Russian Journal of Organic Chemistry, Vol. 41, No. 4, 2005, pp. 473–504. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 4, 2005, pp. 487–516.

REVIEW

Nitrenium Ions and Problem of Direct Electrophilic Amination of Aromatic Compounds

G. I. Borodkin and V. G. Shubin

Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences, pr. Akademika Lavrent'eva 9, Novosibirsk, 630090 Russia
e-mail: gibor@nioch.nsc.ru

Received May 26, 2004

Abstract—Published data on direct electrophilic amination of aromatic compounds are summarized and analyzed on the basis of nitrenium ion properties.

Gennadii Borodkin was born in 1946 in Samara (former Kuibyshev). In 1970, he graduated from the Novosibirsk State University. Candidate of chemical sciences since 1976; Doctor of chemical sciences since 1993; Full Member of the International Academy of Sciences of Ecology, Human Safety, and Nature; Professor at the Organic Chemistry Department, Novosibirsk State University; Leading scientist of the Organic Reaction Mechanisms Laboratory, Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences. Fields of scientific interest: chemistry of carbocations and onium ions, molecular rearrangements, physical organic chemistry, and ecological aspects of electrophilic reactions.

Vyacheslav Shubin was born in 1936 in Esiplevo village, Ivanovo region. In 1959, he graduated from the Moscow State University; Candidate of chemical sciences since 1976; Doctor of chemical sciences, Professor since 1993. Head of a laboratory at the Vorozhtsov Novosibirsk Institute of Organic Chemistry, Siberian Division, Russian Academy of Sciences. Fields of scientific interest: theoretical and applied problems of fine organic synthesis, chemistry of carbocations and organic cationic complexes, molecular rearrangements, "green chemistry."

1. INTRODUCTION

Aromatic amines constitute an important class of organic compounds which give rise to a broad spectrum of practical applications. An arylamino group is a structural fragment of many medical agents (antibiotics, analgetics, antiseptics, etc.) [1–3], pesticides [4], dyes [5, 6], luminophores [6], and materials for lasers and electronics [6, 7]. Aromatic amines are key intermediate products in the synthesis of various practically important organic compounds via diazotization, nucleophilic substitution, and condensations [2, 4, 6]. Arylamines also constitute an important class of chemical carcinogens whose action is based on their enzymatic oxidation to hydroxylamines, followed by amination of DNA fragments [8–16].

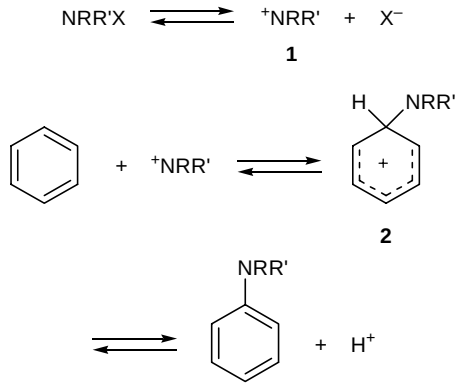
Substitution of hydrogen in an aromatic ring is usually a two- or multistep process including introduction of an intermediate functional group or an atom which is then transformed into amino group [2, 5, 17–20]. An example is the Buchwald–Hartwig reaction which has widely been used in the last decade to convert aryl halides into N-substituted arylamines [20].

The present review discusses methods of direct electrophilic substitution of hydrogen in aromatic

1070-4280/05/4104-0473

compounds by amino group. A number of these methods have been developed in the recent years, and they are based mainly on the concept implying participation of nitrenium ions **1** and cationic σ-complexes **2** as intermediates [16, 21] (Scheme 1).

Scheme 1.



The review was aimed at analyzing and systematizing the data published over the last decade on the direct electrophilc amination of aromatic compounds. Some earlier publications were also involved if it was necessary to understand the problems under discussion and reveal new trends in this field.

2. ELECTRONIC STRUCTURE AND PROPERTIES OF NITRENIUM IONS

Let us consider the electronic structure of nitrenium ions and related electron-deficient species which are usually assumed to be reactive intermediates in electrophilic amination of aromatic compounds. Nitrenium ions possess six electrons and a vacant *p* orbital on the nitrogen atom; therefore, they can exist in the singlet (S) or triplet (T) state [15, 16, 21]. In the singlet state, electrons with antiparallel spins occupy a σ orbital which has a lower energy than *p* orbital (Fig. 1) [15]. In the triplet state, the electron spins are parallel, and they are distributed over partially occupied σ and *p* orbitals. To a first approximation, the energy difference between the singlet and triplet states (ΔE_{ST}) is determined by the diference in the energies of the two nonbonding orbitals (*p* and σ). Insofar as the σ orbital is characterized by a greater *s* order, its energy is lower. On the other hand, electron repulsion and exchange interaction (Hund's rule) favor σ,*p*-configuration. The predominant existence of nitrenium ions in the S- or T-state is important, for this factor determines their reactivity toward arenes. Singlet nitrenium ions possess a vacant *p* orbital and unshared electron pair; therefore, they can act as Lewis acids and bases. By contrast, triplet nitrenium ions possess unpaired electrons which could give rise to radical processes. The energy difference ΔE_{ST} is usually determined directly by photoelectron spectroscopy; however, the application of the same method to large nitrenium ions is difficult because of a vast number of vibrational bands which obscure electronic terms [15]. Therefore, most ΔE_{ST} values were obtained by quantum-chemical calculations.

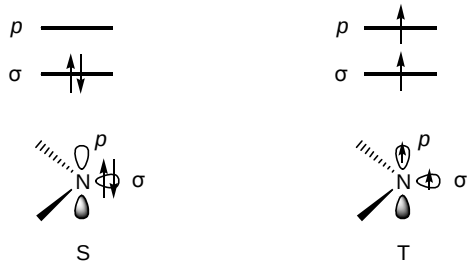
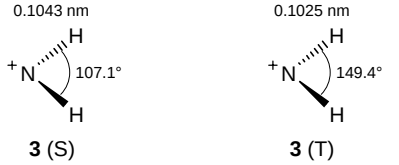


Fig. 1. Schematic representation of the shape of orbitals and their population in nitrenium ions in the singlet and triplet states.

Up to now, quantum-chemical calculations were performed for a wide variety of nitrenium ions: NH_2^+ [22–40], $MeNH^+$ [22, 24, 25, 30, 36, 41], Me_2N^+ [22, 24, 25, 30, 41], $MeAcN^+$ [22], $(CH_2)_2N^+$ [42], $(CH_2)_4N^+$, $(CH_2)_5N^+$ [22, 24, 25], (XCH=CH)MeN^+ (X = H, Cl) [25], $(CH)_2N^+$, CHN_2^+ [43], $(CH)_6N^+$ [44], XN_3^+ (X = O, S, Se, Te) [45], XNH^+ (X = NH_2, PH_2, OR, SH, Cl, F, Br, I, CN, NC_2) [23, 27, 28, 32, 34, 36, 40, 46], $X(CHO)N^+$ [X = N, NH_2, PH_2, OR, SH, $Ph(CH_2)_nO$] [23, 47], $ArNH^+$ [22, 23, 25, 41, 48–65], $ArMeN^+$ [41, 66–69], Ar(*t*-Bu)N^+ [25], $Ph(CHO)N^+$ [23], $ArAcN^+$ [22, 41, 52, 56, 57], Ar_2N^+ [51, 52, 59, 61], X_2N^+ {X = F [27, 28, 40, 70–77], Cl, Br, I [27, 28, 32, 40], X = NH_2, PH_2 [78], N_2 [79–82], N_3 [83, 84], N_4 [85], $(CO)_2$ [81]}, $F(OH)N^+$ [86, 87], $FClN^+$ [40].

Unsubstituted nitrenium ion H_2N^+ (**3**) exists mainly in the triplet state, and the energy difference between the singlet and triplet states was estimated at 89–152 kJ/mol [22–40]. The best agreement with the experimental value (ΔE_{ST} = 125.9 kJ/mol [88]) was obtained by *ab initio* calculations (ΔE_{ST} = 125.8 kJ/mol, CASSCF-MRCI+ZPVE; ΔE_{ST} = 125.6 kJ/mol, TZ2P(*f*,*d*)CASSCF(6,6)-SOCI+ZPVE [33]). *Ab initio*



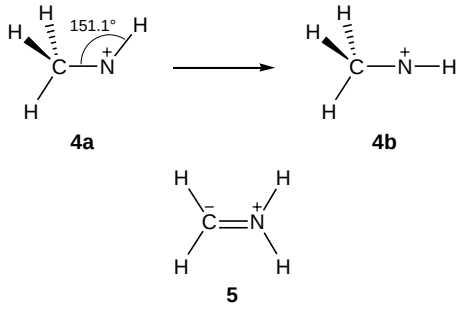
3 (S) **3** (T)

calculations [MP4(SDTQ)/6-311+G(3*d*2*f*,2*p*)//MP2/6-311+G(3*d*,2*p*)] showed that both singlet and triplet states of H_2N^+ ion have an angular structure and that the HNH angle in the triplet state is considerably greater [24].

Using the results of calculation of the potential energy surface for NH_2^+ ion in the X^3B_1 state [26], Osmann *et al*. [38] found that the energy of activation for the transformation of the angular structure into linear is very small, 1.9 kJ/mol. Taking into account that this barrier is lower than the zero-point energy of the bending vibration, NH_2^+ ion may be regarded as quasilinear [89].

According to the calculations [22, 24, 25, 30, 36, 41], the ground state of $MeNH^+$ ion is triplet **4a** with a CNH angle of 151.1° [*ab initio*, HF/6-31G(*d*)], and structure **4a** is converted into linear form **4b** through a low activation barrier (E_a = 4.1 kJ/mol) [24] (Scheme 2). None of the configurations found for the singlet state of $MeNH^+$ corresponds to a minimum on the potential energy surface; the minimum is occupied by structure **5** with a C_{2v} symmetry [24].

Scheme 2.

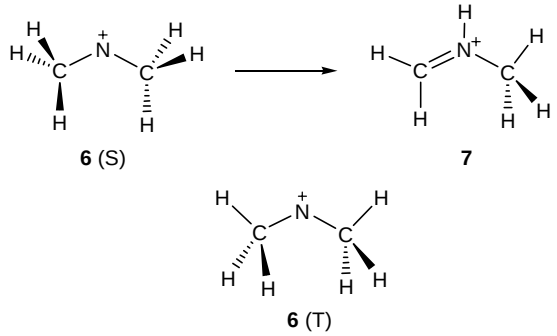


4a **4b**

5

Like $MeNH^+$, the singlet state of dimethylnitrenium ion (S)-**6** does not occupy a minimum on the potential energy surface [MP2(full)/6-31G(*d*)], and it is readily converted into iminium ion **7** [E_a = 18.8 kJ/mol, HF/6-31G(*d*)] [24] (Scheme 3). *Ab initio* [24] and

Scheme 3.

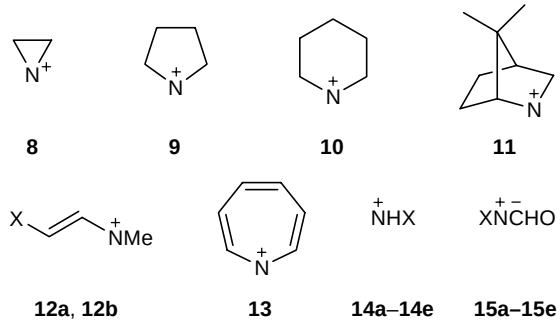


6 (S) **7**

6 (T)

MNDO calculations [22, 25] of Me_2N^+ ion predict greater stability of triplet state (T)-**6** relative to (S)-**6**, while the results of AM1-CI calculations [25] prefer the singlet state.

According to *ab initio* calculations [24, 42], the triplet state of cyclic nitrenium ions $(CH_2)_2N^+$ and $(CH_2)_5N^+$ is more favorable than the singlet state, while with $(CH_2)_4N^+$ the situation is the reverse. Semiempirical MNDO and AM1-CI calculations of ions **8**–**11** predict greater stability of their singlet states [22, 24, 25]. Likewise, the opposite pattern is observed for vinylnitrenium ion (**12a**) [25]. The singlet state was found by *ab initio* calculations to be more favorable for an analog of tropylium ion, azepinyl cation **13**, as well as for cation **12b** [25, 44].

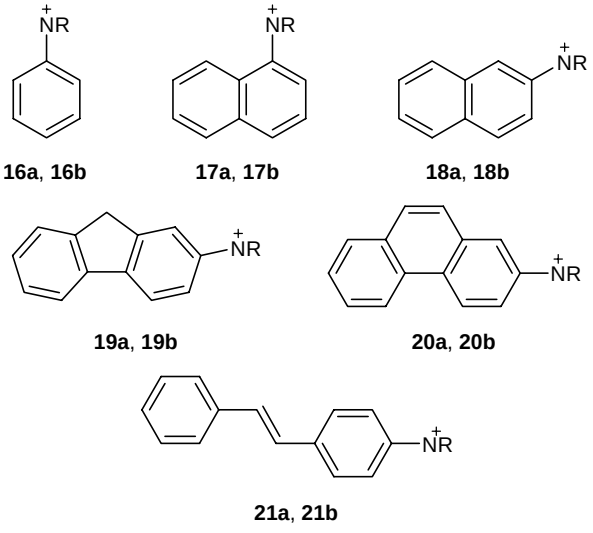


8 **9** **10** **11**

12a, **12b** **13** **14a–14e** **15a–15e**

12, X = H (**a**), Cl (**b**); **14**, **15**, X = NH_2 (**a**), PH_2 (**b**), OH (**c**), OMe (**d**), SH (**e**).

Study of the effect of the X substituent in nitrenium ions XNH^+ (**14a–14e**) and $(OCH)XN^+$ (**15a–15e**) on the relative stability of the S- and T-states showed that donor groups stabilize the singlet state to a greater



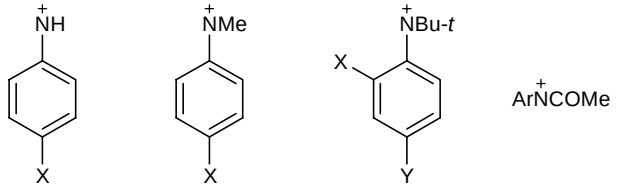
16a, **16b** **17a**, **17b** **18a**, **18b**

19a, **19b** **20a**, **20b**

21a, **21b**

R = H (**a**), Ac (**b**).

extent [23]. High-level *ab initio* calculations (QCISD, B3LYP) predicted greater stability of the triplet state of $NCNH^+$ [34], while $HlgNH^+$ and Hlg_2N^+ (Hlg = F, Cl, Br, I) were found [MP4/6-311G(2*df*)+ZPE] to be more stable in the singlet state [27, 28]. Arylnitrenium ions **16**–**21** are also more stable in the singlet state [22, 25, 49, 51, 53, 57]. Increase in the acceptor power of the substituent in the aromatic ring in nitrenium ions **22**–**24** destabilizes the singlet state relative to triplet [25, 53, 69]. An analogous relation is observed for ions **25a–25c** [57].

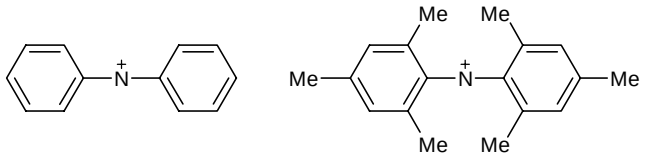


22a–24n **23a–24d** **24a–24d** **25a–25c**

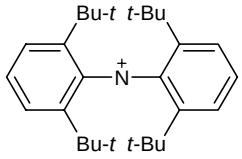
22, X = NMe_2 (**a**), NH_2 (**b**), OH (**c**), MeO (**d**), Me (**e**), CHO (**f**), COOH (**g**), CO_2Me (**h**), COMe (**i**), CF_3 (**j**), CN (**k**), Cl (**l**), F (**m**), NO_2 (**n**); **23**, X = Me (**a**), Cl (**b**), Ph (**c**), MeO (**d**); **24**, X = Y = H (**a**); X = H, Y = Br (**b**); X = Ac, Y = H (**c**), Br (**d**); **25**, Ar = 4-biphenylyl (**a**), 3-pyridyl (**b**), 4-pyrimidinyl (**c**).

A linear correlation between ΔE_{ST} and substituent constants σ^+ (or σ_R^+) was revealed for ions **16a** and **22a–22n**. This fact suggests a strong similarity between arylnitrenium ions and benzyl cations in which resonance interaction between the substituent in the aromatic ring and the cationic center is important [53]. *Ab initio* and AM1 calculations of bi- and polycyclic nitrenium ions **17a**, **18a**, and **26–30** showed that the stability of $ArNH^+$ ions increases with extension of the aromatic π system and that the barrier to interconversion of *syn* and *anti* isomers is fairly high [48, 55]. According to the B3LYP/6-31G* calculations, fluorinated arylnitrenium ion **31** exists in the singlet state, and the energy difference between the singlet and triplet states is as large as ~84 kJ/mol [58]. By contrast, HF/6-31G* calculations showed that the ground state of **31** is triplet and that the energy gap ΔE_{ST} is small (21 kJ/mol) [58].

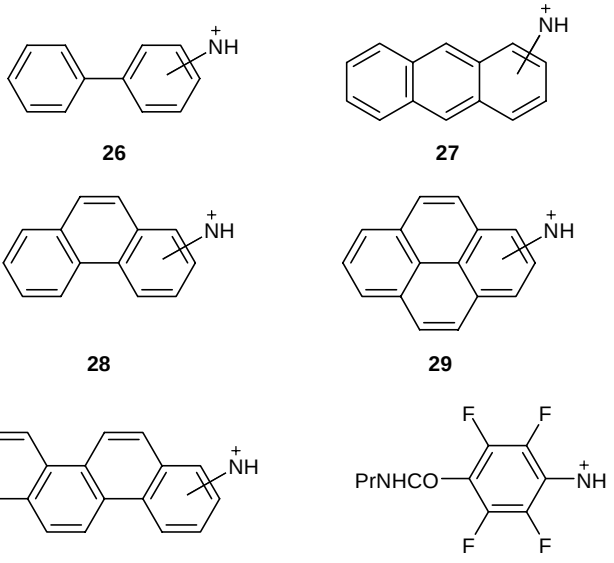
In keeping with the results of AM1 study, the singlet state of arylnitrenium ions $R(Ph)N^+$ becomes less stable than the triplet state as the size of the R substituent rises (*t*-Bu > H) [25]. An analogous effect is produced by rupture of conjugation between the phenyl ring and the NR^+ fragment, caused by introduction of bulky groups into the *ortho* positions in diarylnitrenium ions **32**–**34**; unlike cations **32** and **33**, the triplet state of ion **34** is more stable than the singlet state (AM1) [51].



32 **33**

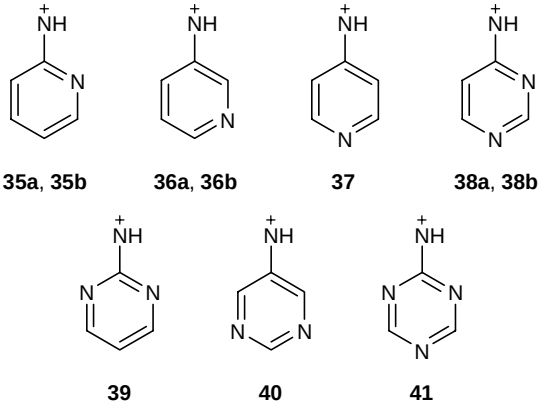


34



26 **27** **28** **29** **30** **31**

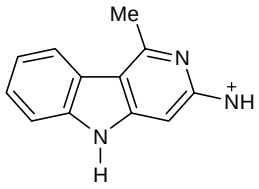
Replacement of a CH fragment in the aromatic ring of arylnitrenium ion by nitrogen atom also destabilizes the S-state relative to T, and the effect becomes stronger in going from *ortho* to *meta* and *para* posi-



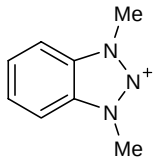
35a, **35b** **36a**, **36b** **37** **38a**, **38b**

39 **40** **41**

35, **36**, **38**, *syn* (**a**), *anti* (**b**).



42a, **42b**



43

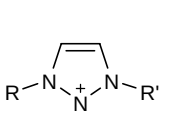
42, *syn* (**a**), *anti* (**b**).

tions, as well as with increase in the number of nitrogen atoms introduced into the ring (cf. ions **35**–**41**) [57]. A large difference in the relative free energies of the *syn* and *anti* isomers of ion **35** in the singlet state (21.8 kJ/mol) was explained [57] by the anomeric effect and by favorable electrostatic interaction between the NH hydrogen atom and lone electron pair on the nitrogen atom in position *2* of the *syn* isomer. The same factors may be responsible for the greater stability of *syn* isomer **42a** relative to *anti* isomer **42b** ($\Delta\Delta H_f$ = 31.8 kJ/mol) [55].

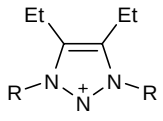
The singlet ground state was found for cyclic nitrenium ions of the dihydrotriazole (**43**–**47**) and tetrahydrotriazole series (**48**–**50**) [90–102]. According to the BPW91/cc-pVDZ *ab initio* calculations, the ΔE_{ST} value for 1,3-dimethylbenzotriazolyl cation **43** is –270.7 kJ/mol, which is well consistent with that found experimentally using the laser flash photolysis technique (–276±13 kJ/mol) [90]. The large absolute value of ΔE_{ST} may be rationalized in terms of the presence of two nitrogen atoms contiguous to the cationic center; their lone electron pairs are involved in conjugation, thus making the dihydrotriazolyl cation system aromatic. The occurrence of conjugation therein follows from the X-ray diffraction data for salts containing cations **44**–**50** [91, 94–96, 98, 100]. The nitrogen–nitrogen bonds in **44**–**50** have intermediate lengths (1.271–1.327 Å) between ordinary N–N (1.425 Å) and double N=N bonds (1.240 Å) [103].

As might be expected for charged systems, the ΔE_{ST} values change considerably if solvation of nitrenium ions **16b**, **25**, and **35**–**41** with water molecules is taken into account in terms of the SM5.42R/BPW91/DZVP model; here, the singlet state is stabilized to a greater extent than the triplet state [57].

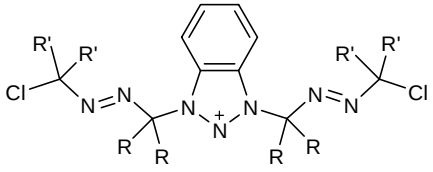
Another factor which may be responsible for the reactivity of nitrenium ions with respect to arenes is the magnitude of the positive charge on the nitrogen atom. Calculations performed by different quantum-chemical methods (Tables 1, 2; Fig. 2) give ambiguous electron density distribution patterns even for a single cation. This ambiguity results in part from different approaches to estimation of charges. Therefore, the most reliable is to consider the charge distribution pat-



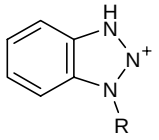
44a–**46c**



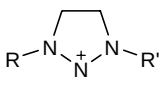
45



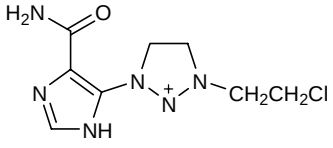
46a, **46b**



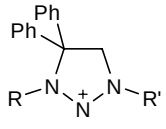
47a, **47b**



48a–**48c**



49



50

44, R = R' = H (**a**); R = Me, R' = $PhCH_2$ (**b**); R = R' = $PhCH_2$ (**c**); **45**, R = 2,4,6-$Cl_3C_6H_2$; **46**, R = R' = Me (**a**); RR' = $(CH_2)_5$ (**b**); **47**, R = H (**a**), OH (**b**); **48**, R = R' = H (**a**), R = H, R' = Ph (**b**); R = Me, R' = Ph (**c**); **50**, R = 2,4,6-$Cl_3C_6H_2$.

Table 1. Calculated (*ab initio*) charges on atoms (q) in nitrenium ions NHX^+ and NXY^+

Ion	$^1A_1$			$^3B_1$		
	q_N	q_H	$q_{X,Y}$	q_N	q_H	$q_{X,Y}$
NH_2^+ [a]	–0.138	0.569	4	–0.28	0.642	
NHF^+ [a]	0.520	0.547	–0.067	0.449	0.655	–0.104
$NHCl^+$ [a]	–0.327	0.512	0.815	–0.561	0.615	0.946
$NHBr^+$ [a]	–0.504	0.494	1.010	–0.608	0.595	1.013
NHI^+ [a]	–0.749	0.471	1.278	–0.867	0.570	1.297
NF_2^+ [a]	1.164		–0.082	1.096		–0.048
NCl_2^+ [a]	–0.204		0.602	–0.378		0.689
NBr_2^+ [a]	–0.470		0.735	–0.572		0.786
NI_2^+ [a]	–0.864		0.932	–0.950		0.975
NMe_2^+ [b]	–0.120		0.560			
$NMeCOMe^+$ [b]	–0.131		0.585 0.546			

[a] MP2/6-31G(*d*) [28].
[b] 3-21G basis set [41].

Table 2. Charges on atoms (q) in aryl-substituted nitrenium ions $PhNR^+$

R	Method	q							Reference
		N	C^1	C^2	C^3	C^4	C^5	C^6	
H	MNDO	0.001	–0.065	0.233	–0.010	0.382	–0.041	0.346	[22]
H	CNDO/2	0.123	[a]	0.112	[a]	0.169	[a]	0.112	[21]
H	HF/3-21G	–0.136	0.220	0.315	0.042	0.274	0.054	0.230	[48]
H	HF/6-31G(*d*)	–0.363[b]	[a]	[a]	[a]	[a]	[a]	[a]	[55]
H	DFT ESP	–0.43	0.44	0.01	–0.12	0.16	–0.07	–0.09	[52]
C(O)Me	DFT ESP	–0.51	0.54	–0.05	–0.10	0.14	–0.06	–0.15	[52]
Ph	DFT ESP	–0.45	0.41	–0.10	–0.08	0.05	–0.10	–0.10	[52]

[a] No data were given.
[b] NPA calculations.

terns obtained in terms of a single quantum-chemical method. The data in Table 1 show that MP2/6-31G(*d*) calculations of nitrenium ions XYN^+ give a negative total charge on the nitrogen atom when X, Y = H, Cl, Br, I. Nonempirical calculations of arylnitrenium ions $Ar(R)N^+$ also showed a negative charge on the nitrogen atom (Table 2, Fig. 2), and in many cases a considerable part of the positive charge is localized on the carbon atoms in the *ortho* and *para* positions with respect to the NR fragment. Correspondingly, aryl-substituted nitrenium ions can act as both N- and C-electrophiles in reactions with arenes. According to

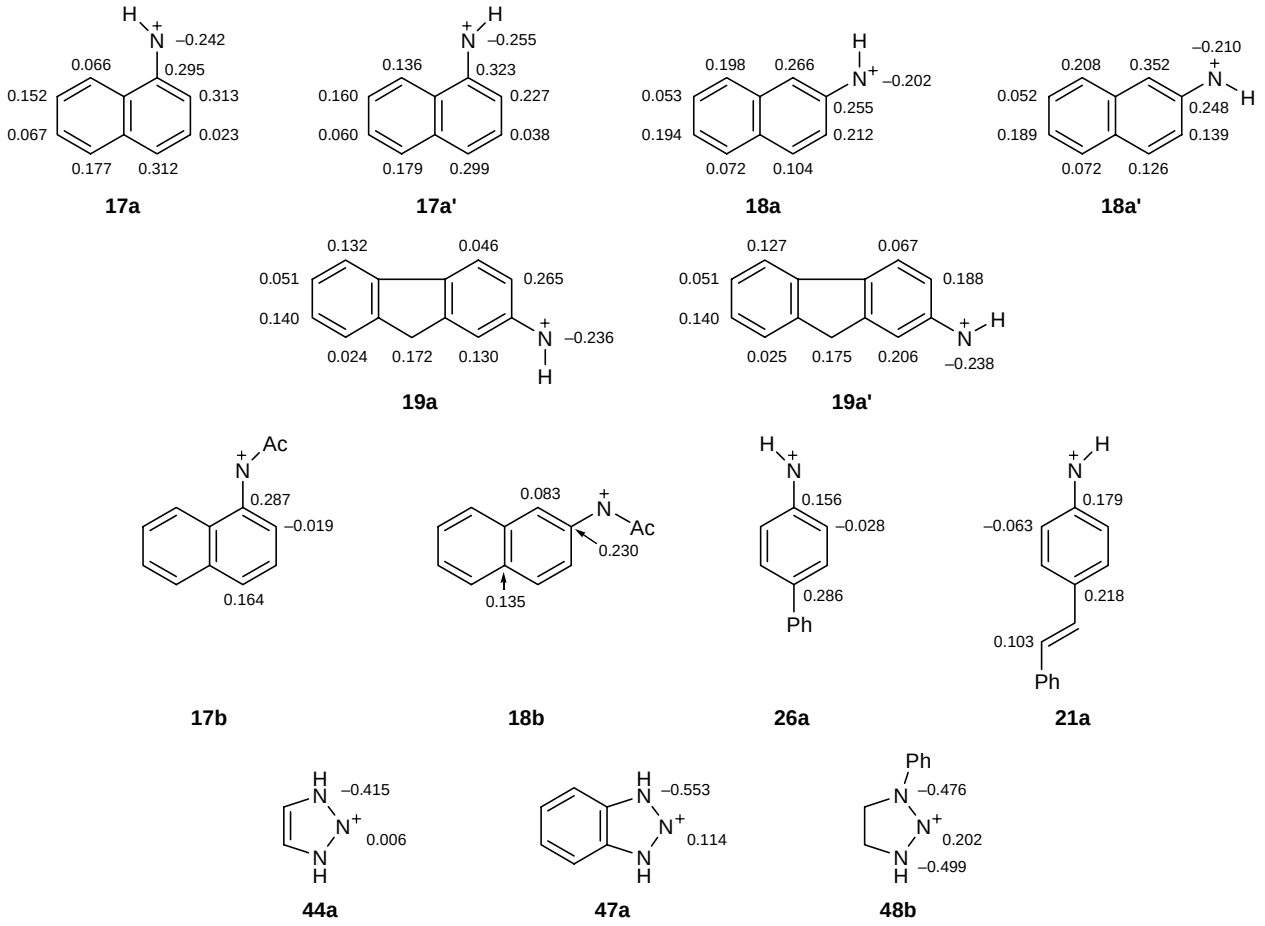


Fig. 2. Calculated Mulliken charges (HF/3-21G; ions **17a**, **18a**, and **19a**) [48] and charge densities (RHF/6-31G*; ions **17b**, **18b**, **21a**, **26a**, **44a**, **47a**, and **48b**) [56, 100].

the UHF/6-31G(*d*) calculations, the nitrenium nitrogen atom in dihydro- and tetrahydroimidazolyl cations possesses a positive charge [100] (Fig. 2).

3. AMINATION OF ARENES WITH VARIOUS REAGENTS

Among up-to-date methods for building up new C_{arom}–N bonds, electrophilic amination attracts a keen interest, for it makes it possible to introduce in one step various amino groups into an aromatic ring [104]. As synthetic equivalents of nitrenium ions, amines having readily departing groups, such as RR'N–Cl, RR'N–OR, and RR'N–SO_3X may be used. More complex compounds whose transformations give rise to $R^1R^2N^+$ ions, e.g., RN_3, $R^1OCON{=}NCOOR^2$, and $R^1R^2N–NR^3R^4$, can also serve as a source of N-centered electrophilic species. These cations can be generated by photolysis of *N*-aminopyridinium and S-aminosulfonium salts and their analogs. In the further treatment, the data are classified with respect to the type of the aminating agent.

3.1. N-Halo Amines

N-Halo amines have long been used as reagents for amination of aromatic compounds (see [105–109] and references therein). The amination of benzene, toluene, *tert*-butylbenzene, *N*,*N*-dimethylaniline, and naphthalene with chloro(dimethyl)amine in nitromethane or nitropropane in the presence of $AlCl_3$ gave the corresponding dimethylamino-substituted arenes in 90, 54, 47, 21, and 32% yield, respectively [105]. Using toluene as an example, it was shown that the isomer ratio of the resulting toluidines (*ortho*:*meta*:*para* = 14:27:59) [105] corresponds to electrophilic character of the process. Chloro(dimethyl)amine reacts in a similar way with benzene, toluene, *tert*-butylbenzene, chlorobenzene, and naphthalene in the presence of 96% H_2SO_4; in the reaction with toluene, the fraction of *meta*-toluidine among isomeric toluidines is considerably greater (*ortho*:*meta*:*para* = 9:53:38) [106]. The amination of benzene was also effected with other dialkyl(chloro)amines R_2NCl [R = Me, Et, Pr; RR = $(CH_2)_5$] and catalysts ($FeCl_3$, $AlCl_3$/$FeSO_4$, H_2SO_4–AcOH) [105, 106].

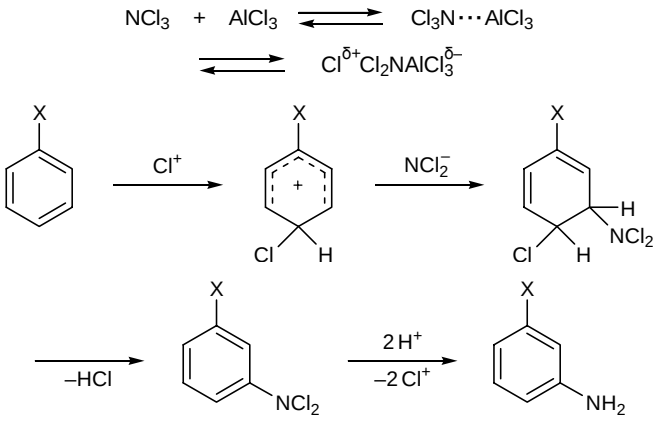
Belen'kaya *et al*. [110] showed that chloroamine reacts with aniline in nonaqueous solvents (diethyl ether, 1,2-dichloroethane, chlorobenzene) in the presence of acid catalysts ($AlCl_3$, KU-23 sulfo cation exchanger, AcOH) to afford *o*- and *p*-phenylenediamines in a low yield (15–20%; Scheme 4).

Scheme 4.

$$PhNH_2 + NH_2Cl \xrightarrow{\text{Catalyst}} o\text{-}C_6H_4(NH_2)_2 + p\text{-}C_6H_4(NH_2)_2 + PhNHNH_2$$

An unusual orientation was observed in the amination of benzene derivatives with $NHCl_2$ or NCl_3 in the presence of $AlCl_3$: *m*-toluidine was obtained from toluene (yield 25 and 42%, respectively), *m*-chloroaniline from chlorobenzene, and 3,5-xylidine from *m*-xylene [107, 108]. This reaction direction was rationalized in terms of the addition–elimination mechanism involving initial attack by Cl^+ ion on the substrate and subsequent addition of NCl_2^- anion [109] (Scheme 5). The yield of toluidine in the reaction of NCl_3 with toluene was shown to depend on the nature of the Lewis acid ($AlCl_3$, 42%; $AlBr_3$, 25%; $SbCl_5$, 3%; $SnCl_4$ and $FeCl_3$, 0%) and solvent (*o*-$C_6H_4Cl_2$, 34%; 1,2,4-$C_6H_3Cl_3$, 30%; H_2O, 30%; $SnCl_4$, 8; $MeNO_2$, Et_2O, and Et_3N, 0%) [108].

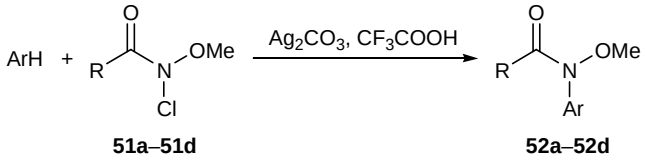
Scheme 5.



X = Me, Cl.

As noted above, the presence of at least one powerful donor substituent on the nitrogen atom increases the stability of nitrenium ion, its singlet state being stabilized to a greater extent than the triplet state. Singlet *N*-acyl-*N*-methoxynitrenium ions are the most probable intermediates in reactions of *N*-chloro-*N*-methoxycarboxamides with arenes catalyzed by Lewis acids [111–113]. Reactions of *N*-chloro derivatives **51a**–**51d** with benzene and substituted benzenes PhX (X = Me, MeO, CO_2Me), as well as with *p*-xylene and naphthalene lead to formation of the corresponding electrophilic amination products in high yields [111, 112] (Scheme 6). Here, the observed orienting effect of the substituent conforms to that typical of electrophilic aromatic substitution [112].

Scheme 6.



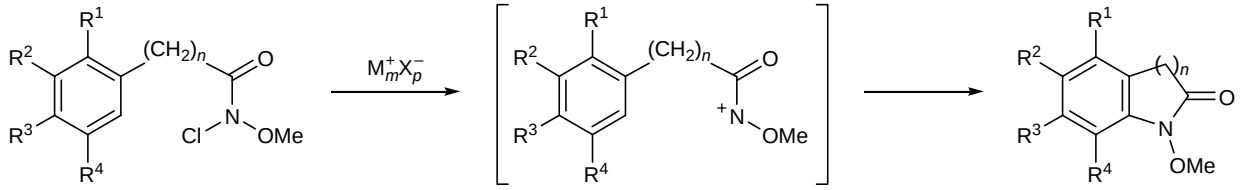
R = $Me(CH_2)_6$ (**a**), Ph (**b**), *t*-BuO (**c**), $PhCH_2O$ (**d**).

Obviously, nitrenium ions are formed as intermediates in intramolecular cyclization of *N*-chloro-*N*-methoxy amides **53a**–**53i**, which is promoted by AgX (X = BF_4, OAc, $OCOCF_3$, OSO_2CF_3), Ag_2X (X = CO_3, SO_4), or $FeSO_4$ [111, 112] (Scheme 7). The yield of 1-methoxy-1,2,3,4-tetrahydroquinolin-2-one (0–87%) from amide **53n** strongly depends on the nature of the salt and solvent and reaction conditions [112]; participation of nitrenium ions in this process follows from the data obtained for deuterium-labeled compound **53g** [112] (Scheme (8). The formation of a considerable amount of compound **55** was interpreted [112] in terms of rearrangement of ion **A** to ion **B** via 1,2-hydrogen shift and subsequent elimination of deuteron (D^+), while indenone **56** was presumed to arise from attack by the nitrenium center on the carbon atom attached to chlorine, followed by migration of chlorine in ion **C**.

Kikugawa *et al*. [113, 114] showed that anhydrous $Zn(OAc)_2$ in nitromethane effectively catalyzes (as Lewis acid) cyclization of *N*-chloro-*N*-methoxycarboxamides obtained from the corresponding *N*-methoxy amides **57**–**61** by the action of *t*-BuOCl. The yield of heterocyclic products **62–66** strongly depended on the initial amide structure (Schemes 9–13). *N*-Chloro-*N*-methoxy-*p*-methoxyphenylacetamide (**67**) gave rise to two regioisomeric compounds **68** and **69**, presumably via intermediate formation of nitrenium ion **D** [113] (Scheme 14).

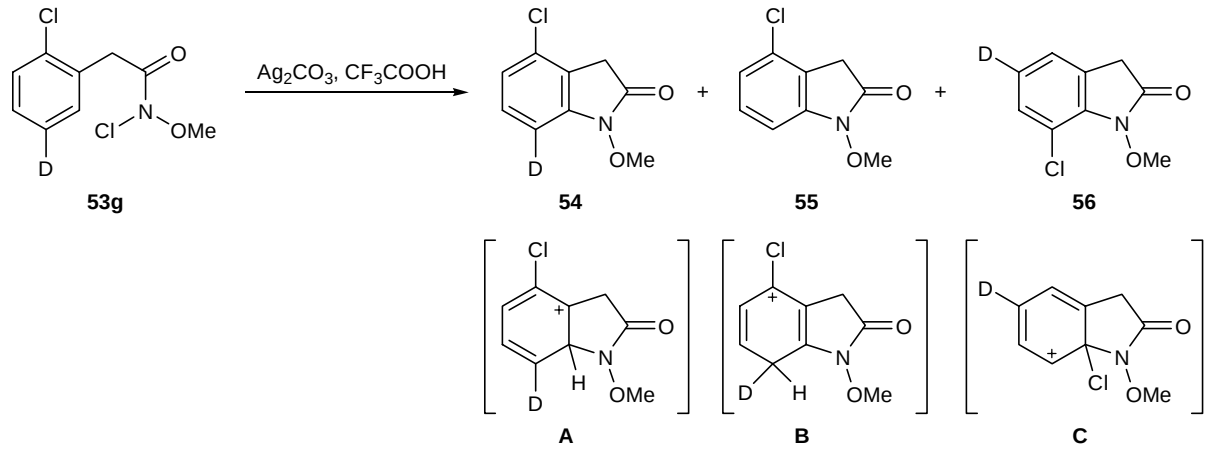
The yield of compounds **71a**–**71f** in the cyclization of *N*-alkoxy-*N*-chloro amides **70a**–**70f** (Scheme 15) depended on the Lewis acid and solvent nature; the best results were obtained with the use of $AgBF_4$ in Et_2O or THF [115]. The presence of a methoxy group in the *para* position of the benzene ring in amides **72a**–**72c** favored formation of spiro compounds **73a-73c** through intermediate nitrenium ions [47, 115] (Scheme 16). Glover *et al*. [116] used deuterated *N*-chloro-*N*-(2-phenylethoxy)acetamide (**74d**) to

Scheme 7.

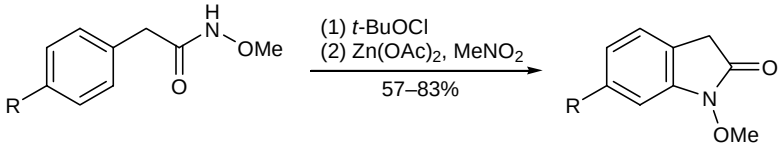


n = 1, $R^1 = R^2 = R^3 = R^4 = H$ (**a**); $R^1 = R^2 = R^4 = H$, $R^3 = Me$ (**b**); $R^1 = Cl$, $R^2 = R^3 = R^4 = H$ (**c**); $R^1 = R^2 = R^3 = H$, $R^4 = Cl$ (**d**); $R^1 = Br$, $R^2 = R^3 = R^4 = H$ (**e**); $R^1 = R^2 = R^3 = H$, $R^4 = Br$ (**f**); $R^1 = Cl$, $R^2 = R^3 = H$, $R^4 = D$ (**g**); $R^1 = R^4 = H$, $R^2 = R^3 = MeO$ (**h**); $R^1 = R^2 = R^4 = H$, $R^3 = Cl$ (**i**), $R^1 = R^2 = R^4 = H$, $R^3 = Br$ (**j**); $R^1 = R^2 = R^4 = H$, $R^3 = Me$ (**k**); $R^1 = R^2 = R^4 = H$, $R^3 = NHCOMe$ (**l**); $R^1 = R^2 = R^4 = H$, $R^3 = NO_2$ (**m**); *n* = 2, $R^1 = R^2 = R^3 = R^4 = H$ (**n**); *n* = 3, $R^1 = R^2 = R^3 = R^4 = H$ (**o**).

Scheme 8.



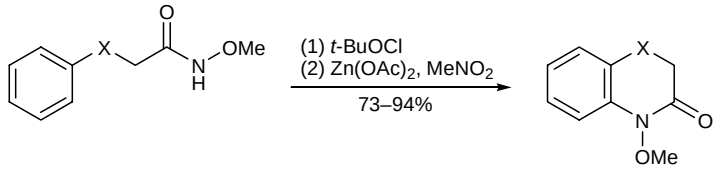
Scheme 9.



57a–57d **62a–62d**

R = H (**a**), Me (**b**), MeO (**c**), Ph (**d**).

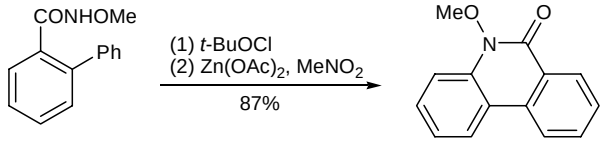
Scheme 10.



58a–58c **63a–63c**

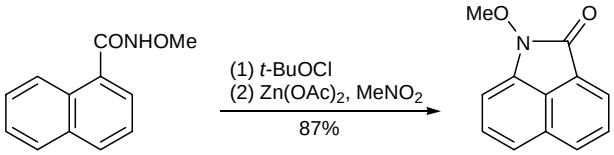
X = CH_2 (**a**), CH_2CH_2 (**b**), O (**c**).

Scheme 11.



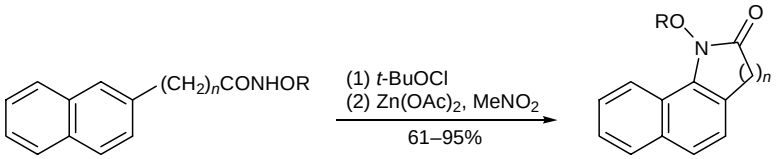
59 **64**

Scheme 12.



60 **65**

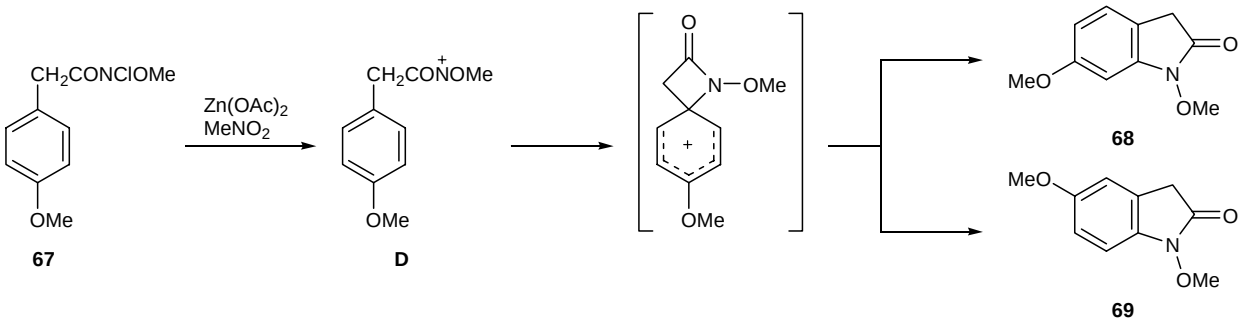
Scheme 13.



61a–61c **66a–66c**

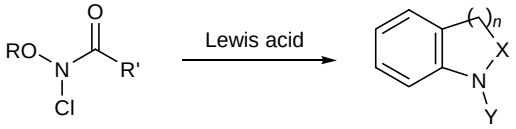
n = 1, R = Me (**a**); *n* = 2, R = Me (**b**), Et (**c**).

Scheme 14.



67 **D** **68** **69**

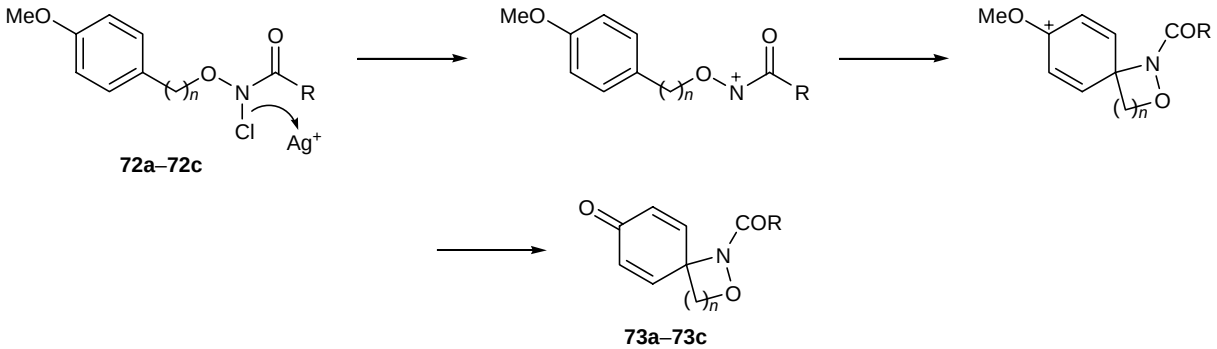
Scheme 15.



70a–70f **71a–71f**

70, R = $Ph(CH_2)_2$, R' = Ph (**a**), Me (**b**); R = $Ph(CH_2)_3$, R' = Ph (**c**); R = Me, R' = $PhCH_2$ (**d**), $Ph(CH_2)_2$ (**e**), $Ph(CH_2)_3$ (**f**); **71**, *n* = 2, X = O, Y = PhCO (**a**), MeCO (**b**); *n* = 3, X = O, Y = PhCO (**c**); X = CO, Y = MeO, *n* = 1 (**d**), 2 (**e**), 3 (**f**).

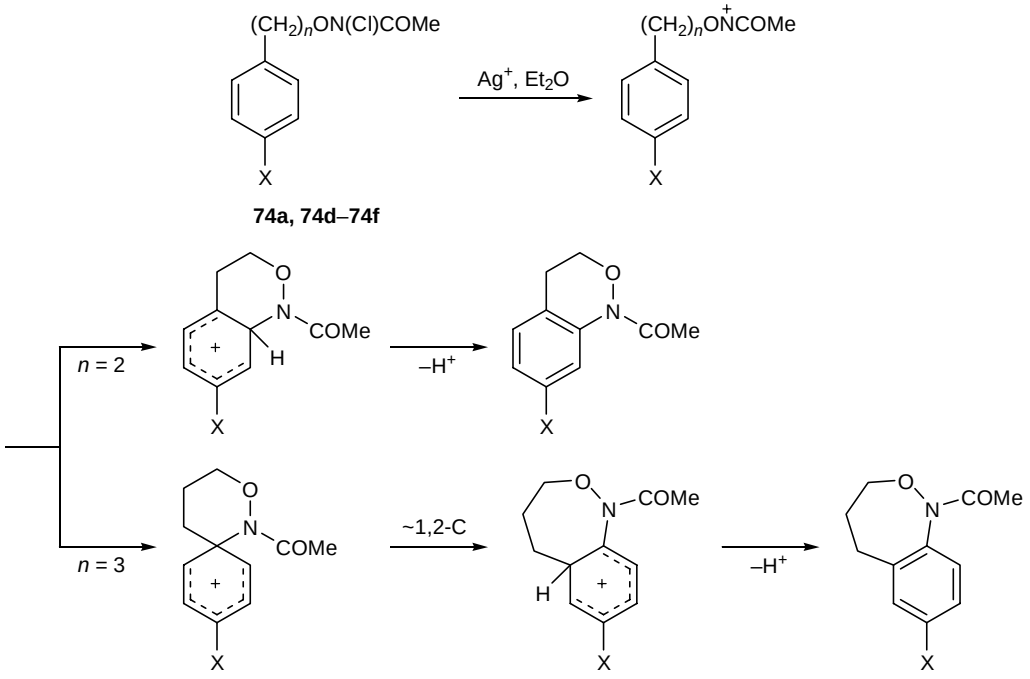
Scheme 16.



72a–72c **73a–73c**

n = 2, R = Me (**a**), Ph (**b**); *n* = 3, R = Ph (**c**).

Scheme 17.



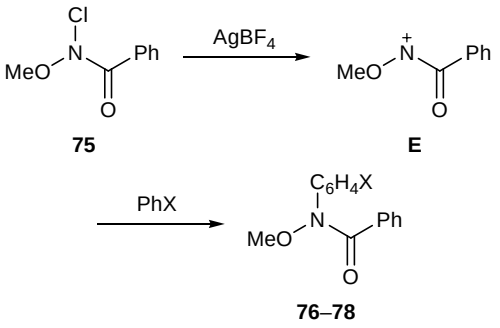
74a, 74d–74f

n = 2, X = H (**a**), D (**d**); *n* = 3, X = H (**e**), D (**f**).

demonstrate that the cyclization occurs via direct attack at the *ortho* position of the benzene ring to afford 3,4-dihydro-1*H*-2,1-benzoxazine (Scheme (17). By contrast, the cyclization of *N*-chloro-*N*-(3-phenylpropoxy)acetamide (**74e**) having a longer hydrocarbon chain involves mainly *ipso* attack by the nitrenium center on the aromatic ring, followed by 1,2-C–C shift (Scheme (17) [116]. *N*-Chloro-*N*-methoxybenzamide (**75**) reacts with benzene or toluene (PhX, X = H, Me) in diethyl ether in the presence of $AgBF_4$ to give

intermolecular amination product **76** (X = H, yield 49%) or a mixture of isomers **77** and **78** (X = *p*-Me, *m*-Me; yield 24 and 20%, respectively; Scheme 18) [115]. In the reaction with toluene, the *ortho*/*para* ratio conforms to that typical of electrophilic aromatic substitution, indicating participation of nitrenium ion **E**.

Scheme 18.

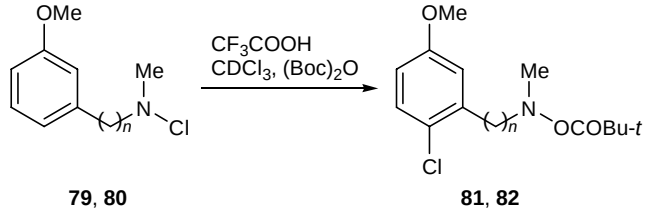


75 **E** **76–78**

76, X = H; **77**, X = *p*-Me; **78**, X = *m*-Me.

The above intramolecular cyclizations of *N*-halo amines occurred in the presence of Lewis acids. No such transformations are likely to be possible in the absence of a catalyst. Lee *et al*. [117] recently showed that reactions of trifluoroacetic acid with *N*-chloro amines **79** and **80** give only the corresponding electrophilic chlorination products **81** and **82** (Scheme 19).

Scheme 19.



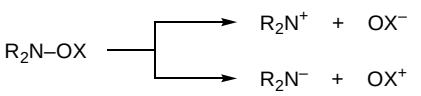
79, **80** **81**, **82**

79, **81**, *n* = 4; **80**, **82**, *n* = 11.

3.2. Reagents like R_2N–OX

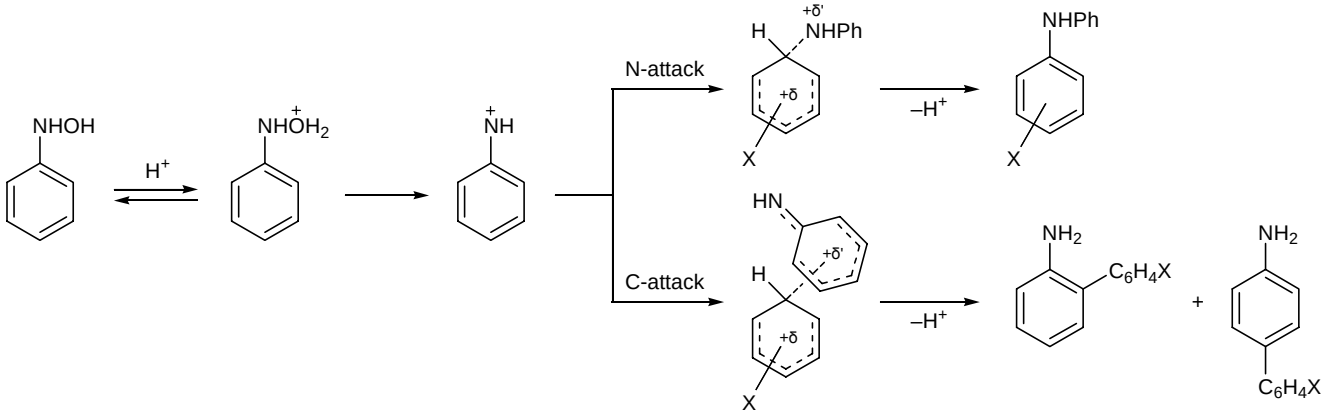
Like *N*-halo amines, R_2N–OX reagents exhibit ambident reactivity: depending on the conditions and nature of the R and X substituents, heterolytic dissociation of the N–O bond could give rise to either nitrenium (R_2N^+) or oxenium ions (OX^+) (Scheme 20). Moreover, ambident reactivity is also intrinsic to nitrenium ions formed during the process, e.g., to arylnitrenium ions which are capable of reacting at both nitrogen and carbon atoms due to considerable charge delocalization over the aromatic ring. Amination of arenes PhX with *N*-phenylhydroxylamine in a mixture of trifluoroacetic and polyphosphoric acids (TFA–PPA) [118] involves both N- and C-attack by phenylnitrenium ion on the substrate (Scheme 21), and the logarithms of the relative substitution rate constants are linearly related to the substituent constants σ^+. The large absolute ρ^+ values for the N- and C-attack (–5.2 and –4.0, respectively) are consistent with participation of nitrenium ion in the rate-determining stage. Addition of polar solvents to TFA–PPA was found to increase the regioselectivity of amination of anisole and toluene with 4-tolylhydroxylamine [119]. The direction of amination of benzene with *N*-phenylhydroxylamine depends on the acidity of the medium [120]. The reaction catalyzed by trifluoroacetic acid gives mainly diphenylamine, while in the presence of a stronger acid, CF_3SO_3H, *p*- and *o*-aminobiphenyls are formed. These results were interpreted assuming that the reaction in CF_3CO_2H involves intermediate formation of phenylnitrenium ion **F** (Scheme 22) whereas trifluoromethanesulfonic acid gives rise to dication **G** (protonated nitrenium ion) which reacts with benzene according to a different scheme.

Scheme 20.

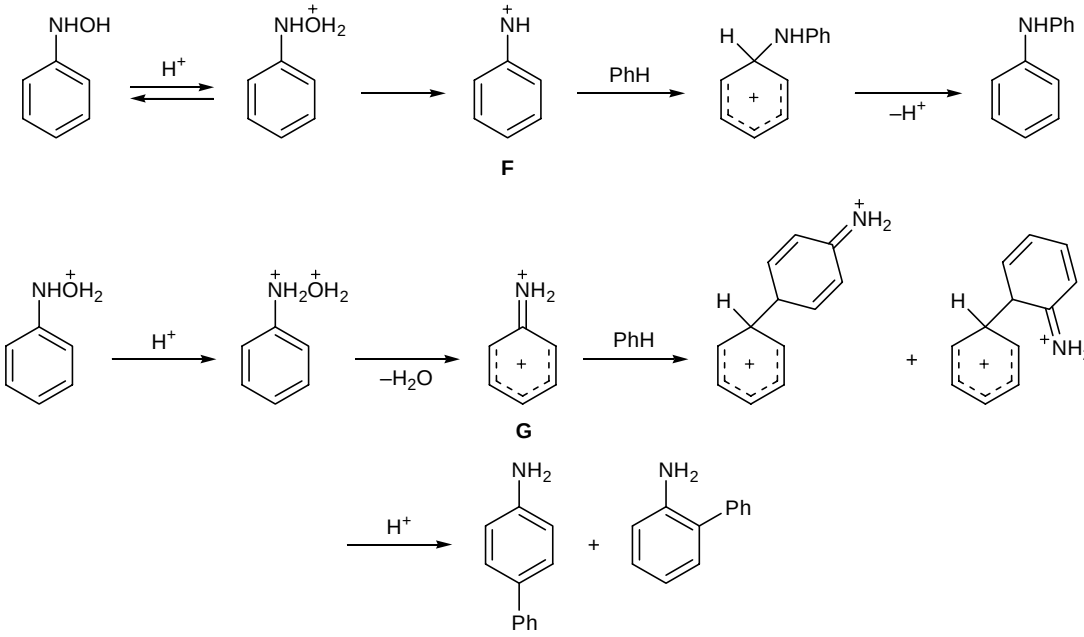


It should be noted that the direction of acid-catalyzed condensation of 2-methoxy-5-*tert*-butylphenylhydroxylamine (**83**) with *p*-*tert*-butylphenol (**84**) almost does not depend on the acidity of the medium. The reactions catalyzed by CF_3CO_2H, *p*-TsOH, and CF_3SO_3H give the same product (**85**, Scheme 23) [121]. Under catalysis by K-10 clay and its cation-exchanged forms (Al^{3+}, Fe^{3+}, Cr^{3+}, Co^{2+}, Mn^{2+}, Ni^{2+}, Cu^{2+}, Ti^{4+}, Zr^{4+}), *N*-phenylhydroxylamine is converted into *p*-nitrosodiphenylamine in 79–100% yield [122]. The fact that the process was not accompanied by the Bamberger rearrangement was explained by the layered structure of the catalyst which hinders attack on the *ortho* position. Decomposition of *N*-phenoxybenzamides **86a**–**86j** by the action of $AlCl_3$ yields mainly *ortho*-substituted phenols **87a**–**87j** (Scheme 24) [123]. The authors believe that a concerted mechanism of the rearrangement is hardly probable and that the reaction involves participation of nitrenium ions. By contrast, the reaction of amide **86a** with a mixture of Brønsted acids CF_3CO_2H and CF_3SO_3H in benzene afforded 2- and 4-hydroxybiphenyls **88a** (6%) and **88b** (3%) and 43% of 2-hydroxyphenyl benzoate (**89**), indicating intermediate formation of oxenium ion **H** (Scheme 25) [123].

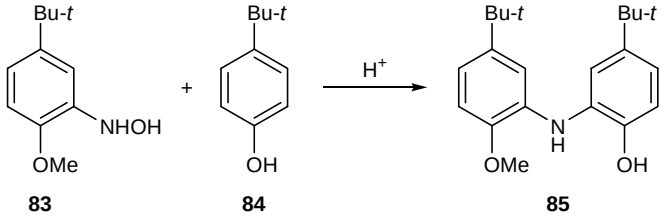
Scheme 21.



Scheme 22.



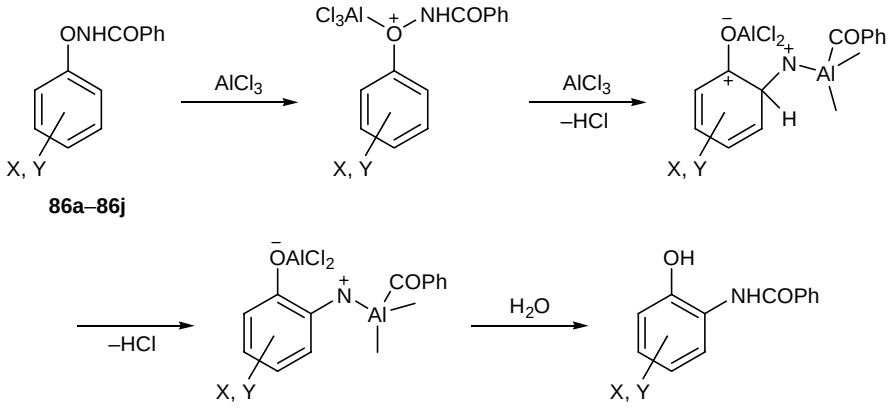
Scheme 23.



83 **84** **85**

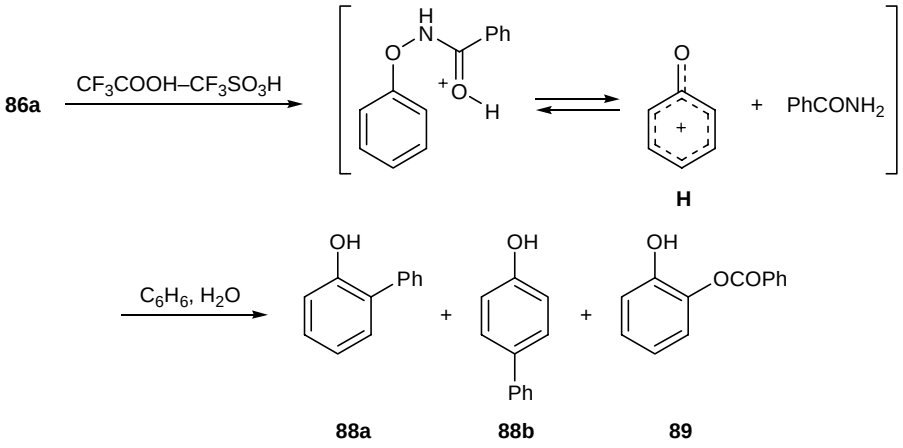
Acyloxy groups OCOR are classed with so-called readily departing groups; therefore, heterolytic dissociation of the N–OCOR bond in polar solvents usually gives the corresponding nitrenium ion. For example, it is believed that solvolysis of 4-*N*-(pivaloyloxy)-2-aminocarboline (**90**) in aqueous acetonitrile occurs through nitrenium ion **I** which reacts with the amine formed during the process along both N- and C-paths to afford secondary and primary amines **91** and **92**, respectively (Scheme 26) [124]. Methanolysis of 2-acetylaminofluorene *N*-sulfate (**93**) in the presence of aniline resulted in formation of amines **94**–**97** (Scheme 27) [125]. Novak *et al*. [126] presumed formation of ion pairs by nitrenium cation and appropriate counterion in the solvolysis of *N*-pivaloyloxy-2-acetylaminofluorene (**98**) and 4-acetylaminobiphenyl

Scheme 24.

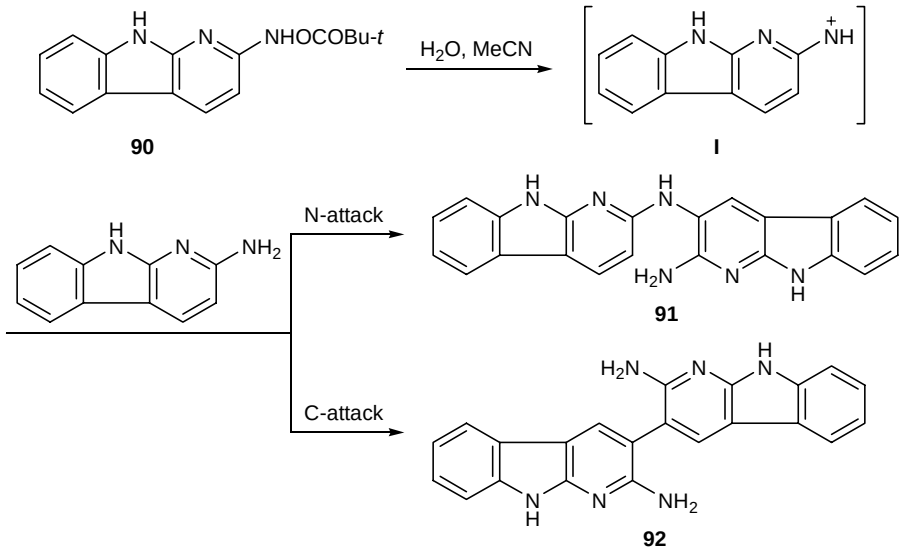


86, Y = H, X = H (**a**), 3-F (**b**), 2-Cl (**c**), 3-Cl (**d**), 4-Cl (**e**), 2-Me (**f**), 4-Me (**g**); X = 2-Cl, Y = 4-Cl (**h**); X = 2-F, Y = 5-Br (**i**); X = 2-Br, Y = 5-Br (**j**); **87**, Y = H, X = H (**a**), 4-F (**b**), 3-Cl (**c**), 4-Cl (**d**), 5-Cl (**e**), 3-Me (**f**), 5-Me (**g**); X = 3-Cl, Y = 5-Cl (**h**); X = 3-F, Y = 6-Br (**i**); X = 3-Br, Y =6-Br (**j**).

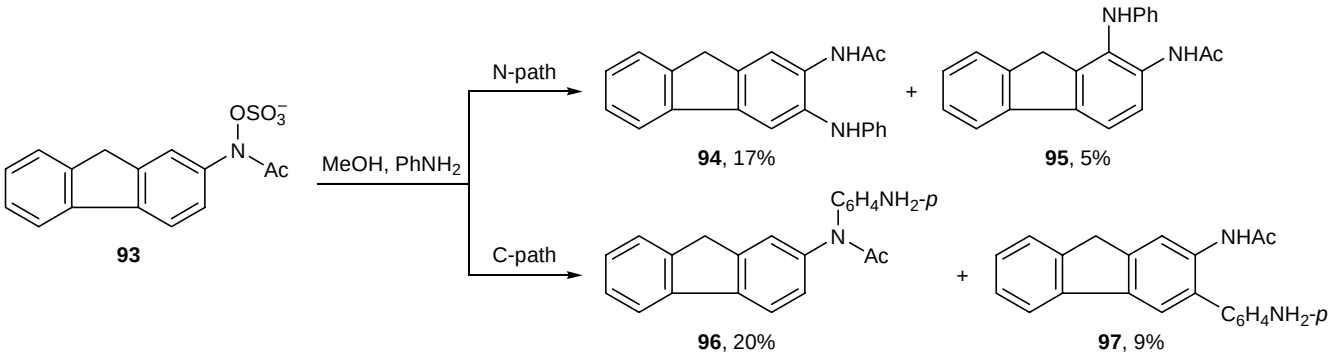
Scheme 25.



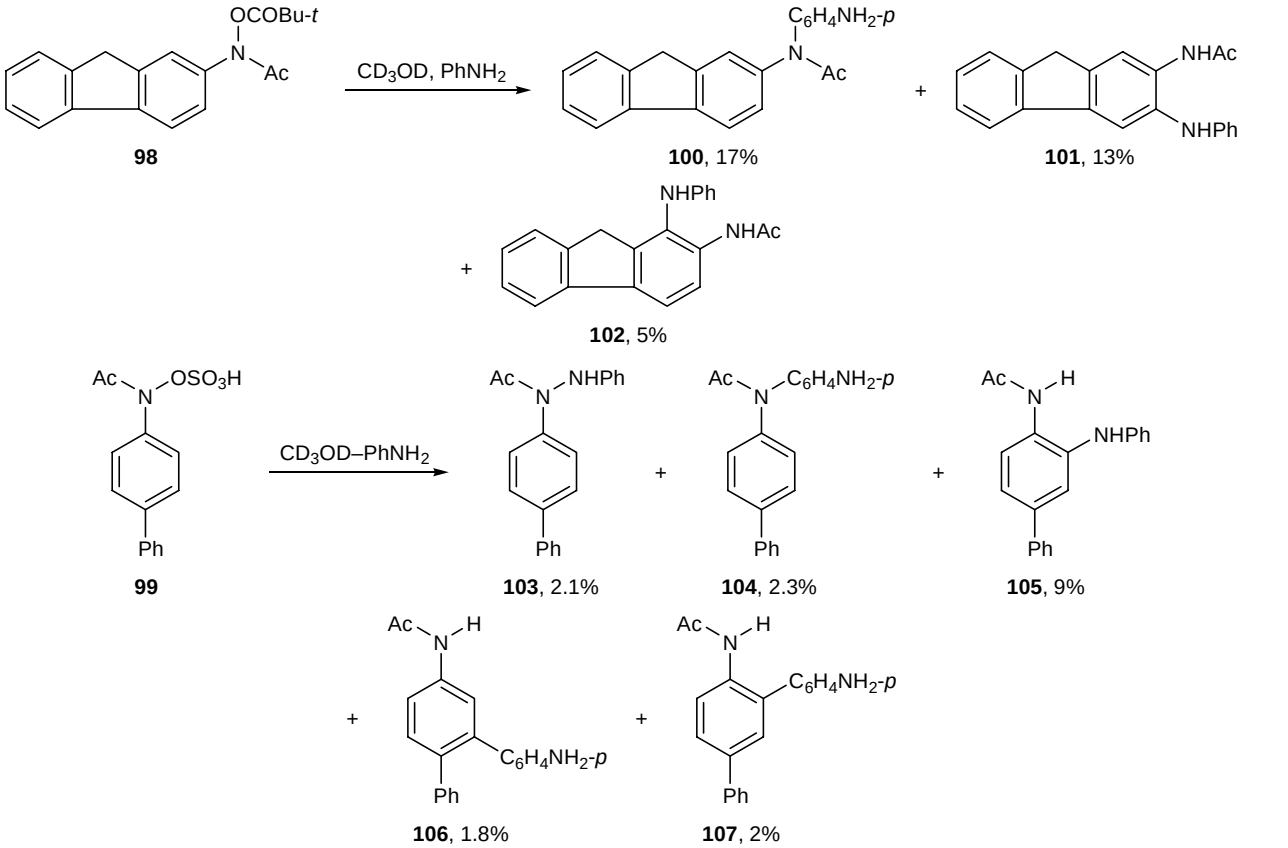
Scheme 26.



Scheme 27.

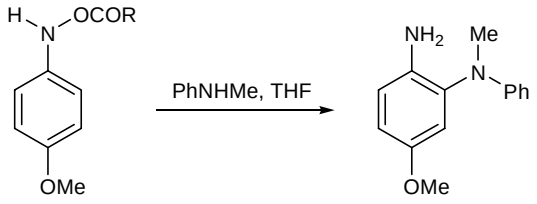


Scheme 28.



N-sulfate (**99**) in CD_3OD–$PhNH_2$, which gave N- and C-substitution products **100–107** (Scheme 28). *N*-Alkoxycarbonyloxy-4-methoxyanilines **108a–108c** react with *N*-methylaniline in THF to form 28–30% of 2-methyl(phenyl)amino-4-methoxyaniline (**109**) [127] (Scheme 29). In the reaction with *meta*-methoxy derivative **110** in CF_3CO_2H, two isomeric products **111** and **112** were obtained [128] (Scheme 30). A different reaction direction was observed for *para*-metoxy derivative **113**. In this case, the products were 6-methoxy-2-methyl-1,2,3,4-tetrahydroquinoline (**114**) and 6-hydroxy-2-methyl-1,2,3,4-tetrahydroquinoline (**115**, demethylation product) which were likely to be formed through intermediate σ-complex **J** [128] (Scheme 31). An analogous mechanism involving formation of spirocyclic intermediates is typical of reactions of *N*-methoxy amide **116** [129], 3-aryl-*N*-methoxypropionamides **117**, and *N*-(3-arylpropionyl)-phthalimides **118** with bis(trifluoroacetoxy)-λ^3-iodanylbenzene or hydroxy(tosyloxy)-λ^3-iodanylbenzene (HTIB) [130–134] (Schemes 32–34). Spirocyclic intermediate **K** is likely to be the key structure in the thermal rearrangement of isoxazolidines **119a–119i** to amines **120a–120i** (Scheme 35) [135].

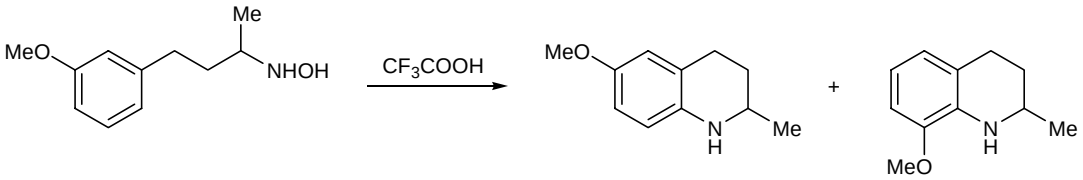
Scheme 29.



108a–**108c** **109**

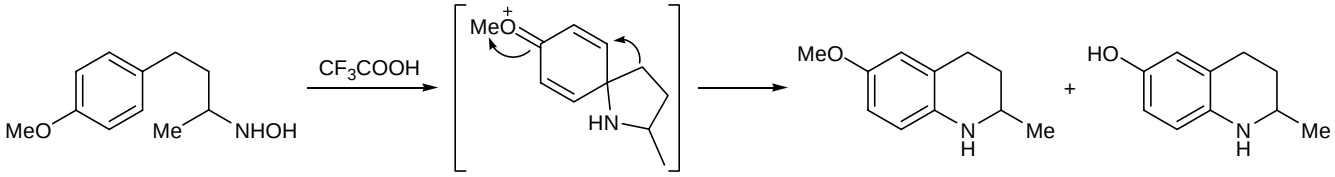
R = Me (**a**), *t*-Bu (**b**), $PhCH_2NHCHMe$ (**c**).

Scheme 30.



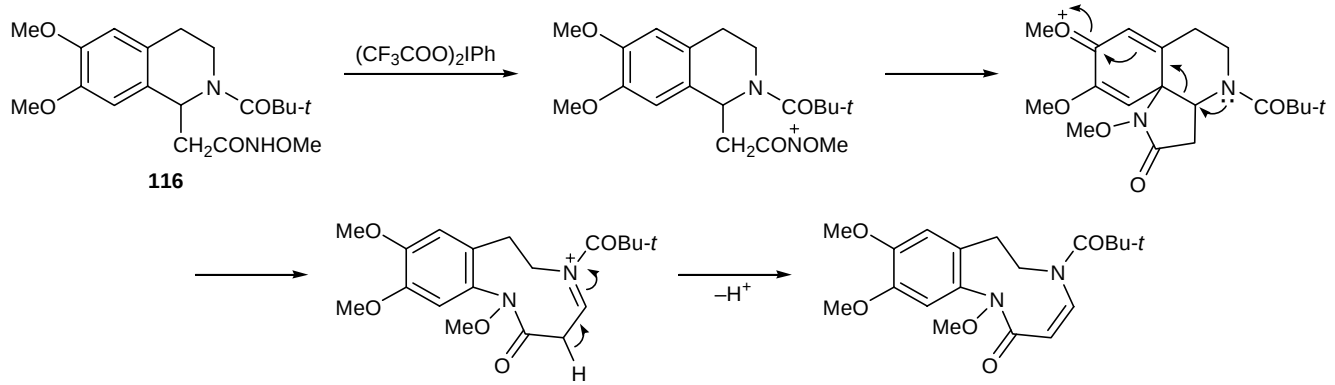
110 **111**, 60% **112**, 10%

Scheme 31.



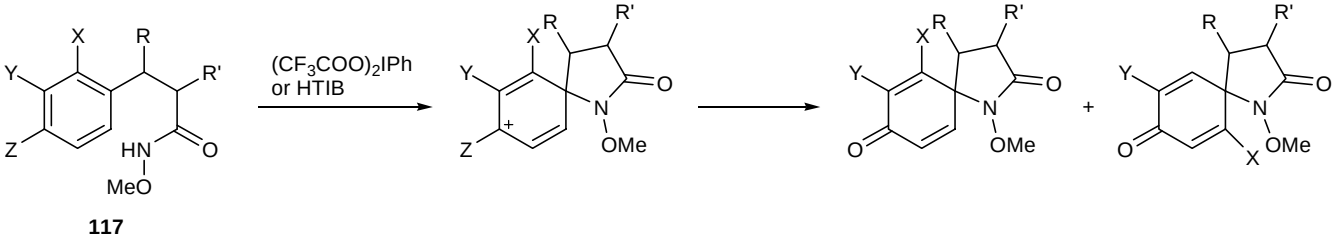
113 **J** **114**, 8% **115**, 20–35%

Scheme 32.



116

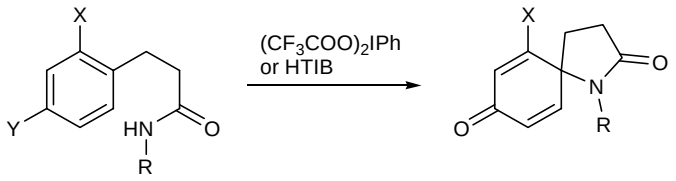
Scheme 33.



117

HTIB is [hydroxy(tosyloxy)-λ^3-iodanyl]benzene.

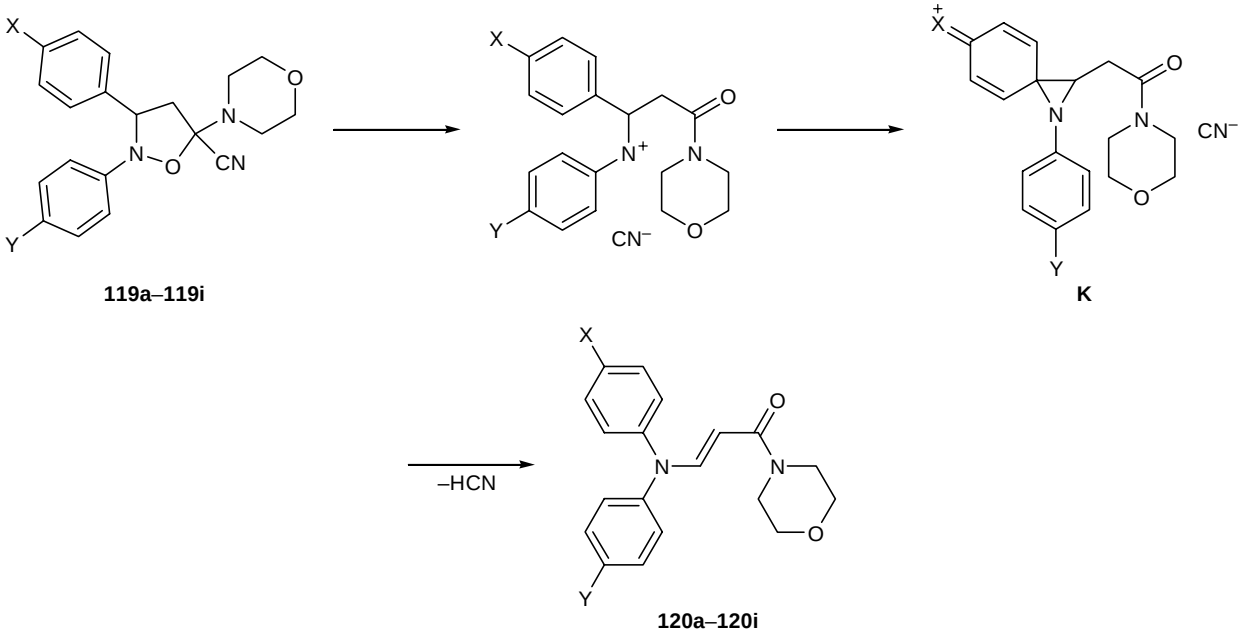
Scheme 34.



118

117, X = H, Me, *i*-Pr, MeO, F, Cl; Y = H, Me, F, Cl; Z = OH, MeO, F, Cl, Br; R = H, Me, Bu; R' = H, Me, Bu, $PhCH_2$; **118**, R = phthalimido, X = H, Y = MeO, Cl, F; X = Y = F.

Scheme 35.



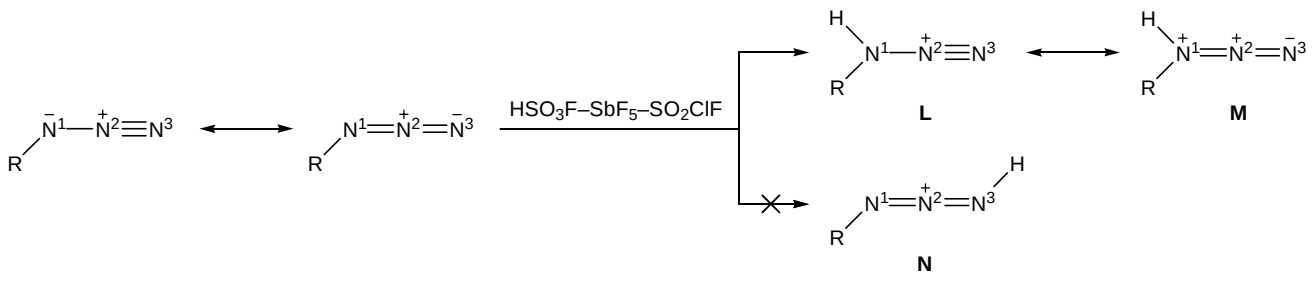
119, **120**, Y = H (**a**), X = OEt (**a**), H (**b**), Cl (**c**), NMe_2 (**d**), NO_2 (**e**); X = H, Y = CN (**f**), MeO (**g**); X = EtO, Y = MeO (**h**), CN (**i**).

3.3. Hydrazoic Acid and Azides

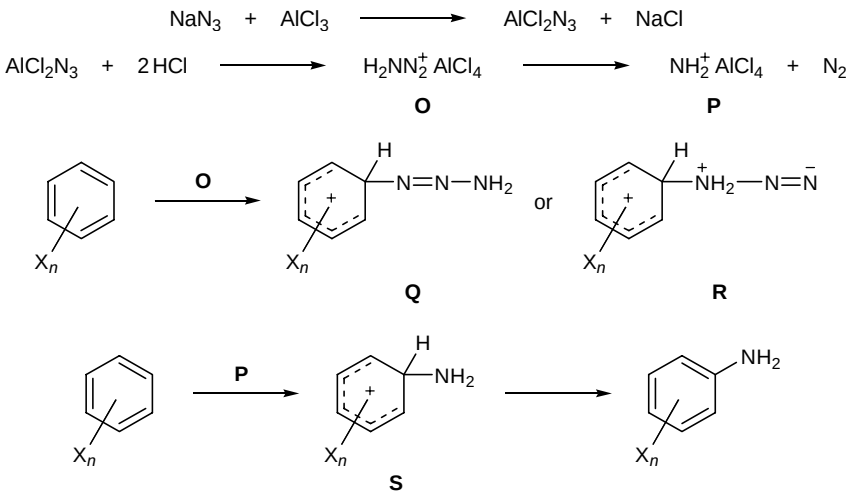
Unlike R_2N–Hlg and R_2N–OX reagents, azides and hydrazoic acid exhibit no ambident reactivity in the amination processes. Mertens *et al*. [136] showed by ^1H, ^{13}C, and ^{15}N NMR spectroscopy that protonation of hydrazoic acid or azides RN_3 (R = Me, Et) in superacidic systems (HSO_3F–SbF_5, HF–SbF_5, HF–BF_3) gives aminodiazonium ions **L** and **M** rather than iminodiazonium ions **N** (Scheme 36).

Presumably, elimination of nitrogen molecule from aminodiazonium ions should lead to the corresponding nitrenium ions. However, the use of hydrazoic acid and superacidic systems is not convenient, so that azides

Scheme 36.



Scheme 37.



and Lewis acids are usually employed as aminating agents. The system NaN_3–$AlCl_3$–HCl was shown to be quite convenient for the amination of arenes [136]. The best yields of amines were obtained from benzene and arenes having electron-donor substituents (benzene, 63%, anisole, 49%; toluene, 73%; *p*-xylene, 70%; mesitylene, 78%; isodurene, 39%), while in the presence of electron-acceptor groups in the benzene ring, the yields were considerably lower (chlorobenzene, 25%; nitrobenzene, 2%). In the above reactions, the aromatic substrate was simultaneously the solvent. Replacement of excess arene by hexane led to reduced yield of the amine, whereas 1,2-dichloroethane and nitromethane turned out to be inapplicable as solvents because of strong complex formation with the catalytic system. By contrast, we showed in [137–139] that the use of hexane and 1,2-dichloroethane as solvents in the amination of mesitylene ensured, respectively, a moderate (40%) and high (86%) yields of 2,4,6-trimethylaniline.

Scheme 37 illustrates the most probable mechanisms of amination of arenes with the system NaN_3–$AlCl_3$–HCl [136, 138, 139]. According to [136], sodium azide initially reacts with $AlCl_3$; therefore, solvents capable of strongly interacting with $AlCl_3$ should inhibit the process. In fact, using mesitylene as an example, we showed [138, 139] that solvents with a large Gutmann donor number (>2), such as THF, sulfolane, $MeNO_2$, and $PhNO_2$, afford a very poor yield of 2,4,6-trimethylaniline (<4%). In the second stage, protonation of $AlCl_2N_3$ gives aminodiazonium ion **O** which loses nitrogen molecule to produce nitrenium ion **P**. Reaction of the latter with arene could give rise to σ-complex **Q** or **R**. AM1 quantum-chemical calculations of such σ-complexes derived from methyl-substituted benzenes (*o*-xylene, mesitylene, durene, and pentamethylbenzene) showed that structures like **Q** are less stable than the corresponding structures like **R**; therefore, participation of the former seems to be unlikely [139]. σ-Complexes **R** are characterized by a very long H_2N–N bond (~3 Å), i.e., they are similar to σ-complexes **S**. The latter can be formed via direct reaction with the nitrenium ion arising from aminodiazonium ion **O** via elimination of N_2 [139]. As noted above, the ground state of nitrenium ion NH_2^+ is triplet ($^3NH_2^+$). Insofar as the formation of σ-complexes like **S** requires singlet state of nitrenium ion, the conversion of arene should depend on the probability for S→T inversion of that ion. This probability increases with rise in the number of heavy atoms in solvent molecule and increase in their atom number. In fact, the conversion of mesitylene and *o*-xylene in the amination with NaN_3–$AlCl_3$–HCl decreases in the series CH_2Cl_2 > $CHCl_3$ > CCl_4, $ClCH_2CH_2Cl$ > $ClCH_2CCl_3$, and CH_2Cl_2 > CH_2Br_2, in keeping with the participation of NH_2^+ as reactive species. Obviously, the rate-determining stage in the amination is formation of σ-complex **S**. Taking into account polar character of the latter, the conversion (η) of methylbenzenes should depend not only on the number of heavy atoms (*N*) in solvent molecule but also on the dielectric constant (ε) of the solvent. This is supported by the existence of the following two-parameter correlations for the reactions with mesitylene (MsH) and *o*-xylene (*o*-XyH) [139]:

$$\eta(\mathrm{MsH}) = (0.29 \pm 0.08) + (0.067 \pm 0.010)\varepsilon - (0.107 \pm 0.023)N_{\mathrm{Cl}};$$
$$r = 0.97,\ s = 0.08,\ n = 9;$$

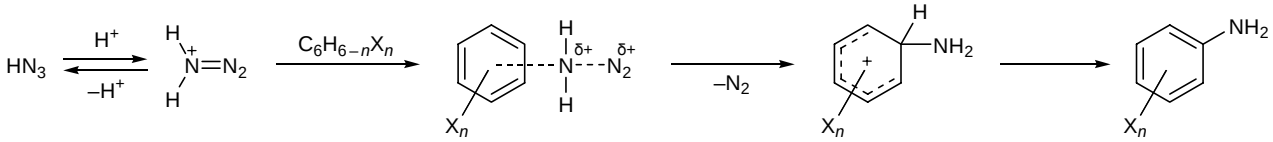
$$\eta(o\text{-XyH}) = (0.40 \pm 0.10) + (0.059 \pm 0.012)\varepsilon - (0.143 \pm 0.027)N_{Cl};$$
$$r = 0.96,\ s = 0.1,\ n = 7.$$

Nitrenium cation NH_2^+ generated in the amination of arenes is a very reactive intermediate species. This follows from the calculated logarithm of the partial rate factor ($\log f_p$) and selectivity factor [$S_f = \log(f_p/f_m)$, where f_m and f_p are, respectively, the partial substitution rate factors at the *meta* and *para* positions) for the amination of toluene with the system NaN_3–$AlCl_3$–HCl: $\log f_p = 0.97$, $S_f = 0.75$; these values approach those found for the alkylation of toluene with MeBr–$GaBr_3$ and EtBr–$GaBr_3$ [139]. The high reactivity of NH_2^+ is responsible for the low selectivity in the amination of arenes [139]. An attempt to increase the selectivity in the amination of *o*-xylene by complex formation of NH_2^+ with 18-crown-6 was unsuccessful: the isomer ratio of 2,3- and 3,4-dimethylanilines did not change to an appreciable extent [139]. Presumably, the reason is strong interaction between 18-crown-6 and acidic medium, which hampers formation of a complex between 18-crown-6 and NH_2^+. According to the AM1 calculations, the crown ether cavity readily accommodates NH_2^+ ion, thus producing a quite strong complex ($\Delta\Delta H_f$ = 296.6 kJ/mol) [139].

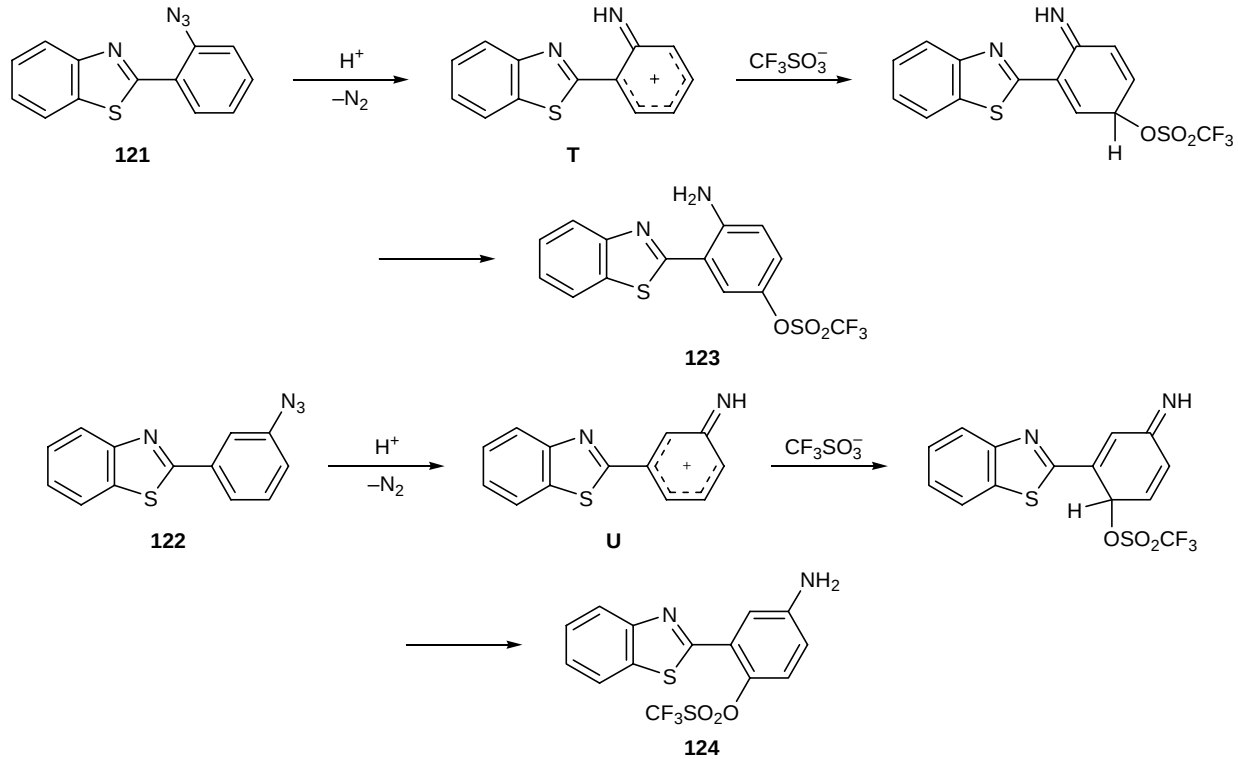
We recently studied the effect of Lewis acids in the amination of mesitylene and *o*-xylene with the systems NaN_3–$MHlg_n$–HCl [140, 141]. The examined Lewis acids can be ranked as follows with respect to their efficiency: $GaCl_3 \sim ZrCl_4 \sim AlCl_3 > AlBr_3 > FeCl_3 > SbCl_5 \gg SnCl_4, TiCl_4 > SbCl_3, GeCl_4$.

According to Takeuchi et al. [142], the amination of arenes with hydrazoic acid in a CF_3SO_3H–CF_3CO_2H mixture (1:3, by volume) yields primary arylamines without formation of appreciable amounts of diamines. The authors presumed that the reaction follows a concerted mechanism involving attack by protonated hydrazoic acid $H_2N_3^+$ on the substrate with simultaneous elimination of nitrogen (Scheme 38). The yield of arylamines depends on the intial arene: it decreases

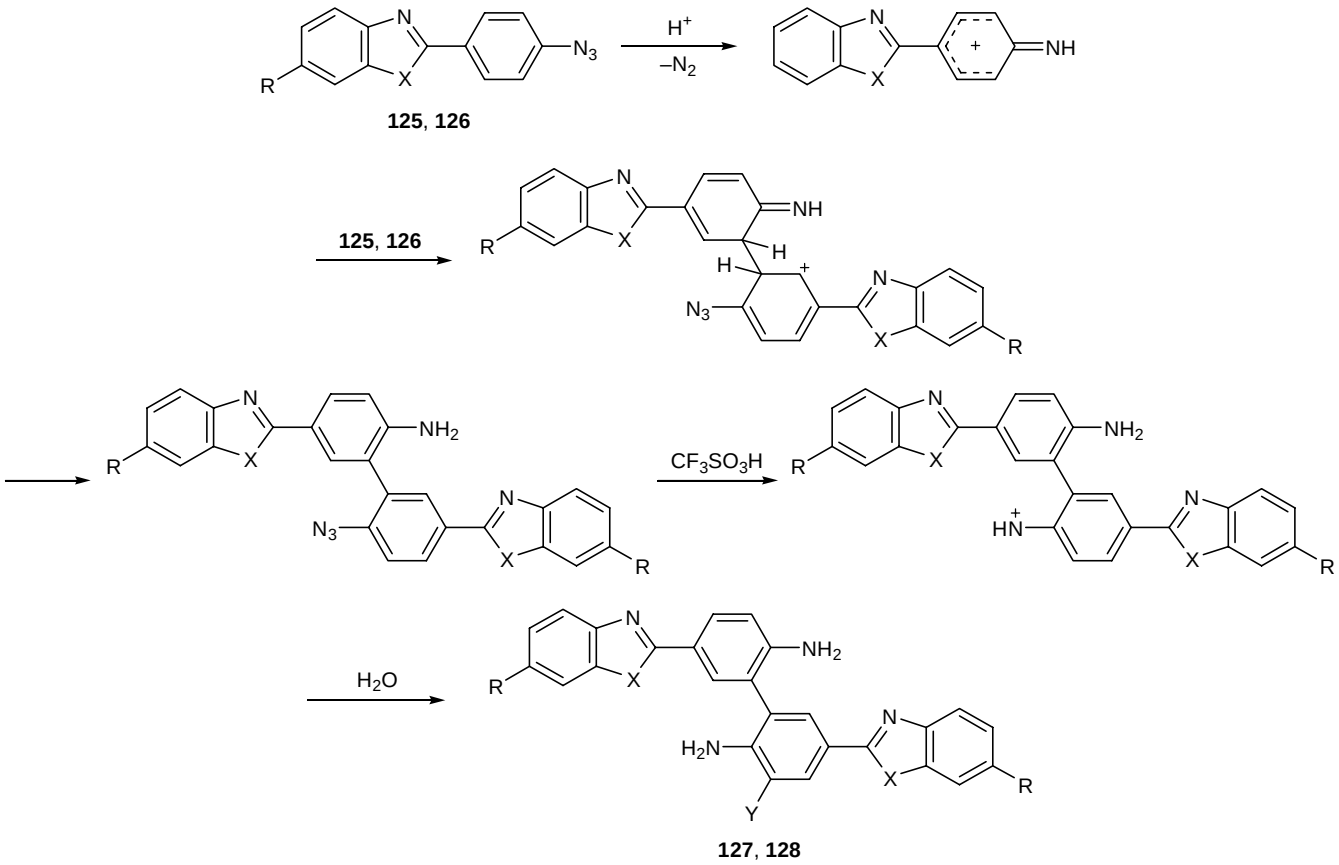
Scheme 38.



Scheme 39.



Scheme 40.



R = H, Me; X = O, S; Y = H, OSO_2CF_3.

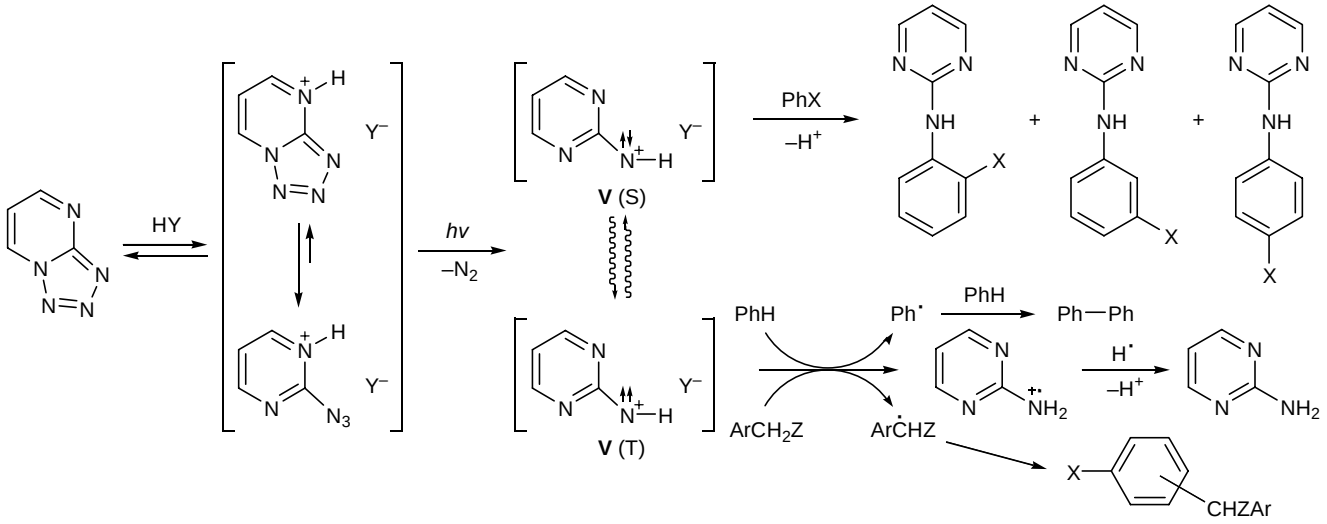
upon introduction of electron-acceptor substituents into the benzene ring. No reaction occurs in the absence of CF_3SO_3H, indicating the necessity of a strongly acidic medium to protonate HN_3.

Reaction of BuN_3 with benzene or mesitylene in CF_3SO_3H–CF_3CO_2H leads to formation of the corresponding *N*-arylbutylamine in a relatively poor yield (5 and 21%, respectively) [142]. Contrastingly, amination of benzene, methylbenzenes, and halobenzenes with trimethylsilyl azide in CF_3SO_3H affords arylamines in a relatively high yield (73–96%) [143]. The amination of monosubstituted benzenes with all the examined azides in acidic medium gives mainly the corresponding *ortho* and *para* isomers, in keeping with electrophilic character of the reactive intermediate. Analogous relations are typical of reactions of monosubstituted benzenes with PhN_3 in CF_3CO_2H, the ρ^+ value in the Hammett equation (–4.5 at 25°C) being somewhat greater than in the amination with PhNHOH ($\rho^+ = -5.2$ at 20°C) [118]. In the latter case, the higher selectivity is likely to result from specific interaction between intermediate nitrenium ion $PhNH^+$ and departing water molecule.

Reactions of 2-(2-azidophenyl)- and 2-(3-azidophenyl)benzothiazoles **121** and **122** with CF_3SO_3H give rise to π-nitrenium ions like **T** and **U** which are trapped by trifluoromethanesulfonate ion to give trifluoromethylsulfonyl-substituted arylamines **123** and **124** [144] (Scheme 39). Analogous reactions of 2-(4-azidophenyl)benzothiazoles and 2-(4-azidophenyl)benzoxazoles **125** and **126** lead to formation of symmetric or unsymmetric benzazolyl-substituted 2,2'-diaminobiphenyls **127** and **128** [144] (Scheme 40).

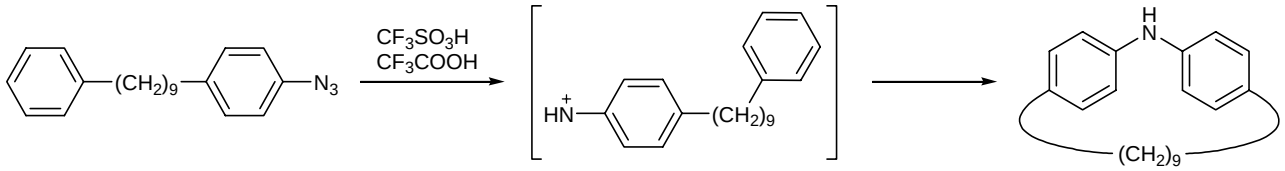
Photochemical amination of benzene and substituted benzenes with tetrazolo[1,5-*a*]pyrimidine in the presence of CF_3CO_2H afforded substituted anilinopyrimidines, as well as 2-aminopyridine, biphenyl, and diarylmethanes [145] (Scheme 41). While considering the heavy-atom effect of the solvent, the authors presumed that substituted anilinopyrimidines are formed through intermediate nitrenium ion **V** in the singlet state and that aminopyrimidine, biphenyl, and diaryl-

Scheme 41.



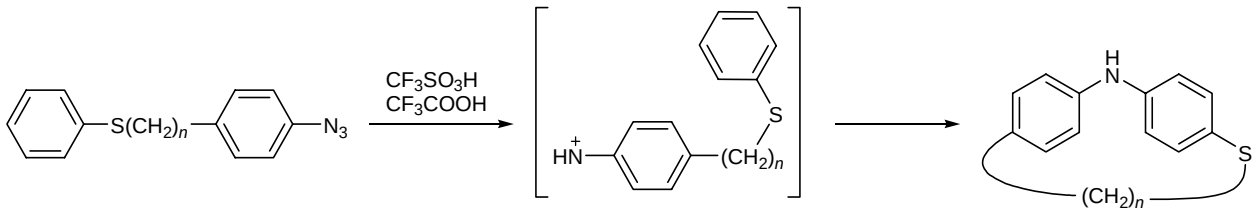
Y = CF_3COO, X = H; X = Me, Ar = Ph, Z = H; X = Et, Ar = Ph, Z = Me; X = MeO, Cl.

Scheme 42.



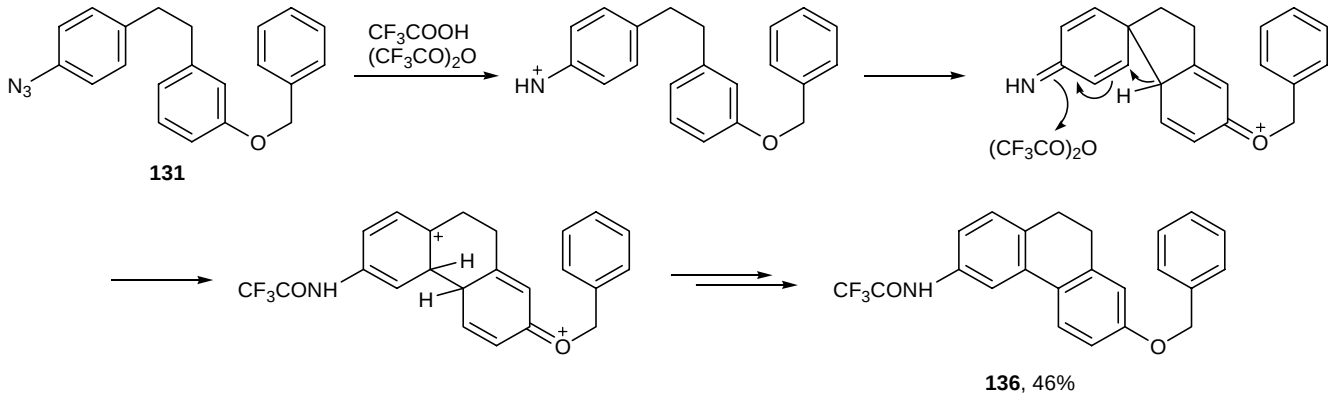
129 **134**, 44%

Scheme 43.



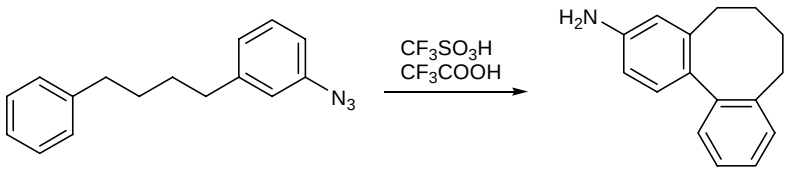
130 (*n* = 7, 9) **135**, 32% (*n* = 7), 16% (*n* = 9)

Scheme 44.



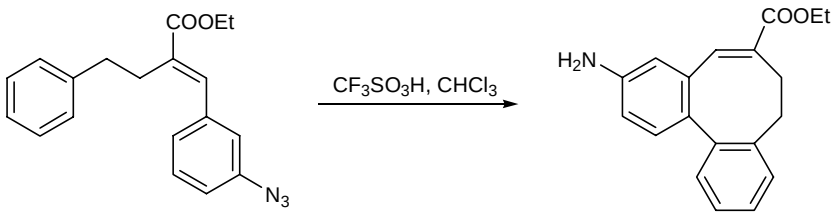
131 **136**, 46%

Scheme 45.



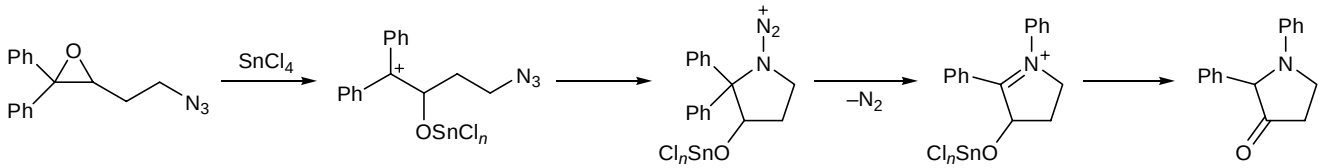
132 **137**

Scheme 46.

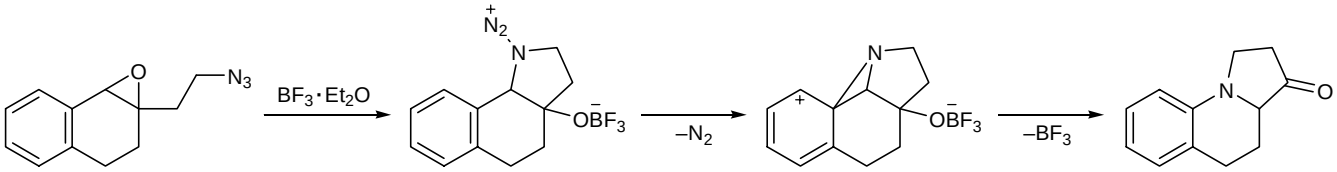


133 **138**, 70%

Scheme 47.



139 **141**, 48%



140 **142**, 94%

methanes originate from the same ion but in the triplet state. According to quantum-chemical calculations, the ground state of 2-pyrimidinylnitrenium ion in the gas phase is triplet, though the energy gap between the triplet and singlet states is small [57]. The formation of nitrenium ion **V** is supported by the existence of a linear correlation between log*k* for the formation of substituted anilinopyrimidines and σ^+ constants of substituents X; here, the relatively low absolute value of ρ^+ (–2.9 at 25°C) indicates higher electrophilicity of the singlet pyrimidylnitrenium ion as compared to phenylnitrenium [118].

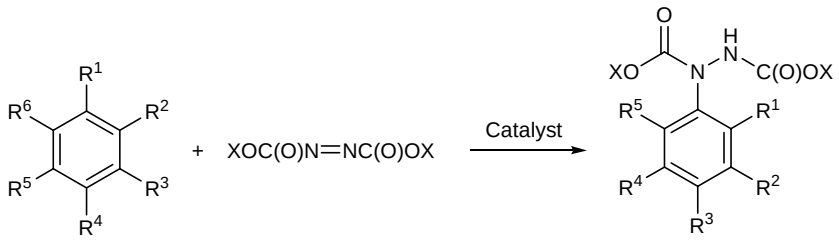
It is believed that acid-catalyzed intramolecular cyclization of arylazides **129** [146], **130** [147], **131** [148], **132**, and **133** [149] involves intermediate formation of the corresponding nitrenium ions (Schemes 42–46) and that the reaction follows either N- or C-path, depending on the initial azide structure; as a result, compounds **134–138** are obtained.

Lang *et al*. [150] showed that epoxy azides **139** and **140** undergo a series of transformations by the action of Lewis acids. These transformations include regioselective amination of the aromatic ring, leading to nitrogen-containing heterocycles **141** and **142** as shown in Scheme 47.

3.4. Azodicarboxylic Esters and Hydrazines

Azo diesters are effective reagents for electrophilic amination of electron-rich aromatic compounds [151–158]. As a rule, Lewis or Brønsted acids are used as catalyst, and the reaction gives mainly substitution products at the *para* position with respect to the most powerful electron-donor substituent in the aromatic ring (Scheme 48). Apart from symmetrical azo diesters like **144a** and **144b**, diesters **148** with dissimilar ester moieties and amido esters **149a–149g** were used in electrophilic amination of arenes **146a**, **146b**, and **147**.

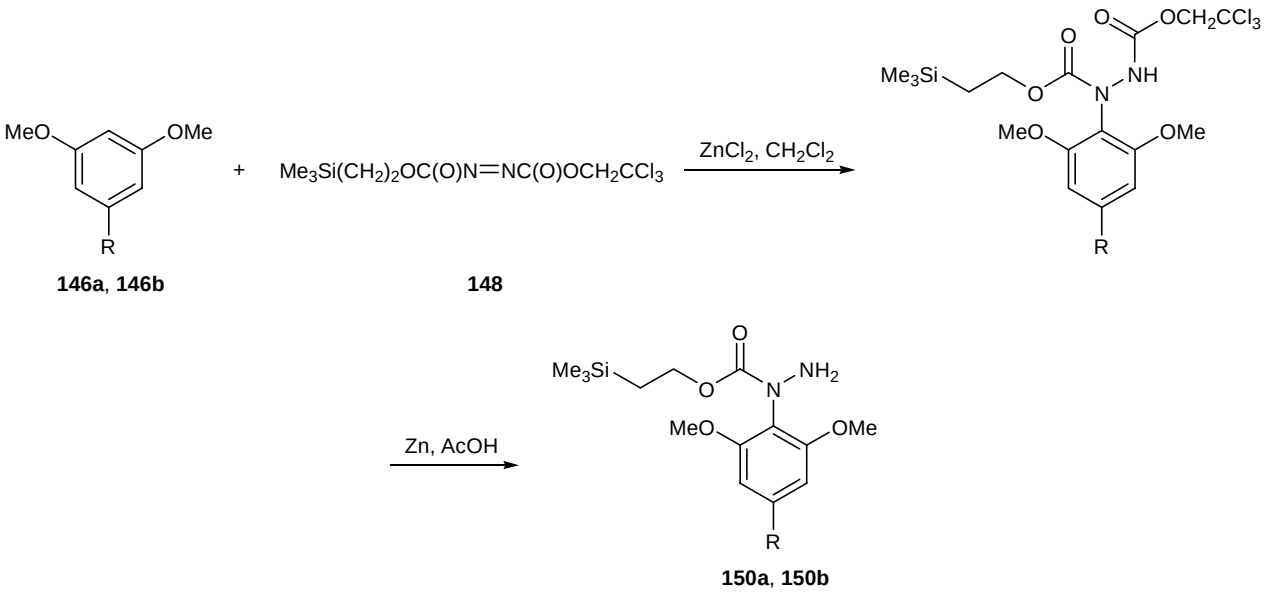
Scheme 48.



143a–143h **144a**, **144b** **145a–145h**

143, R^1 = OH, $R^2 = R^3 = R^4 = R^5 = R^6$ = H (**a**); R^1 = MeO, $R^2 = R^3 = R^4 = R^5 = R^6$ = H (**b**); R^1 = MeO, R^3 = Me, $R^2 = R^4 = R^5 = R^6$ = H (**c**); $R^1 = R^2$ = MeO, $R^3 = R^4 = R^5 = R^6$ = H (**d**); R^1 = MeO, R^2 = Br, $R^3 = R^4 = R^5 = R^6$ = H (**e**); R^1 = MeO, $R^2 = R^3 = R^5 = R^6$ = H, R^4 = Br (**f**); $R^1 = R^3 = R^5$ = MeO, $R^2 = R^4 = R^6$ = H (**g**); $R^1 = R^3$ = MeO, $R^2 = R^4 = R^6$ = H, R^5 = MeCO (**h**); **144**, X = CCl_3CH_2 (**a**), X = Et (**b**); **145**, $R^1 = R^2 = R^4 = R^5$ = H, R^3 = OH, X = CCl_3CH_2 (**a**); $R^1 = R^2 = R^4 = R^5$ = H, R^3 = MeO, X = CCl_3CH_2 (**b**); R^1 = Me, $R^2 = R^4 = R^5$ = H, R^3 = MeO, X = CCl_3CH_2 (**c**); $R^1 = R^4 = R^5$ = H, $R^2 = R^3$ = MeO, X = Et (**d**); $R^1 = R^4 = R^5$ = H, R^2 = Br, R^3 = MeO, X = CCl_3CH_2 (**e**); R^1 = MeO, $R^2 = R^3 = R^5$ = H, R^4 = Br, X = CCl_3CH_2 (**f**); R^1 = MeO, $R^2 = R^4$ = H, $R^3 = R^5$ = MeO, X = CCl_3CH_2 (**g**); R^1 = MeO, $R^2 = R^4$ = H, R^3 = MeO, R^5 = COMe, X = CCl_3CH_2 (**h**).

Scheme 49.



146a, **146b** **148** **150a**, **150b**

As a result, unsymmetrically substituted hydrazines **150a**, **150b**, and **151a–151g** were obtained; the products are convenient synthons for the preparation of heterocyclic compounds [152, 156] (Schemes 49, 50).

The high regioselectivity of the amination was interpreted in terms of formation of an oriented π-complex as shown in Fig. 3 [153]. Arrangement of components in that complex is determined by the maximal orbital coefficients of atoms in the highest occupied molecular orbital of arene, which overlaps the lower unoccupied orbital of the azo reagent; the subsequent formation of σ-complex is followed by elimination of proton [153]. An additional factor ensuring high selectivity in the amination with azo esters is likely to be a large effective volume of the reagent, which hinders its attack on the *ortho* position.

Bicyclic compounds, such as biphenyl derivative **152**, substituted naphthalenes **153** and **154**, and anthracene (**155**) can also be involved in the amination with azo diesters [152, 156, 158] (Schemes 51–54). Electrophilic amination of halogenated phenols **163a**–**163g** with diisopropyl diazenedicarboxylate (**164**) in the presence of $ZrCl_4$ is accompanied by migration of halogen atoms ("halogen dance") to afford amines **165** and **166** [155] (Scheme 55). In the amination of 4-fluorophenol, chloro-substituted compound **165f** was isolated; its formation was explained by migration of the fluorine atom and its subsequent replacement by

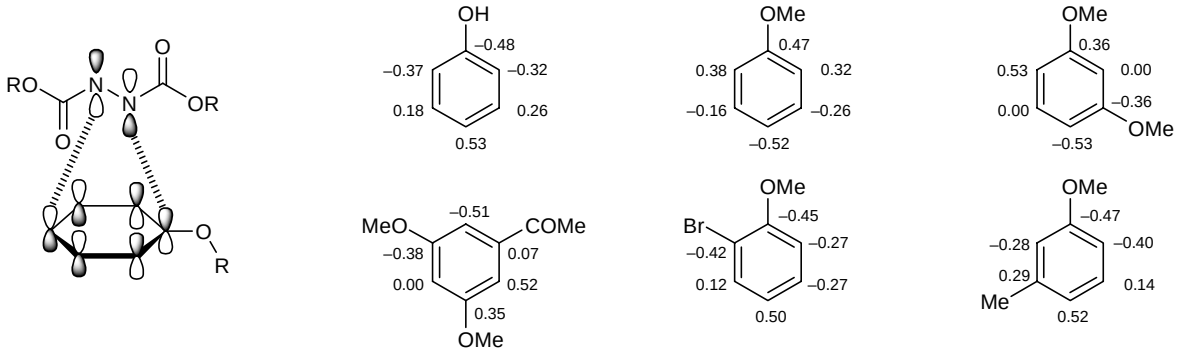
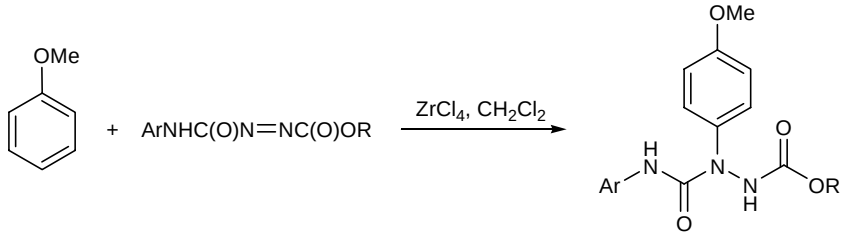


Fig. 3. Schematic representation of the interaction between the HOMO of arene and LUMO of azo reagent in the π-complex derived therefrom and orbital coefficients in the HOMO of some arenes.

chlorine. Groups like NXY behave as readily departing groups. Carbazoles **168a**–**168h** were obtained from *N*-(diarylamino)phthalimides **167a**–**167h** by the action of $AlCl_3$ [159] (Scheme (56). It was presumed that aluminum trichloride induces heterolytic cleavage of the N–N bond in *N*-*p*-tolylaminophthalimide (**169**) in benzene and that *p*-tolylnitrenium ion thus formed reacts with benzene along the C-path to give amines **170** and **171** (Scheme 57) [160]. Likewise, $AlCl_3$ reacts with phenylhydrazines **172a** and **172b** to produce the

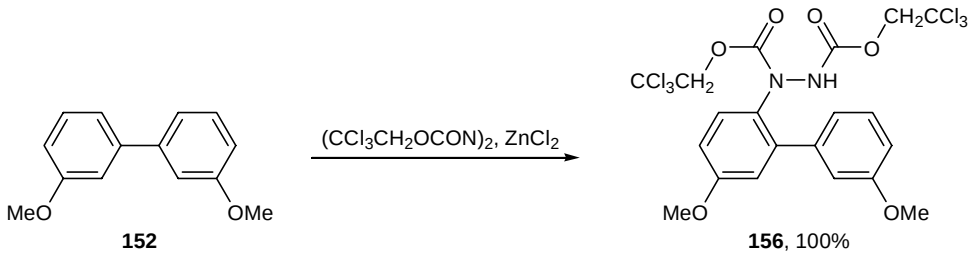
Scheme 50.



147 **149a**–**149g** **151a**–**151g**, 76–93%

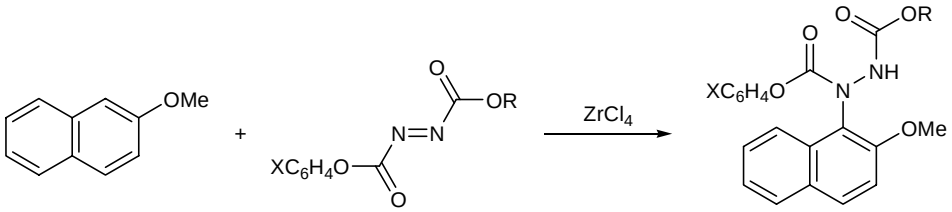
146, **150**, R = H (**a**), MeO (**b**); **149**, **151**, Ar = Ph, R = Et (**a**), *i*-Bu (**b**); Ar = 4-MeC_6H_4, R = Et (**c**); Ar = 4-$MeOC_6H_4$, R = Me (**d**); Ar = 4-FC_6H_4, R = Et (**e**); Ar = 3-ClC_6H_4, R = Et (**f**); Ar = 3,4-$Cl_2C_6H_3$, R = $PhCH_2$ (**g**).

Scheme 51.



152 **156**, 100%

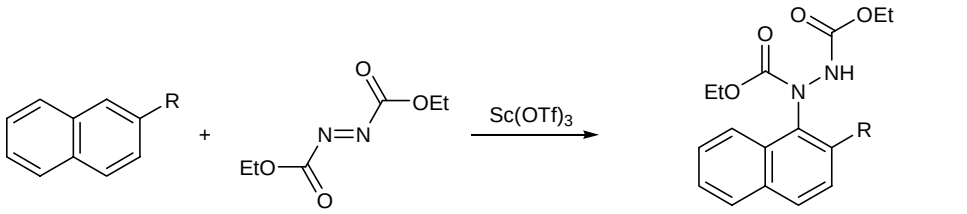
Scheme 52.



153 **144c**, **144d**

157, X = 4-Me, R = Et, 86%
158, X = 4-MeO, R = Me, 95%

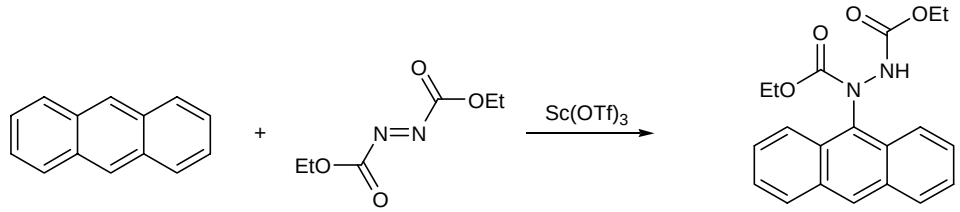
Scheme 53.



154

159, R = H, 78%; **160**, R = Me, 85%
160, R = MeO, 90%

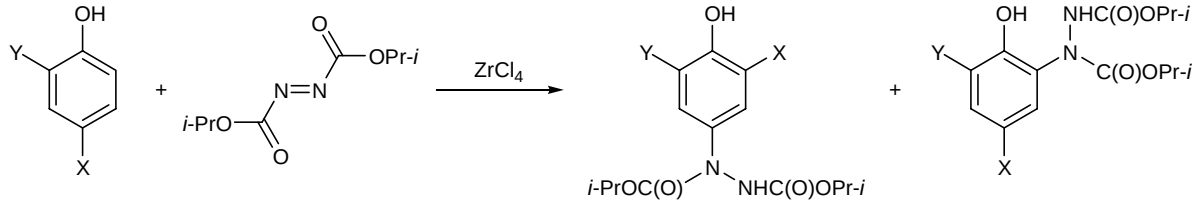
Scheme 54.



155

162, 82%

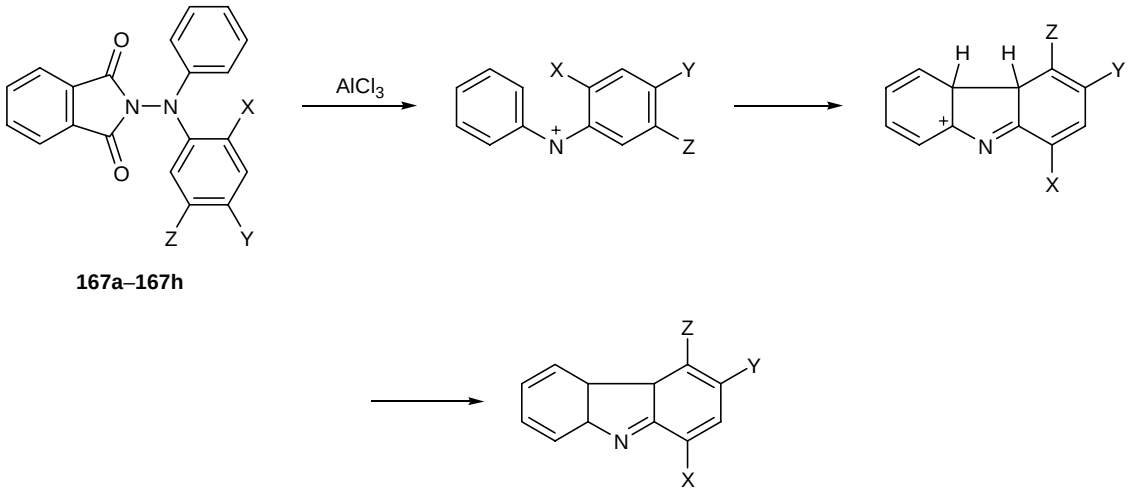
Scheme 55.



163a–**163g** **164** **165a**–**165g**, 5–83% **166a**–**166d**, 10–86%

163, X = Y = Cl (**a**), Br (**b**); Y = H, X = Cl (**c**), Br (**d**), F (**f**), I (**g**); Y = F, X = H (**e**); **165**, X = Y = Cl (**a**), Br (**b**); X = Cl, Y = H (**c**); X = Br, Y = H (**d**); Y = F, X = H (**e**); X = Cl, Y = H (**f**); X = H, Y = H (**g**); **166**, X = Y = Cl (**a**); X = Cl, Y =H (**b**); X = Br, Y = H (**c**); X = I, Y = H (**d**).

Scheme 56.

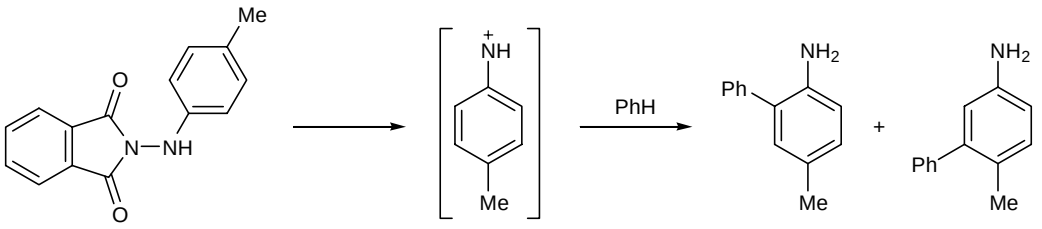


167a–**167h**

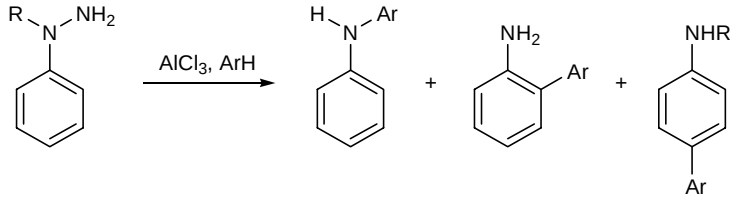
168a–**168h**

167, **168**, X = Y = Z = H (**a**); X = Z = H, Y = Cl (**b**); X = Y = H, Z = Cl (**c**); X = Br, Y = Z = H (**d**); X = Z = H, Y = Me (**e**); X = Y = H, Z = Me (**f**); X = Z = Me, Y = H (**g**); X = Br, Y = Me, Z = H (**h**).

Scheme 57.



Scheme 58.

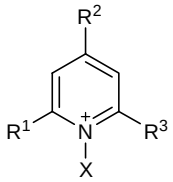


172, R = H (**a**), Me (**b**); **173**, Ar = Ph (**a**), 4-FC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-BrC_6H_4 (**d**), 2,5-$Me_2C_6H_3$ (**e**); **174**, Ar = Ph (**a**), 2-FC_6H_4 (**b**), 2-ClC_6H_4 (**c**), 2-BrC_6H_4 (**d**), 4-ClC_6H_4 (**e**), 4-BrC_6H_4 (**f**), 4-FC_6H_4 (**g**); **175**, R = Me, Ar = Ph (**a**), 2-FC_6H_4 (**b**), 2-BrC_6H_4 (**c**), 2-MeC_6H_4 (**d**), 4-FC_6H_4 (**e**); 4-BrC_6H_4 (**f**), 4-MeC_6H_4 (**g**).

corresponding nitrenium ions which then react with benzene derivatives at both nitrogen and carbon centers, yielding amines **173a**–**173e**, **174a**–**174g**, and **175a**–**175g** [161] (Scheme 58).

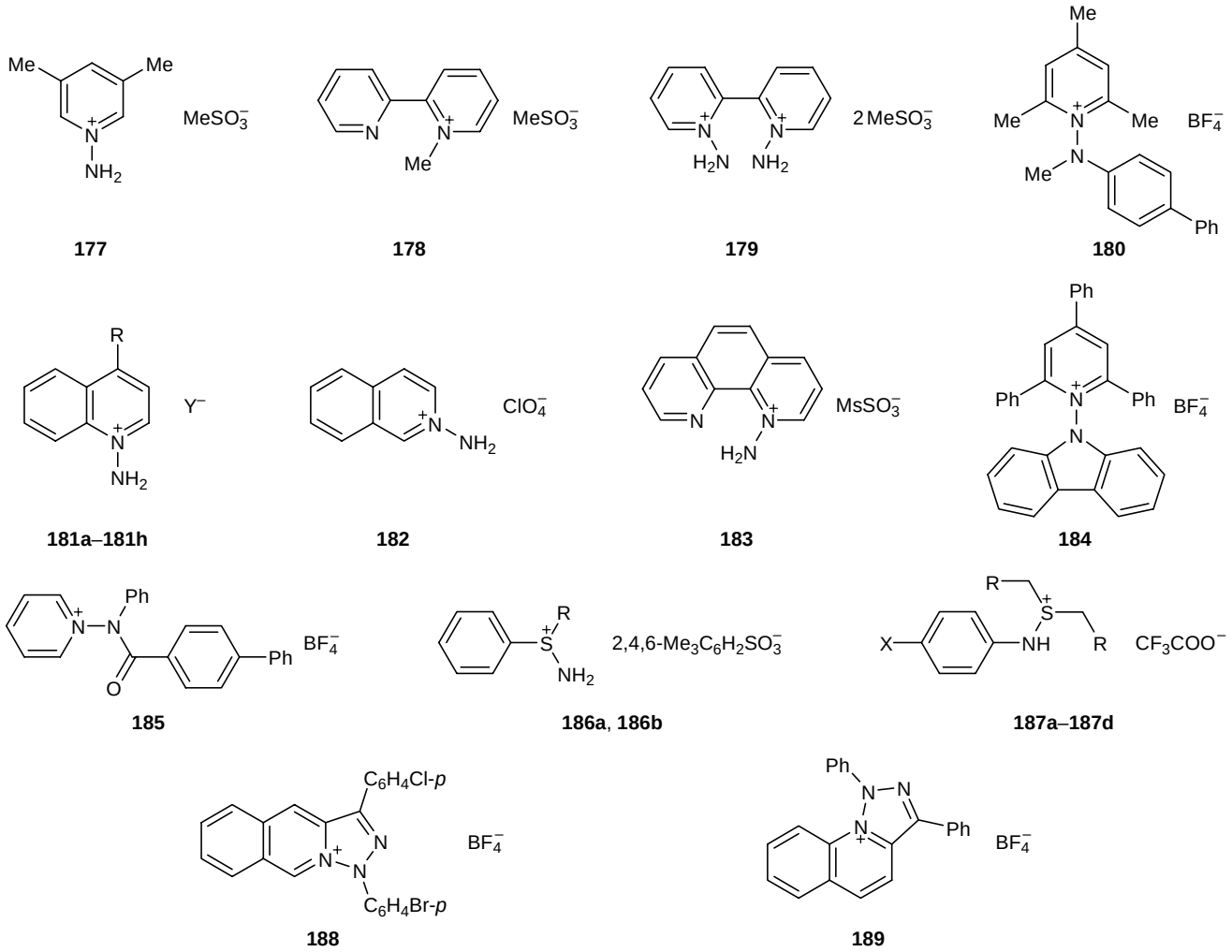
3.5. Aminopyridinium and Aminosulfonium Salts

Direct amination of arenes can be effected via generation of nitrenium ions by thermolysis or photolysis of *N*-aminopyridinium and *S*-aminosulfonium salts and their analogs [162–175]. A wide series of such salts was examined with a view to elucidate the effect of the cation structure and the role of counterion. Photolysis of 1-amino-, 1-methylamino-, and 1,1-dimethylamino-2-methyl-4,6-diphenylpyridinium tetrafluoroborates **176r**, **176t**, and **176v** in benzene or toluene in the presence of CF_3CO_2H led to formation of aniline and isomeric toluidines, respectively, implying participation of nitrenium and alkylnitrenium ions in the singlet state [162, 166] (Scheme 59). Apart from electrophilic substitution products, biphenyl and phenyltolylmethanes are obtained; the latter could be formed according to the radical reaction path with participation of triplet nitrenium ion. The yields of electrophilic substitution products from toluene in the photolysis of salt **176v** were lower than in the photolysis of **176r** and **176t**, while the fraction of phenyltolylmethanes was greater. This may be due to higher rate of the S→T conversion of Me_2N^+ as compared to $MeHN^+$ and H_2N^+ [162]. The low regioselectivity in the reactions of toluene and naphthalene with salts **176** and **177** in the presence of CF_3CO_2H under photolysis conditions indicates high reactivity of $MeHN^+$ and H_2N^+ ions [162, 164]. The same also follows from the low absolute ρ^+ values in the Hammett equation for the reaction of alkylbenzenes with nitrenium ion generated by photolysis of 1-amino-2-methyl-4,6-diphenylpyridinium tetrafluoroborate ($\rho^+ = -2.1$) [162] and 1-amino-



176a–176y

X = NH_2; $R^1 = R^2 = R^3$ = H, Y = Br (**a**), I (**b**), ClO_4 (**c**), $MsSO_3$ (**d**); R^1 = Me, $R^2 = R^3$ = H, Y = I (**e**); R^1 = MeO, $R^2 = R^3$ = H, Y = $MsSO_3$ (**f**), ClO_4 (**g**); $R^1 = R^3$ = H, R^2 = MeO, Y = $MsSO_3$ (**h**); $R^1 = R^3$ = H, R^2 = Me, Y = $MsSO_3$ (**i**); $R^1 = R^3$ = H, R^2 = Ph, Y = $MsSO_3$ (**j**); $R^1 = R^3$ = H, R^2 = MeCO, Y = $MsSO_3$ (**k**); $R^1 = R^3$ = H, R^2 = MeOCO, Y = $MsSO_3$ (**l**); $R^1 = R^3$ = H, R^2 = CH, Y = Br (**m**), ClO_4 (**n**); $MsSO_3$ (**o**); $R^1 = R^3$ = H, $R^2 = NO_2$, Y = $MsSO_3$ (**p**); $R^1 = R^2$ = Me, R^3 = H, Y = $MsSO_3$ (**q**); R^1 = Me, $R^2 = R^3$ = Ph, Y = BF_4 (**r**); $R^1 = R^2 = R^3$ = Ph, Y = ClO_4 (**s**); X = NHMe, R^1 = Me, $R^2 = R^3$ = Ph, Y = BF_4 (**t**); X = PhNH, R^1 = Me, $R^2 = R^3$ = Ph, Y = BF_4 (**u**); X = NMe_2, R^1 = Me, $R^2 = R^3$ = Ph, Y = BF_4 (**v**); X = $(CH_2)_5N$, R^1 = Me, $R^2 = R^3$ = Ph, Y = BF_4 (**w**); X = Ac(Ph)N, $R^1 = R^2 = R^3$ = Ph, Y = BF_4 (**x**); X = NPh_2, $R^1 = R^2 = R^3$ = Me, Y = BF_4 (**y**).



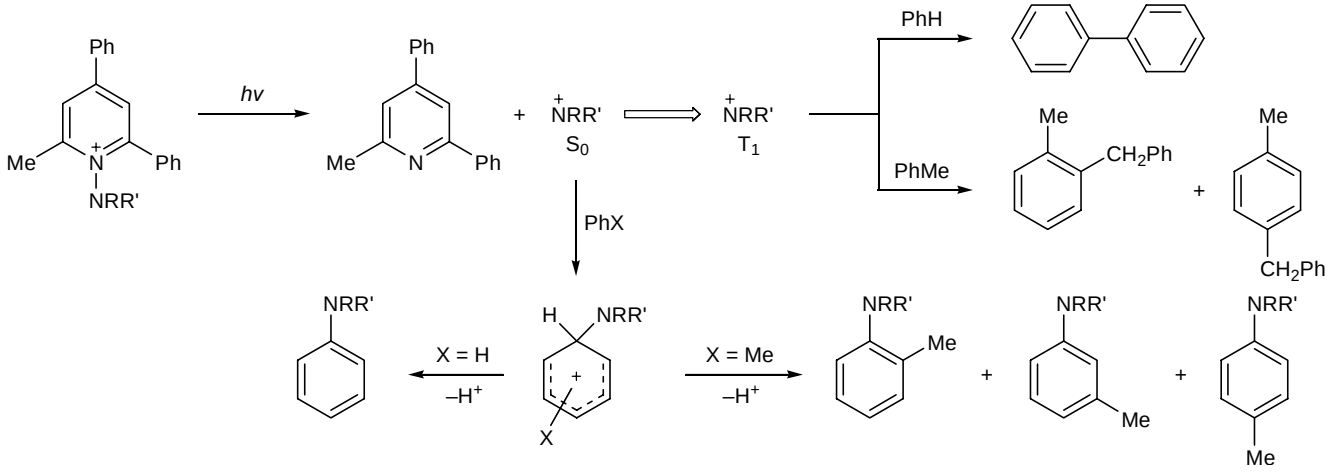
181, R = H, Y = Br (**a**), Cl (**b**), ClO_4 (**c**), $MsSO_3$ (**d**); R = Me, Y = ClO_4 (**e**), $MsSO_3$ (**f**); R = Cl, Y = ClO_4 (**g**), $MsSO_3$ (**h**); **186**, R = Me (**a**), Ph (**b**); **187**, R = X = H (**a**); R = H, X = Me (**b**), NO_2 (**c**); R = Pr, X = NO_2 (**d**).

quinolinium perchlorate ($\rho^+ = -1.9$) [166]. The existence of a linear correlation between log*k* and substituent constants σ^+ for alkyl benzenes suggests a σ-complex-like transition state.

The formation of σ-complexes in electrophilic amination of arenes is supported by the data of [174]. The electron absorption spectra of the reaction mixtures obtained in the photolysis of salt **176t** in the presence of 1-R-3,5-dimethoxybenzenes (R = H, MeO) contained a band with its maximum at λ 330 nm, which was assigned to 1-diphenylamino-2-R-4,6-dimethoxybenzenium ions (R = H, MeO). By contrast, no evidences in favor of formation of σ-complexes were obtained in the reactions of activated arenes (such as mesitylene, 1,3,5-triethylbenzene, durene, pentamethylbenzene, and hexamethylbenzene) with *N*-methyl-4-biphenylylnitrenium ion generated by photolysis of salt **180**: the relative rate constants did not conform to the expected stability of σ-complexes but were consistent with the formation of π-complexes between arylnitrenium ion and arene [172].

The reactivity of *N*-aminopyridinium salts **176** and **177** toward arenes in the presence of CF_3CO_2H strongly depends on the substituent in the pyridine ring and counterion nature [164, 167]. Electron-acceptor substituents increase the selectivity factor S_f = log{2[(*p*-toluidine)%]/[(*m*-toluidine)%]}. The fractions of 1- and 2-aminonaphthalenes in the photolysis of salts **176** and **177** in the system naphthalene–CF_3CO_2H also depend on the structure of the pyridinium fragment and counterion [164]. Analogous relations are typical of quinolinium salts **181** in the system toluene–CF_3CO_2H [167]. The selectivity factor decreases in the series $Cl^- > Br^- > MsSO_3^- > ClO_4^-$, which was inter-

Scheme 59.



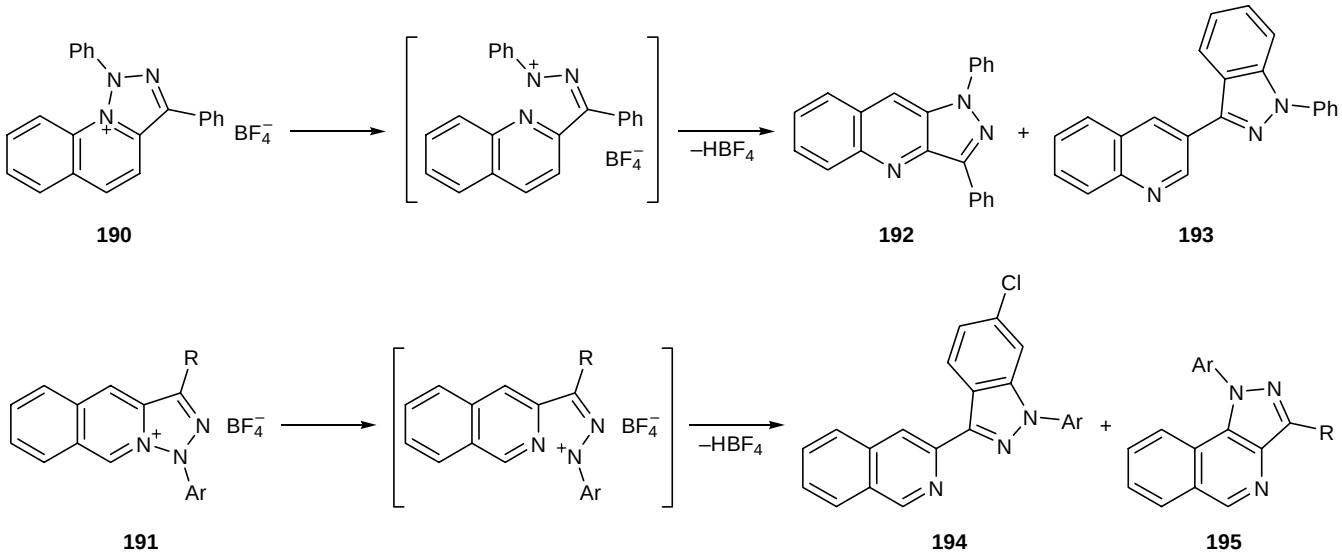
R = R' = H; R = H, R' = Me; R = R' = Me.

preted [167] in terms of variation of the degree of negative charge localization on the anion. The same series, $Br^- > MsSO_3^- > ClO_4^- > I^-$, was found for the photolysis of aminopyridinium salts **176a–176e** [167].

Addition of small amounts of 18-crown-6 to a mixture of benzene with CF_3CO_2H in the photolysis of 1-aminopyridinium and 1-aminoquinolinium mesitylenesulfonates leads to monotonous increase in the yield of aniline, presumably due to stabilization of the singlet state of NH_2^+ ion via interaction with the crown ether [167]. In the photolysis of the corresponding perchlorates, the yield of aniline initially increases and then sharply falls down. A probable reason is the formation of a sandwich-like complex between NH_2^+ and two 18-crown-6 molecules when the concentration of the latter exceeds that corresponding to the maximal yield of aniline. This complex is likely to be less reactive because of hindered approach of benzene molecule to NH_2^+ ion bound into the complex [167]. The yield of aniline and toluidines in the photolysis of salts **176d** and **178** in benzene–CF_3CO_2H or PhMe–CF_3CO_2H decreases on addition of heavy atom-containing solvents (CH_2Cl_2, CH_2Br_2, CH_3I), as well as in the presence of atmospheric oxygen. Presumably, this is the result of increase in the rate of S–T conversion of nitrenium ion [164].

Interaction of nitrenium ion with lone electron pair on the sulfur atom in sulfides is weaker than with

Scheme 60.



191, **194**, **195**, R = 4-ClC_6H_4, Ar = 4-BrC_6H_4.

nitrogen lone electron pair in pyridine derivatives; therefore, the singlet–triplet conversion of nitrenium ions derived from sulfonium salts should proceed at a higher rate. This is consistent with the poor yield of amination products in the photolysis of salts **186a** and **186b** in the systems benzene–CF_3CO_2H and toluene–CF_3CO_2H [164].

Photolysis of salts **176y** and **185** under neutral conditions gave rise to unusual intramolecular cyclization leading to carbazole (yield 24%) [173] (cf. [52]) and *N*-phenylphenanthridinone (yield 65%) [168].

Nitrenium ions can be generated from aminopyridinium salts not only by photolysis but also by thermolysis. However, in the latter case, the presence of at least one electron-donor substituent on the nitrogen atom is necessary. For example, thermolysis of salt **176x** under fairly severe conditions (180°C) in the presence of mesitylene afforded 5% of *N*-phenyl-*N*-(2,4,6-trimethylphenyl)acetamide [163]. 9-Mesitylcarbazole was obtained in 35–45% yield by thermolysis of 1-(9-carbazolyl)-2,4,6-triphenylpyridinium tetrafluoroborate in the presence of mesitylene [171]. The yield increases to 70% under microwave irradiation; less reactive arenes also give rise to the corresponding 9-arylcarbazoles, but with a considerably lower yield (anisole, 56%; *p*-xylene, 20%; toluene, 1%) [176]. [1,2,3]Triazolo[1,5-*a*]quinolinium salt **190** and [1,2,3]-triazolo[1,5-*b*]isoquinolinium salts **191** undergo thermal isomerization with rupture of the N–N bond and formation of new heterocyclic systems **192**–**195** [175] (Scheme 60).

It should be noted that 1-amino-1,10-phenanthrolinium mesitylenesulfonate does not react with mesitylene and anthracene even at a fairly high temperature (150°C) [177], presumably due to very low stability of the corresponding nitrenium ion.

4. RADIOCHEMICAL GENERATION OF NITRENIUM IONS

A specific feature of the radiochemical method for generation of nitrenium ions is that it ensures their reaction with arenes under conditions excluding effects of the counterion and acidic medium, which is important for understanding the mechanisms of these reactions. The procedure is based on β-decay of tritium; for example, phenylnitrenium ion $PhNT^+$ is formed from tritium-labeled aniline (Scheme 61).

Study of electrophilic replacement of hydrogen in benzene and monosubstituted benzenes (such as toluene and nitrobenzene) by phenylnitrenium ion $PhNT^+$ showed that, like in the above described reactions, the process follows both N- and C-paths, yielding diphenylamines and aminobiphenyls, respectively [21, 178–180]. In the reaction with toluene, the product was exclusively 4-methyldiphenylamine [178], while nitrobenzene gave rise to both nitrodiphenylamines (16% of *ortho*, 20% of *meta*, and 8% of *para* isomer) and *o*-, *m*-(40%), and *p*-aminobiphenyls (16%) [179]. Analysis of the experimental and calculation (AM1) results [54] indicated that the composition of products formed in the reaction of benzene with radiochemically generated phenylnitrenium ion is determined by comparable contributions of the equilibrium constants for formation of σ-complexes and rate constants for their deprotonation.

Scheme 61.

$$PhNT_2 \xrightarrow[-\beta^-]{} PhNTHe^+ \longrightarrow PhNT^+ + He$$

5. CONCLUSION

The conception of nitrenium ions is important for understanding mechanisms of direct electrophilic amination of arenes with various reagents. In the present review, we made an attempt to consider these mechanisms in terms of a common concept involving participation of nitrenium ions. However, it should be emphasized that the proposed schemes are often speculative. Undoubtedly, further studies in the field of nitrenium ions, including their "direct observation," should provide clearer realization of the mechanisms of electrophilic amination of arenes and a basis for development of new effective methods of synthesis of aromatic amines.

This review was prepared under financial support by the Russian Foundation for Basic Research (project nos. 02-03-32431 and 02-03-32881).

REFERENCES

1. Mashkovskii, M.D., *Lekarstvennye sredstva* (Drugs), Moscow: Novaya Volna, 2002, vols. 1, 2.
2. Soldatenkov, A.T., Kolyadina, N.M., and Shendrik, I.V., *Osnovy organicheskoi khimii lekarstvennykh veshchestv* (Principles of the Organic Chemistry of Drugs), Moscow: Mir, 2003, p. 8.
3. Lednicer, D., *Strategies for Organic Drug Synthesis and Design*, New York: Wiley, 1998, p. 1.
4. Belan, S.R., Grapov, A.F., and Mel'nikova, G.M., *Novye pestitsidy. Spravochnik* (New Pesticides. Handbook), Moscow: VNIIKhSZR, 2001, p. 1.

5. Gaile, A.A., Somov, V.E., and Varshavskii, O.M., *Aromaticheskie uglevodorody: vydelenie, primenenie, rynok* (Aromatic Hydrocarbons: Isolation, Application, and Market), St. Petersburg: Khimizdat, 2000.
6. Krasovitskii, B.M. and Afanasiadi, L.M., *Mono- i bifluorofory* (Mono- and Bifluorophores), Khar'kov: Inst. Monocryst., 2002.
7. Lehn, J.-M., *Supramolecular Chemistry: Concepts and Perspectives*, Weinheim: VCH, 1995. Translated under the title *Supramolekulyarnaya khimiya*, Novosibirsk: Nauka, Sib. Predpr. Ross. Akad. Nauk, 1998, pp. 111, 167.
8. Benigni, R., Giuliani, A., Franke, R., and Gruska, A., *Chem. Rev*., 2000, vol. 100, p. 3697.
9. McClelland, R.A., Ahmad, A., Dicks, A.P., and Licence, V.E., *J. Am. Chem. Soc*., 1999, vol. 121, p. 3303.
10. McClelland, R.A., Gadosy, T.A., and Ren, D., *Can. J. Chem*., 1998, vol. 76, p. 1327.
11. Novak, M. and Kennedy, S.A., *J. Phys. Org. Chem*., 1998, vol. 11, p. 71.
12. Hoffman, G.R. and Fuchs, R.P.P., *Chem. Res. Toxicol*., 1997, vol. 10, p. 347.
13. McClelland, R.A., Kahley, M.J., and Davidse, P.A., *J. Phys. Org. Chem*., 1996, vol. 9, p. 355.
14. McClelland, R.A., *Tetrahedron*, 1996, vol. 52, p. 6823.
15. Falvey, D.E., *J. Phys. Org. Chem*., 1999, vol. 12, p. 589.
16. Toteva, M.M and O'Donoghue, A.C., *Annu. Rep. Prog. Chem., Sect B: Org. Chem*., 2000, vol. 96, p. 291.
17. *Comprehensive Organic Chemistry*, Barton, D. and Ollis, W.D., Eds., Oxford: Pergamon, 1979, vol. 2. Translated under the title *Obshchaya organicheskaya khimiya*, Moscow: Khimiya, 1982, vol. 3, p. 168.
18. De Vos, D.E., Dams, M., Sels, B.F., and Jacobs, P.A., *Chem. Rev*., 2002, vol. 102, p. 3615.
19. Adams, J.P. and Paterson, J.R., *J. Chem. Soc., Perkin Trans. 1*, 2000, p. 3695.
20. Wolfe, J.P., Wagaw, S., Marcoux, J.-F., and Buchwald, S.L., *Acc. Chem. Res*., 1998, vol. 31, p. 805; Hartwig, J.F., *Angew. Chem., Int. Ed. Engl*., 1998, vol. 37, p. 2046; Belfield, A.J., Brown, G.R., and Foubister, A.J., *Tetrahedron*, 1999, vol. 55, p. 11399.
21. Simonova, T.P., Nefedov, V.D., Toropova, M.A., and Kirillov, N.F., *Usp. Khim*., 1992, vol. 61, p. 1061.
22. Ford, G.P. and Scribner, J.D., *J. Am. Chem. Soc*., 1981, vol. 103, p. 4281.
23. Glover, S.A. and Scott, A.P., *Tetrahedron*, 1989, vol. 45, p. 1763.
24. Ford, G.P. and Herman, P.S., *J. Am. Chem. Soc*., 1989, vol. 111, p. 3987.
25. Falvey, D.E. and Cramer, C.J., *Tetrahedron Lett*., 1992, vol. 33, p. 1705.
26. Barclay, V.J., Hamilton, I.P., and Jensen, P., *J. Chem. Phys*., 1993, vol. 99, p. 9709.
27. Gobbi, A. and Frenking, G., *Chem. Commun*., 1993, p. 1162.
28. Gobbi, A. and Frenking, G., *Bull. Chem. Soc. Jpn*., 1993, vol. 66, p. 3153.
29. Cramer, C.J., Dulles, F.J., Storer, J.W., and Worthington, S.E., *Chem. Phys. Lett*., 1994, vol. 218, p. 387.
30. Wright, T.G. and Miller, T.A., *J. Phys. Chem*., 1996, vol. 100, p. 4408.
31. Osmann, G., Bunker, P.R., Jensen, P., and Kraemer, W.P., *J. Mol. Spectrosc*., 1997, vol. 186, p. 319.
32. Milburn, R.K., Rodriquez, C.F., and Hopkinson, A.C., *J. Phys. Chem. B*, 1997, vol. 101, p. 1837.
33. Van Huis, T.J., Leininger, M.L., Sherrill, C.D., and Schaefer, H.F., *Collect. Czech. Chem. Commun*., 1998, vol. 63, p. 1107.
34. Gonzalez, C., Restrepo-Cossio, A., Marquez, M., Wiberg, K.B., and De Rosa, M., *J. Phys. Chem. A*, 1998, vol. 102, p. 2732.
35. Stephens, J.C., Yamaguchi, Y., Sherrill, C.D., and Schaefer, H.F., *J. Phys. Chem. A*, 1998, vol. 102, p. 3999.
36. Marquez, M., Mari, F., and Gonzalez, C.A., *J. Phys. Chem. A*, 1999, vol. 103, p. 6191.
37. Stephens, J.C., Yamaguchi, Y., and Schaefer, H.F., *J. Mol. Struct. (Theochem)*, 1999, vols. 461–462, p. 41.
38. Osmann, G., Bunker, P.R., Kraemer, W.P., and Jensen, P., *Chem. Phys. Lett*., 2000, vol. 318, p. 597.
39. Dixon, D.A., Feller, D., and Peterson, K.A., *J. Chem. Phys*., 2001, vol. 115, p. 2576.
40. Bronzolino, N. and Gzandinetti, F., *J. Mol. Struct. (Theochem)*, 2003, vol. 635, p. 221.
41. Ford, G.P. and Herman, P.S., *J. Mol. Struct. (Theochem)*, 1990, vol. 204, p. 121.
42. Cramer, C.J. and Worthington, S.E., *J. Phys. Chem*., 1995, vol. 99, p. 1462.
43. Krogh-Jespersen, K., *Tetrahedron Lett*., 1980, vol. 21, p. 4553.
44. Smith, D.A. and Bitar, J., *J. Org. Chem*., 1993, vol. 58, p. 6.
45. Li, Q.S. and Cheng, L.P., *J. Phys. Chem. A*, 2003, vol. 107, p. 5561.
46. Ding, Y.-H., Li, Z.-S., Huang, X.-R., and Sun, C.-C., *J. Phys. Chem. A*, 2001, vol. 105, p. 7085.
47. Glover, S.A., Scott, A.P., and Tarrant, G.J., Abstracts of Papers, *Electronic Conf. on Heterocyclic Chemistry*, June 24–July 22, 1996, p. 1.
48. Ford, G.P. and Herman, P.S., *J. Mol. Struct. (Theochem)*, 1991, vol. 236, p. 269.
49. Cramer, C.J., Dulles, F.J., and Falvey, D.E., *J. Am. Chem. Soc*., 1994, vol. 116, p. 9787.

50. Shcherbinin, M.B., Erusalimskii, G.B., Bal'tser, A.E., Bazanov, A.G., and Ostrovskii, V.A., *Russ. J. Org. Chem*., 1995, vol. 31, p. 1622.
51. Cramer, C.J. and Falvey, D.E., *Tetrahedron Lett*., 1997, vol. 38, p. 1515.
52. Moran, R.J., Cramer, C., and Falvey, D.E., *J. Org. Chem*., 1997, vol. 62, p. 2742.
53. Sullivan, M.B., Brown, K., Cramer, C.J., and Truhlar, D.G., *J. Am. Chem. Soc*., 1998, vol. 120, p. 11778.
54. Simonova, T.P., Shurov, S.N., Nefedov, V.D., Toropova, M.A., and Avrorin, V.V., *Russ. J. Org. Chem*., 1998, vol. 34, p. 74.
55. Ford, G.P., Herman, P.S., and Thompson, J.W., *J. Comput. Chem*., 1999, vol. 20, p. 231.
56. Novak, M. and Lin, J., *J. Org. Chem*., 1999, vol. 64, p. 6032.
57. Sullivan, M.B. and Cramer, C.J., *J. Am. Chem. Soc*., 2000, vol. 122, p. 5588.
58. Pol'shakov, D.A., Tsentalovich, Yu.P., and Gritsan, N.P., *Izv. Ross. Akad. Nauk, Ser. Khim*., 2000, p. 49.
59. Novak, M. and Rajagopal, S., *Adv. Phys. Org. Chem*., 2001, vol. 36, p. 167.
60. Zhu, P., Ong, S.Y., Chan, P.Y., Leung, K.H., and Phillips, D.L., *J. Am. Chem. Soc*., 2001, vol. 123, p. 2645.
61. Zhu, P., Ong, S.Y., Chan, P.Y., Poon, Y.F., Leung, K.H., and Phillips, D.L., *Chem. Eur. J*., 2001, vol. 7, p. 4928.
62. Parks, J.M., Ford, G.P., and Cramer, C.J., *J. Org. Chem*., 2001, vol. 66, p. 8997.
63. Chan, P.Y., Ong, S.Y., Zhu, P., Leung, K.H., and Phillips, D.L., *J. Org. Chem*., 2003, vol. 68, p. 5265.
64. Chan, P.Y., Ong, S.Y., Zhu, P., Zhao, C., and Phillips, D.L., *J. Phys. Chem. A*, 2003, vol. 107, p. 8067.
65. O'Brien, S.E., Browne, H.L., Bradshaw, T.D., Westwell, A.D., Stevens, M.F.G., and Laughton, C.A., *Org. Biomol. Chem*., 2003, vol. 1, p. 493.
66. Ford, G.P. and Herman, P.S., *J. Chem. Soc., Perkin Trans. 2*, 1991, p. 607.
67. Novak, M., Kahley, M.J., Lin, J., Kennedy, S.A., and Swanegan, L.A., *J. Am. Chem. Soc*., 1994, vol. 116, p. 11626.
68. Cramer, C.J., Truhlar, D.G., and Falvey, D.E., *J. Am. Chem. Soc*., 1997, vol. 119, p. 12338.
69. Srivastava, S., Ruane, P.H., Toscano, J.P., Sullivan, M.B., Cramer, C.J., Chiapperino, D., Reed, E.C., and Falvey, D.E., *J. Am. Chem. Soc*., 2000, vol. 122, p. 8271.
70. Grandinetti, F., Hrusak, J., Schroder, D., Karrass, S., and Schwarz, H., *J. Am. Chem. Soc*., 1992, vol. 114, p. 2806.
71. Cacace, F. and Pepi, F., *J. Phys. Chem*., 1994, vol. 98, p. 8009.
72. Cacace, F., Grandinetti, F., and Pepi, F., *Inorg. Chem*., 1995, vol. 34, p. 1325.
73. Hiraoka, K., Nasu, M., Fujimaki, S., and Yamabe, S., *J. Phys. Chem*., 1995, vol. 99, p. 15822.
74. Ricca, A., *Chem. Phys. Lett*., 1998, vol. 294, p. 454.
75. Aschi, M., Grandinetti, F., and Vinciguerra, V., *Chem. Eur. J*., 1998, vol. 4, p. 2366.
76. Aschi, M. and Grandinetti, F., *J. Mol. Struct. (Theochem)*, 2000, vol. 497, p. 205.
77. Grandinetti, F. and Vinciguerra, V., *Int. J. Mass. Spectrom*., 2002, vol. 216, p. 285.
78. Schoeller, W.W. and Busch, T., *Chem. Ber*., 1990, vol. 123, p. 971.
79. Nguyen, M.T. and Ha, T.-K., *Chem. Phys. Lett*., 2000, vol. 317, p. 135.
80. Vij, A., Wilson, W.W., Vij, V., Tham, F.S., Sheehy, J.A., and Christe, K.O., *J. Am. Chem. Soc*., 2001, vol. 123, p. 6308.
81. Kerkines, I.S.K., Papakondylis, A., and Mavridis, A., *J. Phys. Chem. A*, 2002, vol. 106, p. 4435.
82. Dixon, D.A., Feller, D., Christe, K.O., Wilson, W.W., Vij, A., Vij, V., Jenkins, H.D.B., Olson, R.M., and Gordon, M.S., *J. Am. Chem. Soc*., 2004, vol. 126, p. 834.
83. Liu, Y.D., Zhao, J.F., and Li, Q.S., *Theor. Chem. Acc*., 2002, vol. 107, p. 140.
84. Li, Q.S. and Zhao, J.F., *J. Phys. Chem. A*, 2002, vol. 106, p. 5928.
85. Li, Q.S., Wang, L.J., and Xu, W.G., *Theor. Chem. Acc*., 2000, vol. 104, p. 67.
86. Cacace, F., Grandinetti, F., and Pepi, F., *Angew. Chem., Int. Ed. Engl*., 1994, vol. 33, p. 123.
87. Aschi, M., Cacace, F., Grandinetti, F., and Pepi, F., *J. Phys. Chem*., 1994, vol. 98, p. 2713.
88. Gibson, S.T., Greene, J.P., and Berkowitz, J., *J. Chem. Phys*., 1985, vol. 83, p. 4319.
89. Kabbadj, Y., Huet, T.R., Uy, D., and Oka, T., *J. Mol. Spectrosc*., 1996, vol. 175, p. 277.
90. McIlroy, S., Cramer, C.J., and Falvey, D.E., *Org. Lett*., 2000, vol. 2, p. 2451.
91. Boche, G., Andrews, P., Harms, K., Marsch, M., Rangappa, K.S., Schimeczek, M., and Willeke, C., *J. Am. Chem. Soc*., 1996, vol. 118, p. 4925.
92. Boche, G., Rangappa, K., Harms, K., and Marsch, M., *Z. Crystallogr*., 1996, vol. 211, p. 581.
93. Boche, G., Marsch, M., Willeke, C., and Harms, K., *Z. Crystallogr*., 1996, vol. 211, p. 583.
94. Wirschun, W. and Jochims, J.C., *Synthesis*, 1997, p. 233.
95. Sridhar, M.A., Lokanath, N.K., Shashidhara, P.J., Bhadre, G.D.G., and Rangappa, K.S., *Z. Crystallogr. New Cryst. Struct*., 1997, vol. 212, p. 33.

96. Wirschun, W., Winkler, M., Lutz, K., and Jochims, J.C., *J. Chem. Soc., Perkin Trans. 1*, 1998, p. 1755.
97. Al-Soud, Y.A., Shrestha-Dawadi, P.B., Winkler, M., Wirschun, W., and Jochims, J.C., *J. Chem. Soc., Perkin Trans. 1*, 1998, p. 3759.
98. Hoffmann, F. and Griehl, C., *J. Mol. Struct*., 1998, vol. 440, p. 113.
99. Katritzky, A.R., Zhang, G.-F., Pernak, J., and Fan, W.-Q., *Heterocycles*, 1993, vol. 36, p. 1253.
100. Robert, M., Neudeck, A., Boche, G., Willeke, C., Rangappa, K.S., and Andrews, P., *New J. Chem*., 1998, vol. 22, p. 1437.
101. Pause, L., Robert, M., Heinicke, J., and Kuhl, O., *J. Chem. Soc., Perkin Trans. 2*, 2001, p. 1383.
102. Trifonov, R.E., Alkorta, I., Ostrovskii, V.A., and Elguero, J., *Heterocycles*, 2000, vol. 52, p. 291.
103. Allen, F.H., Kennard, O., Watson, D.G., Brammer, L., Orpen, G., and Taylor, R., *J. Chem. Soc., Perkin Trans. 2*, 1987, p. S1.
104. *Current Trends in Organic Synthesis*, Scolastico, C. and Nicotra, F., Eds., New York: Plenum, 1998, p. 97.
105. Bock, H. and Kompa, K.-L., *Chem. Ber*., 1966, vol. 99, p. 1361.
106. Bock, H. and Kompa, K.-L., *Chem. Ber*., 1966, vol. 99, p. 1357.
107. Kovacic, P., Lange, R.M., Foote, J.L., Goralski, C.T., Hiller, J.J., and Levisky, J.A., *J. Am. Chem. Soc*., 1964, vol. 86, p. 1650.
108. Kovacic, P., Goralski, C.T., Hiller, J.J., Levisky, J.A., and Lange, R.M., *J. Am. Chem. Soc*., 1965, vol. 87, p. 1262.
109. Kovacic, P., Lowery, M.K., and Field, K.W., *Chem. Rev*., 1970, vol. 70, p. 639.
110. Belen'kaya, R.S., Verevkin, S.P., Zimichev, A.V., and Rozhnov, A.M., *Zh. Org. Khim*., 1993, vol. 29, p. 570.
111. Kikugawa, Y. and Kawase, M., *J. Am. Chem. Soc*., 1984, vol. 106, p. 5728.
112. Kawase, M., Kitamura, T., and Kikugawa, Y., *J. Org. Chem*., 1989, vol. 54, p. 3394.
113. Kikugawa, Y. and Shimada, M., *Chem. Lett*., 1987, p. 1771.
114. Kikugawa, Y., Shimada, M., and Matsumoto, K., *Heterocycles*, 1994, vol. 37, p. 293.
115. Glover, S.A., Goosen, A., McCleland, C.W., and Schoonraad, J.L., *Tetrahedron*, 1987, vol. 43, p. 2577.
116. Glover, S.A., Rowbottom, C.A., Scott, A.P., and Schoonraad, J.L., *Tetrahedron*, 1990, vol. 46, p. 7247.
117. Lee, S.J., Terrazas, M.S., Pippel, D.J., and Beak, P., *J. Am. Chem. Soc*., 2003, vol. 125, p. 7307.
118. Takeuchi, H., Taniguchi, T., and Ueda, T., *J. Chem. Soc., Perkin Trans. 2*, 2000, p. 295.
119. Takeuchi, H., Tateiwa, J.-i., Hata, S., Tsutsumi, K., and Osaki, Y., *Eur. J. Org. Chem*., 2003, p. 3920.
120. Shudo, K., Ohta, T., and Okamoto, T., *J. Am. Chem. Soc*., 1981, vol. 103, p. 645.
121. Spence, J.D., Raymond, A.E., and Norton, D.E., *Tetrahedron Lett*., 2003, vol. 44, p. 849.
122. Naicker, K.P, Pitchumani, K., and Varma, R.S., *Catal. Lett*., 1998, vol. 54, p. 165.
123. Miyazawa, E., Sakamoto, T., and Kikugawa, Y., *J. Chem. Soc., Perkin Trans. 2*, 1998, p. 7.
124. Novak, M. and Kazerani, S., *J. Am. Chem. Soc*., 2000, vol. 122, p. 3606.
125. Novak, M. and Rangappa, K.S., *J. Org. Chem*., 1992, vol. 57, p. 1285.
126. Novak, M., Rangappa, K.S., and Manitsas, R.K., *J. Org. Chem*., 1993, vol. 58, p. 7813.
127. Meier, C. and Boche, G., *Tetrahedron Lett*., 1990, vol. 31, p. 1693.
128. Kawase, M. and Kikugawa, Y., *Chem. Pharm. Bull*., 1981, vol. 29, p. 1615.
129. Kikugawa, Y. and Kawase, M., *Chem. Commun*., 1991, p. 1354.
130. Wardrop, D.J., Burge, M.S., Zhang, W., and Ortiz, J.A., *Tetrahedron Lett*., 2003, vol. 44, p. 2587.
131. Wardrop, D.J., Landrie, C.L., and Ortiz, J.A., *Synlett*, 2003, p. 1352.
132. Miyazawa, E., Sakamoto, T., and Kikugawa, Y., *J. Org. Chem*., 2003, vol. 68, p. 5429.
133. Miyazawa, E., Sakamoto, T., and Kikugawa, Y., *Heterocycles*, 2003, vol. 59, p. 149.
134. Kikugawa, Y., Nagashima, A., Sakamoto, T., Miyarawa, E., and Shiiya, M., *J. Org. Chem*., 2003, vol. 68, p. 6739.
135. Liard, A., Nguyen, T.-H., Smir, A.I.D., Vaultier, M., Derdour, A., and Mortier, J., *Chem. Eur. J*., 2003, vol. 9, p. 1000.
136. Mertens, A., Lammertsma, K., Arvanaghi, M., and Olah, G.A., *J. Am. Chem. Soc*., 1983, vol. 105, p. 5657.
137. Borodkin, G.I., Popov, S.A., and Shubin, V.G., Abstracts of Papers, *Int. Conf. "Reaction Mechanisms and Organic Intermediates,"* St. Petersburg: Nauch.-Issled. Inst. Khim. Sankt-Peterburg Gos. Univ., 2001, p. 87.
138. Borodkin, G.I., Popov, S.A., Pokrovskii, L.M., and Shubin, V.G., *Russ. J. Org. Chem*., 2003, vol. 39, p. 747.
139. Borodkin, G.I., Elanov, I.R., Popov, S.A., Pokrovskii, L.M., and Shubin, V.G., *Russ. J. Org. Chem*., 2003, vol. 39, p. 672.
140. Borodkin, G.I., Bessonov, A.A., Popov, S.A., and Shubin, V.G., *Materialy Vserossiiskoi nauchnoi molodezhnoi konferentsii "pod znakom sigma"* (Proc. All-Russia Scientific Youth Conf. "Under the Sigma Sign"), Omsk, 2003, p. 55.

141. Borodkin, G.I., Bessonov, A.A., Andreev, R.V., and Shubin, V.G., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 755.
142. Takeuchi, H., Adachi, T., Nishiguchi, H., Itou, K., and Koyama, K., *J. Chem. Soc., Perkin Trans. 1*, 1993, p. 867.
143. Olah, G.A. and Ernst, T.D., *J. Org. Chem.*, 1989, vol. 54, p. 1203.
144. Stevens, M.F.G., Shi, D.-F., and Castro, A., *J. Chem. Soc., Perkin Trans. 1*, 1996, p. 83.
145. Takeuchi, H. and Watanabe, K., *J. Phys. Org. Chem.*, 1998, vol. 11, p. 478.
146. Abramovitch, R.A. and Shi, Q., *Heterocycles*, 1994, vol. 38, p. 2147.
147. Abramovitch, R.A., Ye, X., Pennington, W.T., Schimek, G., and Bogdal, D., *J. Org. Chem.*, 2000, vol. 65, p. 343.
148. Abramovitch, R.A. and Ye, X., *J. Org. Chem.*, 1999, vol. 64, p. 5904.
149. Abramovitch, R.A., Miller, J., and Souza, A.J.C., *Tetrahedron Lett.*, 2003, vol. 44, p. 6965.
150. Lang, S., Kennedy, A.R., Murphy, J.A., and Payne, A.H., *Org. Lett.*, 2003, vol. 5, p. 3655.
151. Zaltsgendler, I., Leblanc, Y., and Bernstein, M.A., *Tetrahedron Lett.*, 1993, vol. 34, p. 2441.
152. Mitchell, H. and Leblanc, Y., *J. Org. Chem.*, 1994, vol. 59, p. 682.
153. Leblanc, Y. and Boudreault, N., *J. Org. Chem.*, 1995, vol. 60, p. 4268.
154. Dufresne, C., Leblanc, Y., Berthelette, C., and McCooeye, C., *Synth. Commun.*, 1997, vol. 27, p. 3613.
155. Bombek, S., Lenarsic, R., Kocevar, M., Saint-Jalmes, L., Desmurs, J.-R., and Polanc, S., *Chem. Commun.*, 2002, p. 1494.
156. Lenarsic, R., Kocevar, M., and Polanc, S., *J. Org. Chem.*, 1999, vol. 64, p. 2558.
157. Yadav, J.S., Reddy, B.V.S., Kumar, G.M., and Madan, C., *Synlett*, 2001, p. 1781.
158. Yadav, J.S., Reddy, B.V.S., Veerendhar, G., Rao, R.S., and Nagaiah, K., *Chem. Lett.*, 2002, p. 318.
159. Kikugawa, Y., Aoki, Y., and Sakamoto, T., *J. Org. Chem.*, 2001, vol. 66, p. 8612.
160. Ohwada, A., Li, H., Sakamoto, T., and Kikugawa, Y., *Heterocycles*, 1997, vol. 46, p. 225.
161. Ohwada, A., Nara, S., Sakamoto, T., and Kikugawa, Y., *J. Chem. Soc., Perkin Trans. 1*, 2001, p. 3064.
162. Takeuchi, H., *Chem. Commun.*, 1987, p. 961.
163. Abramovitch, R.A., Evertz, K., Huttner, G., Gibson, H.H., and Weems, H.G., *Chem. Commun.*, 1988, p. 325.
164. Takeuchi, H., Hayakawa, S., and Murai, H., *Chem. Commun.*, 1988, p. 1287.
165. Takeuchi, H. and Koyama, K., *J. Chem. Soc., Perkin Trans. 1*, 1988, p. 2277.
166. Takeuchi, H., Hayakawa, S., Tanahashi, T., Kobayashi, A., Adachi, T., and Higuchi, D., *J. Chem. Soc., Perkin Trans. 2*, 1991, p. 847.
167. Takeuchi, H., Higuchi, D., and Adachi, T., *J. Chem. Soc., Perkin Trans. 1*, 1991, p. 1525.
168. Abramovitch, R.A. and Shi, Q., *Heterocycles*, 1994, vol. 37, p. 1463.
169. Srivastava, S., Kercher, M., and Falvey, D.E., *J. Org. Chem.*, 1999, vol. 64, p. 5853.
170. Takeuchi, H., Taniguchi, T., Masuzawa, M., and Isoda, K., *J. Chem. Soc., Perkin Trans. 2*, 1998, p. 1743.
171. Bogdal, D., *Heterocycles*, 2000, vol. 53, p. 2679.
172. Chiapperino, D., McIlroy, S., and Falvey, D.E., *J. Am. Chem. Soc.*, 2002, vol. 124, p. 3567.
173. McIlroy, S., Moran, R.J., and Falvey, D.E., *J. Phys. Chem. A*, 2000, vol. 104, p. 11154.
174. McIlroy, S. and Falvey, D.E., *J. Am. Chem. Soc.*, 2001, vol. 123, p. 11329.
175. Beres, M., Hajos, G., Riedl, Z., Soos, T., Timari, G., and Messmer, A., *J. Org. Chem.* 1999, vol. 64, p. 5499.
176. Bogdal, D., *ARKIVOC*, 2001, vol. 6, p. 109.
177. Andreev, R.V., Borodkin, G.I., Gatilov, Yu.V., Shakirov, M.M., and Shubin, V.G., *Russ. J. Org. Chem.*, 2004, vol. 40, p. 567.
178. Nefedov, V.D., Toropova, M.A., Simonova, T.P., Avrorin, V.V., and Vorontsov, A.M., *Zh. Org. Khim.*, 1990, vol. 26, p. 1133.
179. Nefedov, V.D., Toropova, M.A., Simonova, T.P., Avrorin, V.V., and Kaso Pen'ya, R., *Zh. Org. Khim.*, 1992, vol. 28, p. 2272.
180. Simonova, T.P., Nefedov, V.D., Toropova, M.A., Avrorin, V.V., and Kirillov, N.F., *Russ. J. Org. Chem.*, 1995, vol. 31, p. 1499.