounds.[2–18]

It is well known that aromatic compounds undergo substitution reactions initiated by an either electrophilic or nucleophilic attack on the C(sp^2) carbons of an aromatic ring.[19] Electrophilic aromatic substitution of hydrogen (for which the symbol S_EAr is usually used, while H is omitted) is a well-developed synthetic procedure which is widely used for structural modification of aromatic compounds. In the S_EAr reactions, the cationic nature of intermediate σ^H adducts facilitates the elimination of a proton, and the cleavage of the C(sp^3)–H bond takes place easily enabling the system to restore the lost aromaticity (Scheme 1).[19]



Scheme 1

This is not the case with the anionic σ^H adducts, which are derived from a nucleophilic attack on unsubstituted carbon of an aromatic ring. Due to difficulties associated with elimination of hydrogen with pair of electrons from anionic σ^H adducts (in

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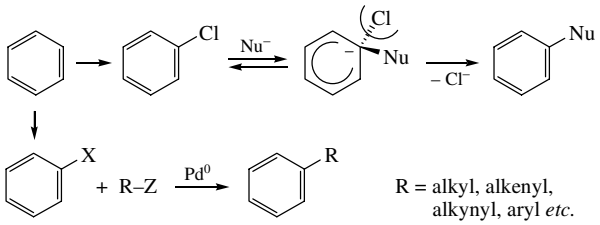
summary, the hydride ion), development of the S_N^H methodology has been lagged behind the S_EAr and $S_N^{ipso}Ar$ reactions for a long time. A remarkable progress in studying both oxidative and elimination versions of the S_N^H reactions has been achieved only during the last two to three decades.[1–18]

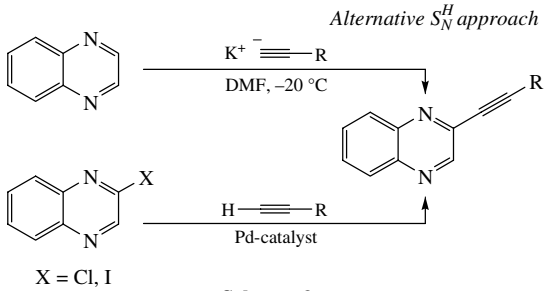
Note that aromatic compounds have wide applications in practice; in order to modify their structure, industrial organic synthesis often exploits electrophilic chlorination followed by a nucleophilic displacement reaction $S_N^{ipso}Ar$ accompanied by departure of the chloride anion. The situation is far from ideal from a chemical point of view (chlorination–dechlorination), to say nothing of its poor correspondence to the green chemistry principles.[20] Another powerful synthetic tool of the advanced chemistry of aromatic compounds is a set of palladium-catalysed cross-coupling reactions enabling one to build a variety of C(sp^2)–C or C(sp^2)–X (X is a heteroatom) bonds. These methods are known as the Heck, Stille, Suzuki–Mijaura, Sonogashira, Kumada, Negishi, Buchwald–Hartwig, Hijama and Tsuji-Trost reactions.[21] Most of them are also based on the use of aryl halides (Scheme 2).



X = Cl, Br, I, $B(OH)_2$; R–Z = organoelement compound

Scheme 2

Meanwhile, there are coupling reactions which do not require metal complex catalysis or the presence of halogen in an aromatic substrate, and these are the S_N^H reactions.[1–16] For instance, the S_N^H methodology has been used to introduce acetylenic fragments into quinoxalines, and this approach is an alternative way for the well-known palladium-catalysed Sonogashira cross-coupling reaction (Scheme 3).[22]



X = Cl, I

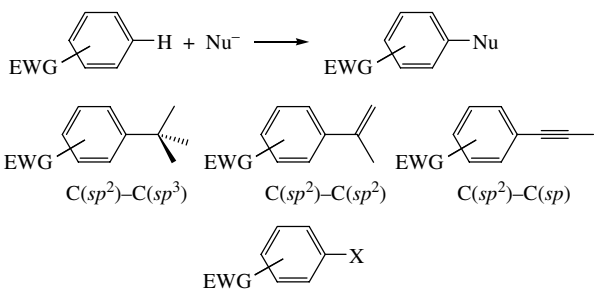
Scheme 3

What are advantages of the S_N^H methodology? First, it provides new effective methods to build a variety of chemical bonds. Second, a direct nucleophilic attack on the C(sp^2)–H carbon enables one to avoid toxic chlorinated intermediates and to carry out the process following the principles of green chemistry,[16] such as atom efficiency, shorter synthesis, less hazardous chemicals, waste prevention, *etc*.[20]

A detailed study of the nucleophilic aromatic substitution of hydrogen has been initiated at the Urals State Technical University (Ekaterinburg, Russia) in the 1970s.[2] At that time, nucleophilic aromatic substitutions were associated mainly with the *ipso*-attack at a ring carbon C(sp^2)–X bearing a halogen or other good leaving group X (S_NAr^{ipso}), and the overwhelming majority of textbooks on organic chemistry stated that, as a rule, hydrogen is not displaced from aromatic ring because very strong basic hydride ion H^- has to be displaced in this case.[19] In the first review on nucleophilic aromatic displacement of hydrogen, it was suggested to use the symbols S_N^H in order to distinguish these reactions from the classical nucleophilic substitutions $S_N^{ipso}Ar$.[2] Later, a number of reviews have been published,[3–18] and also the book '*Nucleophilic Aromatic Substitution of Hydrogen*', which accumulated a considerable body of data on conditions, kinetics, structure of intermediates, electrochemical and mathematic modeling, as well as plausible mechanisms and the general concept of the S_N^H reactions.[1] Many research groups contributed to the field, for example, Professor M. Makosza developed the so-called vicarious nucleophilic substitution of hydrogen,[4,6,8,9,15,23,24] which proved to be an elimination version of the S_N^H reactions. Professor H. C. van der Plas modified the Chichibabin reaction[25] and suggested to use the very effective liquid ammonia–potassium permanganate oxidative system for the amination of azaaromatics.[3,5,26] In the course of these studies, it has been established that ring carbon atoms bearing hydrogen are more vulnerable for a nucleophilic attack than those bearing halogen or other good leaving groups,[26] and the S_N^H methodology proved to be an efficient tool to build carbon–carbon and carbon–heteroatom chemical bonds between an aromatic ring and a variety of nucleophilic reagents. Therefore, Professor F. Terrier referred to the S_N^H reactions as a fascinating subject of the last decade.[7]

This article is mainly based on the results of our research group, and it cannot pretend for a comprehensive consideration of this promising area of organic synthesis. We focus our attention on the S_N^H reactions, their scope and limitations.

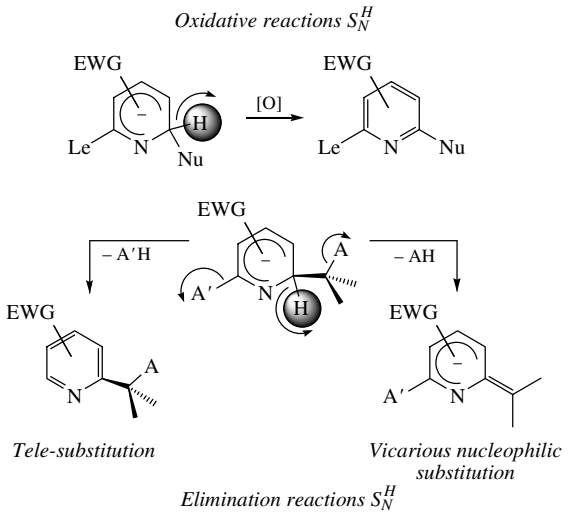
The general scheme of the S_N^H reactions is very similar to that of the $S_N^{ipso}Ar$, and it suggests the interaction of π-deficient aromatic (heteroaromatic) compounds with nucleophiles. Electron-withdrawing groups, such as NO_2, N=O, C=O, cyano, and CF_3 are, as a rule, necessary to promote the ability of arenes to react with nucleophiles. A similar activation can be reached by incorporating heteroatoms, such as C=N and its cationic forms C=NR^+, C=NH^+, =S^+, =O^+ and N-oxides C=N^+–O^-. Indeed, azinium, pyrilium, thiapyrilium and tropylium cations, as well as activated nitroannulenes, azaazulenes, arene–metal complexes and porphyrins, nitro and aza activated arenes, azoles and azines, and other π-deficient systems proved to be appropriate substrates for the S_N^H reactions.[1] The π-deficiency of aromatics is a requirement of the S_N^H reactions limiting the scope of their application relative to that for metal-catalysed cross-couplings. As for reagents for the S_N^H reactions are concerned, they involve a great deal of C-, O-, N-, P- and S-centered nucleophiles, halides, peroxides, *etc*., thus enabling one to perform nucleophilic alkylation, alkenylation, alkynylation, aminoarylation, hydroxyarylation, hetarylation, amination, hydroxylation, alkoxylation, cyanation and halogenation,[1–15] carboranylation,[27] ferrocenylation[28] and other types of reactions (Scheme 4).



X = O-, N-, S-, P-centered nucleophiles

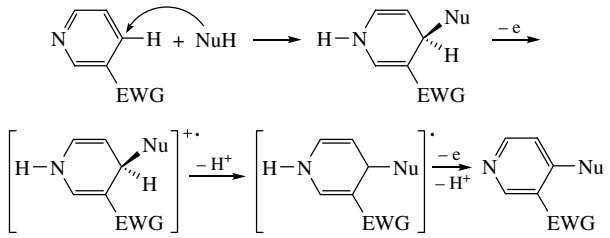
Scheme 4

A considerable body of published data[1–18] on the S_N^H reactions shows that these reactions are of fundamental importance in the chemistry of electron-deficient aromatics, and they occur through two principal pathways: (i) the addition–oxidation $S_N^H(AO)$ scheme, which is based on using an outer oxidant[1–3,5,13,14,16,18,26] and (ii) the addition–elimination $S_N^H(AE)$ scheme, which suggests the presence of an auxiliary group in either a nucleophile (A) or an aromatic ring (A′).[4,6,8,9,15,23,24] Both schemes are complementary to each other, since they have in common that a proton and two electrons have to be departed from intermediate σ^H adducts either by the action of an outer oxidant[1] or due to the elimination of an auxiliary group (A or A′),[15] facilitating the departure of hydrogen as a proton (Scheme 5).[18]



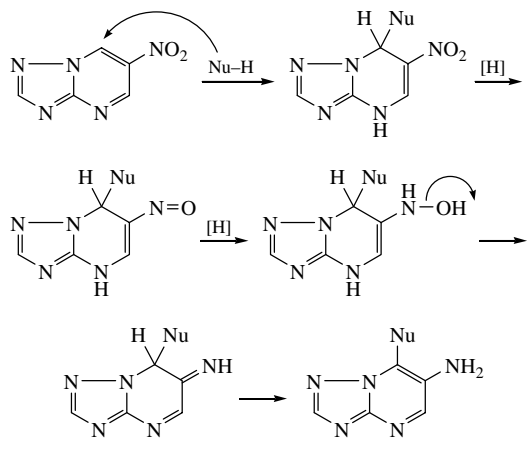
Scheme 5

In spite of a continuous discussion regarding hydride ion elimination, the stepwise mechanism involving successive electron–proton–electron (EPE) transfer appears to be the most plausible pathway (Scheme 6).[18]



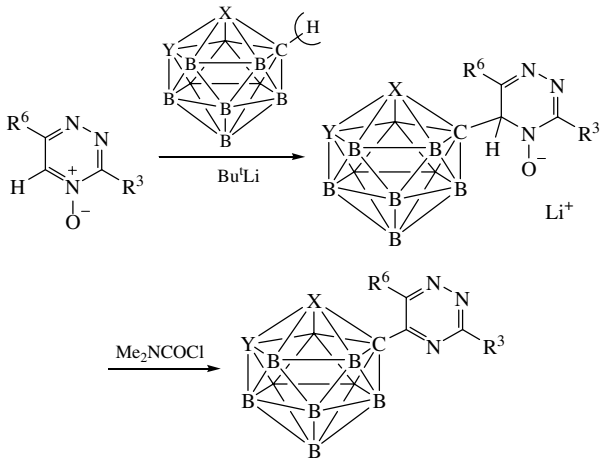
Scheme 6

The aromatisation of σ^H adducts is a crucial step in the majority of the S_N^H reactions,[1,18] although sometimes it requires unusual conditions. The aromatisation of the σ^H adducts derived from 6-nitro-1,2,4-triazolo[1,5-*a*]pyrimidines can be initiated by reduction of the nitro group in the dihydropyrimidine intermediate.[29] The most plausible mechanism of this auto-aromatisation involves water elimination from the intermediate hydroxyamino compound with the hydroxy fragment acting as an auxiliary group. Finally, a prototropic rearrangement of the heterocyclic imine affords an amino compound in a good yield (Scheme 7).[29]



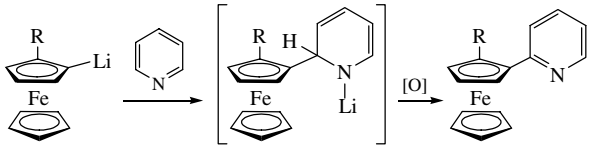
Scheme 7

The scope of the S_N^H reactions can be illustrated by the following examples. Carbanions generated from carboranes can replace hydrogen in pyrazines, triazine-*N*-oxides and other π-deficient systems. This approach to incorporate boron-containing fragments into heterocyclic molecules is effective for the synthesis of compounds that can be used as new ligands and agents for the neutron-capture therapy of cancer (Scheme 8).[27]



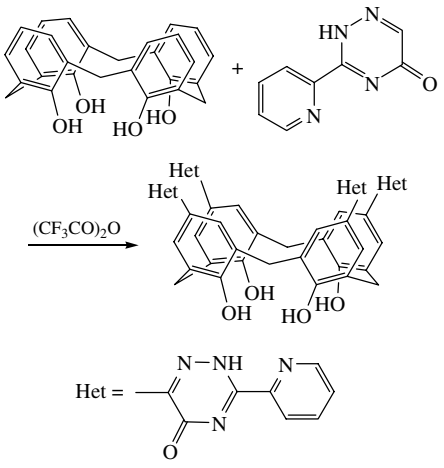
Scheme 8

The modification of pyridines with the lithium salts of monosubstituted ferrocenes is based on the S_N^H process, which provides an access to new derivatives of metal complexes, including those possessing planar chirality (Scheme 9).[28]



Scheme 9

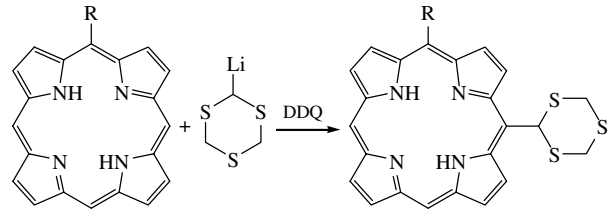
Another area of application for the S_N^H methodology concerns macrocycles (calixarenes, calixhetarens and porphyrins), which



Scheme 10

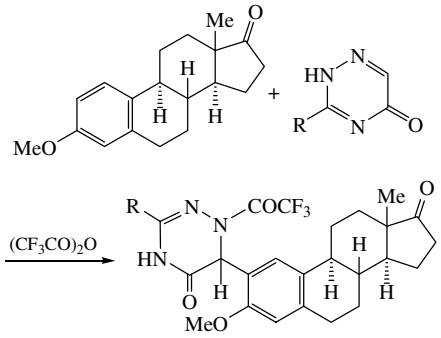
are widely used as ligands in supramolecular chemistry. The modification of the upper rim of calix[4]phenols through the S_N^H C–C coupling with electron-deficient triazinones is a new approach to change molecular cavities of these compounds, opening new possibilities for design of highly selective ligands.[30] The same approach has been applied to modify calixpyrroles and calixfurans (Scheme 10).[31]

The substitution of hydrogen in porphyrins by the action of carbanions (butyllithium or dithianyllithium) in the presence of DDQ as an oxidant is another interesting application of the S_N^H methodology to the chemistry of macrocycles, which seems a promising route to the derivatisation of these important heterocyclic photosensitisers for the photodynamic therapy of cancer (Scheme 11).[32]



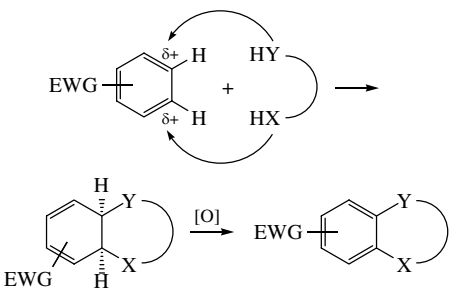
Scheme 11

Intramolecular S_N^H reactions have been used to modify the structures of fluoroquinolones, derivatives of a well-known family of antibacterials,[33] while intermolecular C–C couplings have been successfully applied to the structure modification of steroids, an important class of bioregulators (Scheme 12).[34]



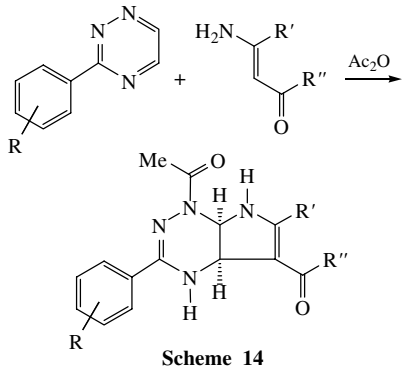
Scheme 12

In addition to the well-known route to fused heterocyclic systems, which is based on the displacement of two leaving groups in an aromatic ring, the S_N^H methodology exploits tandem nucleophilic addition–addition (A_N–A_N), addition–substitution of hydrogen (A_N–S_N^H), and double substitution of hydrogen reactions (S_N^H–S_N^H) on two neighbouring carbons (Scheme 13).[1,14,35–43]



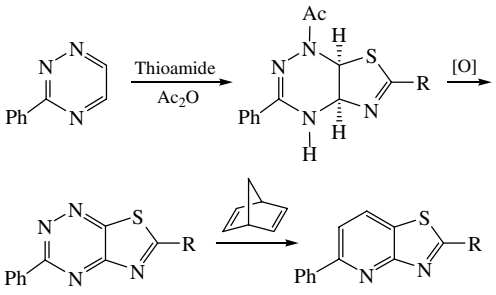
Scheme 13

The synthesis of fused derivatives by using the tandem A_N–A_N, A_N–S_N^H and S_N^H–S_N^H reactions is a very constructive concept.[1,14,35–43] A variety of 1,4-diazines condensed with five- and six-membered heterocycles have been obtained by reacting 1,4-diazinium (pyrazinium, quinoxalinium, pyrido[2,3-*b*]pyrazinium, pteridinium, *etc*.) salts with enamines, diketones, ureas, thioureas, thioamides, thiohydrazides, dithiocarbamates, iminoesters, amidines, amidrazones, 1,2-diamines, amidoximes and other 1,3- and 1,4-bifunctional nucleophiles.[1,14,35–38] The tandem reactions of bifunctional nucleophiles at C-5 and C-6 of the 1,2,4-triazine ring proved to be an efficient route to condensed 1,2,4-triazines.[1,14,39–43] In particular, the reaction of 3-aryl-1,2,4-triazines, activated by acetic anhydride with β-aminovinyl ketones or β-aminocrotonate in acetic anhydride proceeds very smoothly and regioselectively leading to the derivatives of 1*H*-pyrrolo-[3,2-*e*]-1,2,4-triazines (Scheme 14).[43]



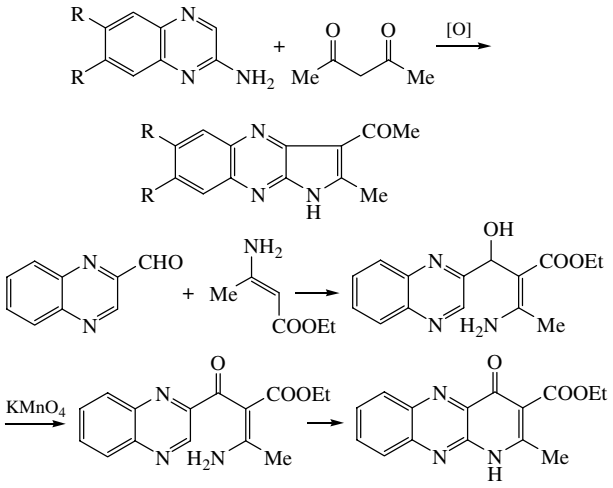
Scheme 14

Scheme 15 shows that not only condensed 1,2,4-triazines but also fused pyridines can be obtained through the tandem S_N^H–S_N^H reactions of 1,2,4-triazines.[44]



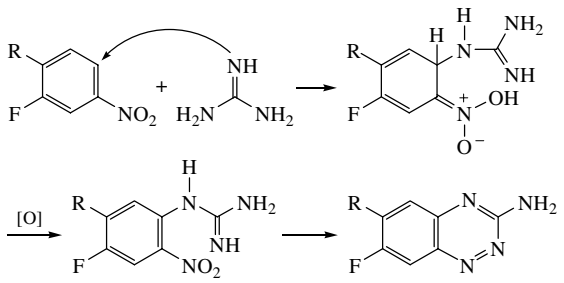
Scheme 15

An effective approach to condensed azaheterocycles is the use of intramolecular nucleophilic substitution of hydrogen in combination with condensation on an *exo*-cyclic substituent. The key role of the S_N^H step has been demonstared by the synthesis of quinoxalines condensed with five- and seven-membered rings from 2-aminoquinoxaline[45] or quinoxaline-2-carbaldehyde (Scheme 16).[46]



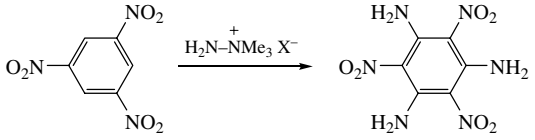
Scheme 16

The synthesis of fluorinated 1,2,4-benzotriazines illustrates the advantage of the oxidative S_N^H reaction as a key step in the modification of fluorinated nitrobenzenes with guanidine followed by annelation of the 1,2,4-triazine ring (Scheme 17).[47]



Scheme 17

The S_N^H methodology is important in both materials science and industry. Indeed, a new strategy for obtaining di- and terpyridines and their luminescent ruthenium chelates,[48,49] as well as the large-scale synthesis of *para*-nitroaniline from nitrobenzene, and also direct amination of 1,3,5-trinitrobenzene into 1,3,5-triamino-2,4,6-trinitrobenzene (Scheme 18) have been advanced. Note that these chlorine-free technologies are not only technically effective but also environmentally friendly and consistent with the principles of green chemistry.[16,20]



Scheme 18

In conclusion, note that the S_N^H methodology and related reactions belong to a rapidly developing area of organic chemistry. Experimental data demonstrate that the S_N^H reactions are similar to S_EAr, and they reflect a fundamental nature of aromatic systems. They provide facile routes to new carbon–carbon C(sp^2)–C(sp^3), C(sp^2)–C(sp^2) and C(sp^2)–C(sp) bonds, as well as C(sp^2)–O, C(sp^2)–N, C(sp^2)–P, C(sp^2)–S and C(sp^2)–Hal bonds, *i.e.*, the chemical bonds the formation of which has earlier been associated with electrophilic aromatic substitution reactions. We believe that the S_N^H methodology is a promising synthetic tool, which will be especially useful in the future when the role of coal as a raw material will be much higher. Then, the S_N^H methods for chemical transformations of pyridine bases are supposed to be in a great demand.

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References

1 O. N. Chupakhin, V. N. Charushin and H. C. van der Plas, *Nucleophilic Aromatic Substitution of Hydrogen*, New York, Academic Press, 1994.
2 O. N. Chupakhin and I. Ya. Postovsky, *Usp. Khim.*, 1976, **45**, 908 (*Russ. Chem. Rev.*, 1976, **45**, 454).
3 H. C. van der Plas and M. Wozniak, *Croat. Chem. Acta*, 1986, **95**, 33.
4 M. Makosza and J. Winiarski, *Acc. Chem. Res.*, 1987, **20**, 282.
5 O. N. Chupakhin, V. N. Charushin and H. C. van der Plas, *Tetrahedron*, 1988, **44**, 1.
6 M. Makosza, *Usp. Khim.*, 1989, **58**, 1298 (*Russ. Chem. Rev.*, 1989, **58**, 747).
7 F. Terrier, in *Organic Nitro Chemistry Series*, ed. H. Feuer, VCN Publishers, New York, 1991.
8 M. Makosza, *Pol. J. Chem.*, 1992, **66**, 3.
9 M. Makosza, *Izv. Akad. Nauk, Ser. Khim.*, 1996, 531 (*Russ. Chem. Bull.*, 1996, **45**, 491).
10 D. N. Kozhevnikov, V. L. Rusinov and O. N. Chupakhin, *Usp. Khim.*, 1998, **67**, 707 (*Russ. Chem. Rev.*, 1998, **67**, 633).
11 A. V. Gulevskaya and A. F. Pozharskii, *Targets in Heterocyclic Systems*, 1999, **2**, 101.
12 D. N. Kozhevnikov, V. L. Rusinov and O. N. Chupakhin, *Adv. Heterocycl. Chem.*, 2002, **82**, 26.
13 O. N. Chupakhin and D. N. Beresnev, *Usp. Khim.*, 2002, **71**, 803 (*Russ. Chem. Rev.*, 2002, **71**, 707).
14 V. N. Charushin and O. N. Chupakhin, *Pure Appl. Chem.*, 2004, **76**, 1621.
15 M. Makosza and K. Wojciechowskii, *Chem. Rev.*, 2004, **104**, 2631.
16 O. N. Chupakhin and V. N. Charushin, in *Green Chemistry in Russia*, eds. V. Lunin, P. Tundo and E. Lokteva, INCA, 2005, p. 19.
17 I. N. Egorov, G. V. Zyryanov, V. L. Rusinov and O. N. Chupakhin, *Usp. Khim.*, 2005, **74**, 1176 (*Russ. Chem. Rev.*, 2005, **74**, 1073).
18 A. I. Matern, V. N. Charushin and O. N. Chupakhin, *Usp. Khim.*, 2007, **76**, 27 (*Russ. Chem. Rev.*, 2007, **76**, 23).
19 R. Morrison and R. Boyd, *Organic Chemistry*, 2nd edn., Allyn and Backon, Inc., Boston, 1970.
20 I. Arends, R. Sheldon and U. Hanefeld, *Green Chemistry and Catalysis*, Wiley-VCH, Weinheim, 2007.
21 *Name Reactions and Reagents in Organic Synthesis*, 2nd edn., eds. B. P. Mundy, M. G. Ellerd and F. G. Favaloro, Jr., Wiley-Interscience, New York, 2005.
22 D. N. Kozhevnikov, V. N. Kozhevnikov, A. M. Prokhorov, M. M. Ustinova, V. L. Rusinov, O. N. Chupakhin, G. G. Aleksandrov and B. Konig, *Tetrahedron Lett.*, 2006, **47**, 869.
23 (*a*) M. Makosza and M. Bialecki, *J. Org. Chem.*, 1992, **57**, 4784; (*b*) Z. Wrobel and M. Makosza, *Tetrahedron*, 1997, **53**, 5501.
24 D. N. Kozhevnikov, V. L. Rusinov, O. N. Chupakhin, M. Makosza, A. Rykowski and E. Wolinska, *Eur. J. Org. Chem.*, 2002, 1412.
25 A. F. Pozharsky and A. M. Simonov, *Aminirovanie geterotsiklov po Chichibabinu* (*Chichibabin Amination of Heterocycles*), Rostov-on-Don University Press, USSR, 1971.
26 H. C. van der Plas, V. N. Charushin and A. Veldhuizen, *J. Org. Chem.*, 1983, **48**, 1354.
27 (*a*) O. N. Chupakhin, A. M. Prokhorov, D. N. Kozhevnikov, V. L. Rusinov, V. N. Kalinin, V. A. Olshevskaya, I. V. Glukhov and M. Yu. Antipin, *Mendeleev Commun.*, 2003, 165; (*b*) A. M. Prokhorov, D. N. Kozhevnikov, V. L. Rusinov, O. N. Chupakhin, I. V. Glukhov, M. Yu. Antipin, O. N. Kazheva, A. N. Chekhlov and O. A. Dyachenko, *Organometallics*, 2006, **25**, 2972.
28 O. N. Chupakhin, I. A. Utepova, I. S. Kovalev, V. L. Rusinov and Z. A. Starikova, *Eur. J . Org. Chem.*, 2007, 857.
29 G. L. Rusinov, E. B. Gorbunov, V. N. Charushin and O. N. Chupakhin, *Tetrahedron Lett.*, 2007, **48**, 5873.
30 D. G. Beresnev, N. A. Itsikson, O. N. Chupakhin, V. N. Charushin, M. I. Kodess, A. I. Butakov, G. L. Rusinov, Yu. Yu. Morzherin, A. I. Konovalov and I. S. Antipin, *J. Org. Chem.*, 2006, **71**, 8272.
31 (*a*) O. N. Chupakhin, G. L. Rusinov, D. G. Beresnev, S. Sh. Bashirov, M. G. P. M. S. Neves and J. A. S. Cavaleiro, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 155 (*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 160); (*b*) O. N. Chupakhin, G. L. Rusinov, N. A. Itsikson and D. G. Beresnev, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 1297 (*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 1351); (*c*) O. N. Chupakhin, N. A. Itsikson, S. Sh. Bashirov, D. G. Beresnev and G. L. Rusinov, *Heterocycles*, 2005, **67**, 543.
32 (*a*) M. O. Senge and I. Bischoff, *Heterocycles*, 2005, **65**, 879; (*b*) M. B. Bakar, K. Dahms and M. O. Senge, *Abstracts of the 15th European Symposium on Organic Chemistry*, University College Dublin, Ireland, 2007, p. 52.
33 O. N. Chupakhin, Yu. A. Azev, S. G. Alexeev, S. V. Shorshnev, E. Tsoi and V. N. Charushin, *Mendeleev Commun.*, 1992, 151.
34 O. N. Chupakhin, D. G. Beresnev and N. A. Itsikson, *Mendeleev Commun.*, 2006, 95.
35 V. N. Charushin and O. N. Chupakhin, *Usp. Khim.*, 1984, **53**, 1648 (*Russ. Chem. Rev.*, 1984, **53**, 956).
36 (*a*) V. N. Charushin, O. N. Chupakhin and H. C. van der Plas, *Adv. Heterocycl. Chem.*, 1988, **43**, 301; (*b*) V. N. Charushin, O. N. Chupakhin and A. I. Rezvukhin, *Heterocycles*, 1981, **16**, 195; (*c*) V. N. Charushin, G. A. Mokrushina, G. M. Petrova, G. G. Alexandrov and O. N. Chupakhin, *Mendeleev Commun.*, 1998, 133.
37 (*a*) V. N. Charushin, O. N. Chupakhin and A. I. Chernyshev, *Prog. Nucl. Magn. Reson. Spectrosc.*, 1988, **20**, 95; (*b*) V. N. Charushin, A. I. Chernyshev, N. N. Sorokin and O. N. Chupakhin, *Org. Magn. Reson.*, 1984, **22**, 775; (*c*) V. N. Charushin, N. N. Sorokin, A. I. Chernyshev, V. G. Baklykov, V. G. Ponizovsky and O. N. Chupakhin, *Magn. Reson. Chem.*, 1986, **24**, 777.

38 (*a*) G. L. Rusinov, P. A. Slepukhin, V. N. Charushin, O. A. Dyachenko, O. N. Kazheva, A. N. Chekhlov, E. V. Verbitsky, M. I. Kodess and O. N. Chupakhin, *Mendeleev Commun*., 2006, 26; (*b*) G. L. Rusinov, P. A. Slepukhin, V. N. Charushin and O. N. Chupakhin, *Mendeleev Commun*., 2001, 78.

39 (*a*) V. N. Charushin, S. G. Alexeev, O. N. Chupakhin and H. C. van der Plas, *Adv. Heterocycl. Chem*., 1989, **46**, 73; (*b*) S. G. Alexeev, V. N. Charushin, O. N. Chupakhin and G. G. Alexandrov, *Tetrahedron Lett.*, 1988, **29**, 1431; (*c*) A. M. Prokhorov, D. N. Kozhevnikov, V. L. Rusinov and O. N. Chupakhin, *Pol. J. Chem*., 2003, **77**, 1157.

40 O. N. Chupakhin, B. V. Rudakov, S. G. Alexeev and V. N. Charushin, *Heterocycles*, 1992, **33**, 931.

41 O. N. Chupakhin, G. L. Rusinov, D. G. Beresnev, V. N. Charushin and H. Neunhoeffer, *J. Heterocycl. Chem*., 2001, **38**, 901.

42 V. N. Charushin, N. N. Mochulskaya, A. A. Andreiko, M. I. Kodess and O. N. Chupakhin, *Mendeleev Commun*., 2002, 28.

43 (*a*) V. N. Charushin, N. N. Mochulskaya, A. A. Andreiko, V. I. Filyakova, M. I. Kodess and O. N. Chupakhin, *Tetrahedron Lett.*, 2003, **44**, 2421; (*b*) N. N. Mochul'skaya, A. A. Andreiko, M. I. Kodess, E. B. Vasil'eva, V. I. Filyakova, A. T. Gubaidullin, I. A. Litvinov, O. G. Sinyashin, G. G. Alexandrov and V. N. Charushin, *Izv. Akad. Nauk, Ser. Khim*., 2004, 1228 (*Russ. Chem. Bull., Int. Ed*., 2004, **53**, 1279).

44 M. M. Krayushkin, V. N. Yarovenko, I. P. Sedishev, A. A. Andreiko, N. N. Mochulskaya and V. N. Charushin, *Mendeleev Commun*., 2005, 151.

45 S. K. Kotovskaya, V. N. Charushin, N. M. Perova, M. I. Kodess and O. N. Chupakhin, *Synth. Commun*., 2004, **34**, 2531.

46 (*a*) M. G. Ponizovsky, A. M. Boguslavsky, M. I. Kodess, V. N. Charushin and O. N. Chupakhin, *Mendeleev Commun*., 2002, 68; (*b*) V. N. Charushin, A. M. Boguslavsky, M. G. Ponyzovsky, M. I. Kodess, A. N. Chekhlov, Sh. G. Mikoyan and S. M. Aldoshin, *Izv. Akad. Nauk, Ser. Khim*., 2004, 1216 (*Russ. Chem. Bull., Int. Ed*., 2004, **53**, 1267).

47 G. A. Zhumabaeva, S. K. Kotovskaya, N. N. Perova, V. N. Charushin and O. N. Chupakhin, *Izv. Akad. Nauk, Ser. Khim*., 2006, 1196 (*Russ. Chem. Bull., Int. Ed*., 2006, **55**, 1243).

48 (*a*) D. N. Kozhevnikov, V. N. Kozhevnikov, T. V. Nikitina, V. L. Rusinov, O. N. Chupakhin and H. Neunhoeffer, *Mendeleev Commun*., 2002, 30; (*b*) D. N. Kozhevnikov, V. N. Kozhevnikov, T. V. Nikitina, V. L. Rusinov, O. N. Chupakhin, I. L. Eremenko and G. G. Aleksandrov, *Tetrahedron Lett*., 2002, **43**, 4923; (*c*) V. N. Kozhevnikov, D. N. Kozhevnikov, T. V. Nikitina, V. L. Rusinov, O. N. Chupakhin, M. Zabel and B. Konig, *J. Org. Chem*., 2003, **68**, 2882.

49 (*a*) V. N. Kozhevnikov, D. N. Kozhevnikov, V. L. Rusinov, O. N. Chupakhin and B. König, *Synthesis*, 2003, 2400; (*b*) V. N. Kozhevnikov, D. N. Kozhevnikov, O. V. Shabunina, V. L. Rusinov, O. N. Chupakhin, M. Zabel and B. Konig, *Mendeleev Commun*., 2005, 6; (*c*) V. N. Kozhevnikov, D. N. Kozhevnikov, O. V. Shabunina, V. L. Rusinov and O. N. Chupakhin, *Tetrahedron Lett*., 2005, **46**, 1791.

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