The role of polysubstituted heterocycles in the synthesis of bi- and polycyclic heterocycles*

B. STANOVNIK

Department of Chemistry, E. Kardelj University of Ljubljana, 61000 Ljubljana

Received 19 March 1982

This review presents the syntheses and some transformations of the *s*-triazolo[1,5-*x*]azines, 2-methyl-*s*-triazolo[1,5-*x*]azines, *s*-triazolo[1,5-*x*]-azine 3-oxides, *N*-heteroarylcyanoamines and *N*-heteroaryl-*N*-methyl-cyanoamines, azino-pyrimidines and -pyrimidine 3-oxides including purines and pteridines, substituted 2-aminooxazolo-azines, pyrazolo[3,4-*c*]pyridazines and *O*-, *S*-, and/or *N*-methylation with *N*,*N*-dimethylformamide dimethyl acetal.

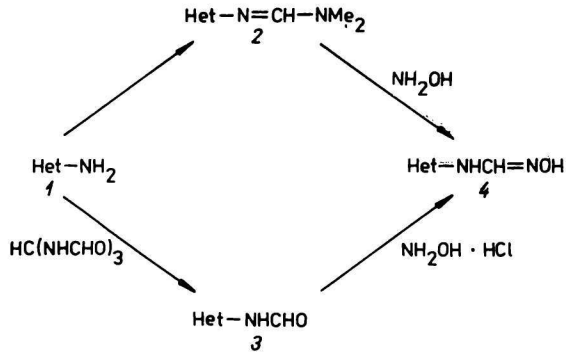
В обзоре приведены синтезы и некоторые превращения *s*-триазоло-[1,5-*x*]азинов, 2-метил-*s*-триазоло[1,5-*x*]азинов, *s*-триазоло[1,5-*x*]азин-3-оксидов, *N*-гетероарилцианоаминов и *N*-гетероарил-*N*-метилциа-ноаминов, азино-пиримидинов и азино-пиримидин-3-оксидов, включая пурины и птеридины, замещенные 2-аминооксазоло-азины, пиразо-ло[3,4-*c*]пиридазины и *O*-, *S*- или *N*-метилирование диметилацеталем *N*,*N*-диметилформамида.

N-Heteroarylformamidines, *N*-heteroarylacetamidines, *N*-heteroarylform-amide oximes, and *N*-heteroarylacetamide oximes are versatile intermediates for the preparation of various heterocyclic systems, especially when the corresponding amide, formamide oxime or acetamide oxime group is attached either at α-position to ring nitrogen atom, or in *ortho* position to amino, cyano or hydroxy group.

N-Heteroarylformamide oximes and N-heteroarylacetamide oximes

N-Heteroarylformamide oximes *4* (Scheme 1) can be prepared either from the corresponding heterocyclic amines *1* and *N*,*N*-dimethylformamide dimethyl acetal followed by treatment with hydroxylamine, or, in some instances, from the formylamino heterocycles *3* with hydroxylamine [1]. The latter method, which presents an alternative method for the preparation of *N*-heteroarylformamide

* Based on a paper presented at the VIIth Symposium on Chemistry of Heterocyclic Compounds, Bratislava, August 31—September 3, 1981.



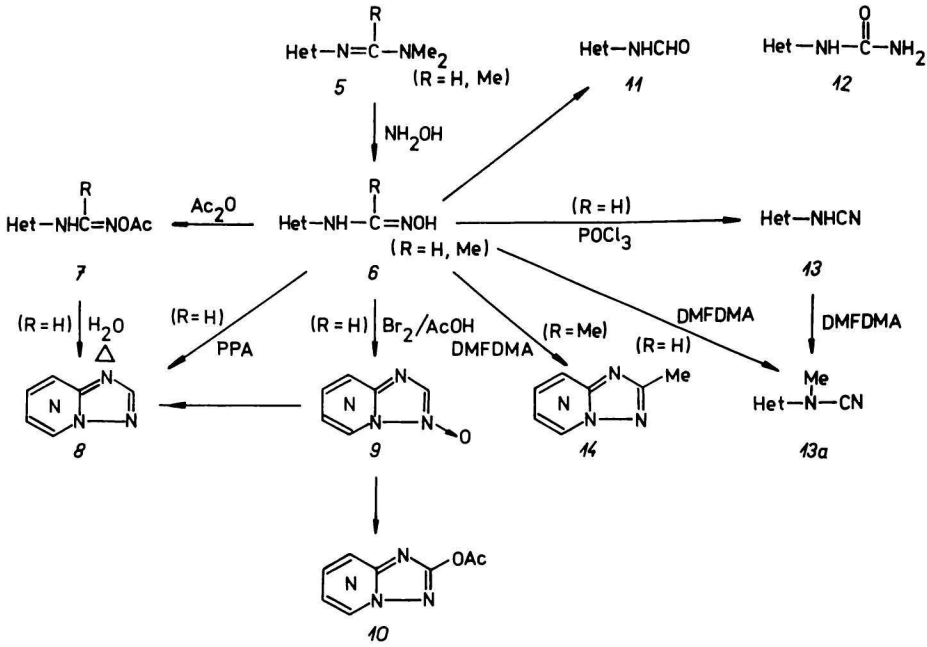
Scheme 1

a	Het = 2-pyridyl	*k*	6-chloropyrazin-2-yl
b	5-nitropyrid-2-yl	*l*	4,6-bismorpholino-1,3,5-triazin-2-yl
c	4-pyridyl	*m*	1-chloropyrido[2,3-*d*]pyridazin-4-yl
d	3-pyridazinyl	*n*	4-chloropyrido[2,3-*d*]pyridazin-1-yl
e	6-chloropyridazin-3-yl	*o*	2,4-dihydroxypyrimid-5-yl
f	4,5-dimethyl-6-chloropyridazin-3-yl	*p*	2,6-dimethylpyrimid-4-yl
g	2-pyrimidinyl	*r*	4-dimethylamino-6-chloro-1,3,5-triazin-2-yl
h	4,6-dimethylpyrimidinyl	*s*	4-ethylthio-6-methylamino-1,3,5-triazin-2-yl
i	2-pyrazinyl	*t*	4,6-bis(ethylthio)-1,3,5-triazin-2-yl
j	5-chloropyrazin-2-yl	*u*	4,6-dimethoxy-1,3,5-triazin-2-yl

oximes, as compared to the previously described method [2, 3], is limited only to 2-formylaminopyrimidines and formylamino-1,3,5-triazines, in which the amino group is a part of the guanidine structural element [1]. Since the nucleophilic character of an amino group attached to the heterocyclic ring is strongly decreased (many formylating agents reported in the literature [4, 5] such as formic acid, formates, formamides, mixed anhydrides and others, frequently afford the formylated compounds in low yields, and in the case of 1,3,5-triazines the reaction completely fails [6]), more powerful formylating agents have been introduced [7]. We found that trisformamidomethane, previously used for the synthesis of various heterocyclic systems as the reagent for introducing of one carbon unit into a heterocyclic ring [7, 8], is the most useful formylating agent affording the corresponding formylamino derivatives in pyrimidine and *s*-triazine series, even with the least reactive heterocyclic amines, in yields up to 95%. [1].

In an analogous manner *N*-heteroarylacetamide oximes were obtained from the corresponding heterocyclic amines and *N*,*N*-dimethylacetamide dimethyl acetal and subsequent treatment of acetamidine derivative with hydroxylamine [9].

The structure and the free energies of rotational barriers, ΔG, about $=CH—NMe_2$ bond in *N'*-heteroaryl-*N*,*N*-dimethylformamidines *2* and *N'*-heteroaryl-*N*,*N*-dimethylacetamidines *5* ($R=CH_3$) (Scheme 2) have been

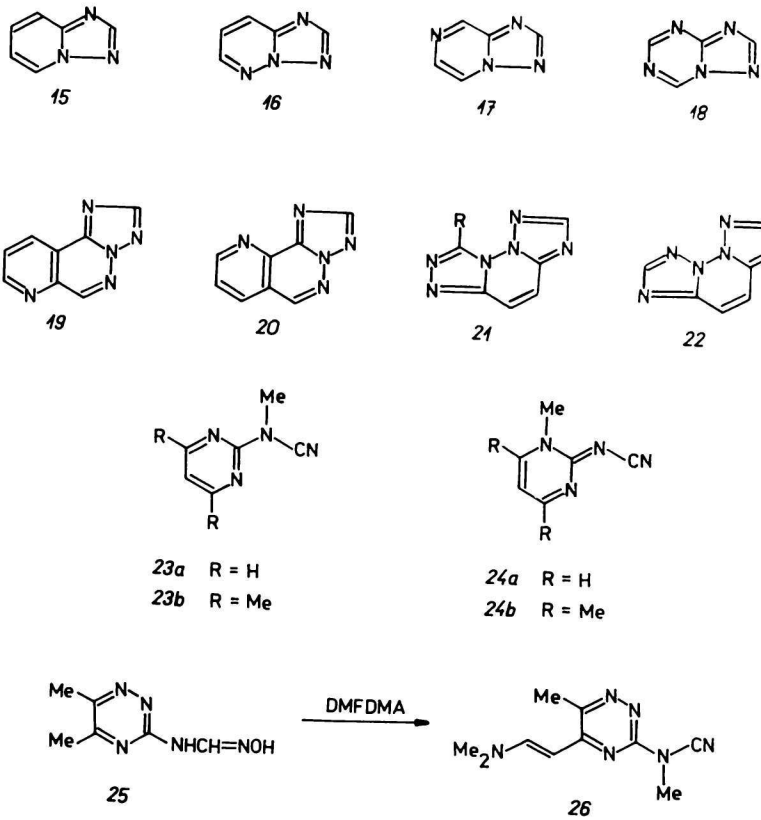


Scheme 2

found to be in the range 54.4—90.4 kJ mol^{-1} [10, 11], and the structures of *N*-heteroarylformamide oximes *4* were determined by comparison of the coupling constants of *N*-heteroarylformamide oximes-^{14}N and -^{15}N labelled compounds [12].

s-Triazolo[1,5-x]azines and s-triazolo[1,5-x]azine 3-oxides

s-Triazolo[1,5-*x*]azines (*8*) can be prepared by the following methods: by a Dimroth rearrangement of *s*-triazolo[4,3-*x*]azines, especially in pyrimidine and *s*-triazine series [13], by the reaction of 3-amino-*s*-triazole with 1,3-dicarbonyl compounds or β-keto esters [14], oxidative cyclization of *N*-heteroarylamidines [15—17], cyclization of *N*-aminoazinium salts, prepared from heterocyclic amines and *O*-mesitylenesulfonylhydroxylamine with formic acid, acetic anhydride, benzoyl chloride, *etc.* [18—21]. Cyclodehydration of *N*-heteroarylformamide oximes *6* (R = H) in polyphosphoric acid appeared to be a general one [2, 3]. By this method various, at position 2 unsubstituted, fused *s*-triazolo[1,5-*x*] systems were prepared (Scheme 3): *s*-triazolo[1,5-*a*]pyridine (*15*), *s*-triazolo[1,5-*b*]pyridazine (*16*), *s*-triazolo[1,5-*a*]pyrazine (*17*), *s*-triazolo[1,5-*a*]-1,3,5-triazine (*18*), pyrido-[3,2-*d*]-*s*-triazolo[1,5-*b*]pyridazine (*19*), isomeric pyrido[2,3-*d*]-*s*-triazolo[1,5-



Scheme 3

-*b*]pyridazine (*20*), *s*-triazolo[4,3-*b*]-*s*-triazolo[5′,1′-*f*]pyridazine (*21*), and bis--*s*-triazolo[1,5-*b*: 5′,1′-*f*]pyridazine (*22*) [3].

In some instances, a Beckmann rearrangement into urea derivatives *12* took place when oximes *6* (R = H) were treated with polyphosphoric acid (*e.g.* from 2-pyridylformamide oxime *N*-pyridylurea was obtained [22], by the treatment with lead tetraacetate *N*-cyanoamino compounds *13* were isolated [23]) whereas hydrolysis into formylamino derivatives *11* was observed [24].

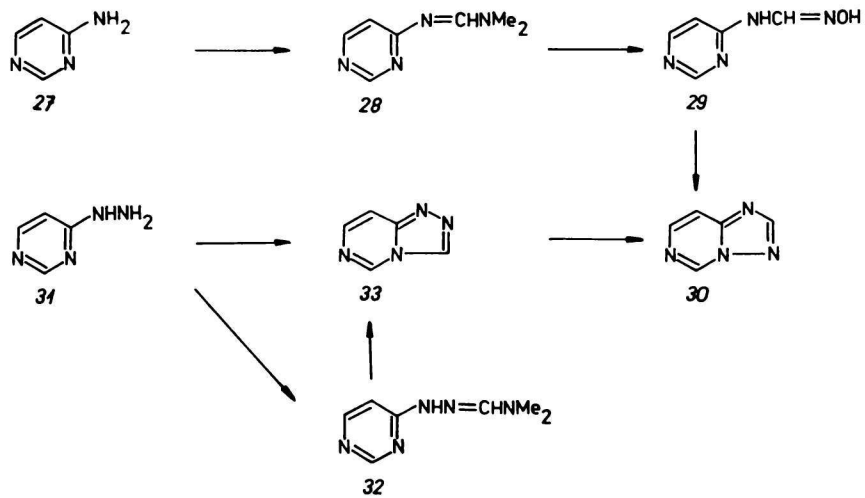
In order to overcome these difficulties, *N*-heteroarylformamide oximes *6* (R = H) were converted with acetic anhydride into *N*-heteroaryl-*O*-acetylformamide oximes *7*, which could be cyclized by heating in aqueous solution into *s*-triazolo[1,5-*x*]azines [25]. In this way *s*-triazolo[1,5-*a*]pyridine, *s*-triazolo-[1,5-*a*]pyrazine, and 6-chloro-*s*-triazolo[1,5-*b*]pyridazine were prepared (Scheme 2).

A general route for the preparation of *s*-triazolo[1,5-*x*]azine 3-oxides *9* represents the oxidation of *N*-heteroarylformamide oximes *6* (R = H) with bromine in acetic acid or *N*-bromosuccinimide in chloroform. The 3-oxides *9* could be deoxygenated by hydrogen in the presence of palladium/carbon as catalyst or with phosphorous trichloride. With acetic anhydride they can be rearranged into the corresponding 2-acetoxy derivatives *10* [24, 26].

N-Heteroarylacetamide oximes *6* ($R = CH_3$) cyclize in the presence of *N*,*N*-dimethylformamide dimethyl acetal to give 2-methyl-*s*-triazolo[1,5-*x*]azines *14*. Similar results were obtained also by heating acetamide oximes in polyphosphoric acid or by heating in phosphorous oxychloride in chloroform or chloroform and pyridine [9]. This transformation represents an extension of the previously described "oxime method" [2, 3] (Scheme 2).

In the reaction of *N*-heteroarylformamide oximes *6* (R = H) with *N*,*N*-dimethylformamide dimethyl acetal *N*-heteroaryl-*N*-methylcyanoamines *13a* were obtained as the main products. However, in some instances, cyanoimino derivatives, methylated at ring nitrogen were isolated. For example, *N*-(pyrimidinyl-2)formamide oxime *4g* and its 4,6-dimethyl derivative *4h* gave a mixture of the products *23* and *24* (Scheme 3). *N*,*N*-Dimethylformamide dimethyl acetal reacts also with activated methyl groups to give the corresponding enamines. For example, *N*-(5,6-dimethyl-1,2,4-triazin-3-yl)formamide oxime *25* gave 5-[2-(*N*,*N*-dimethylamino)ethen-1-yl]-3-(*N*-methylcyanoamino)-6-methyl-1,2,4-triazine *26*.

From 4-aminopyrimidine (*27*) (Scheme 4) *s*-triazolo[1,5-*c*]pyrimidine (*30*) was obtained by this method. The same bicyclic systems were prepared also from



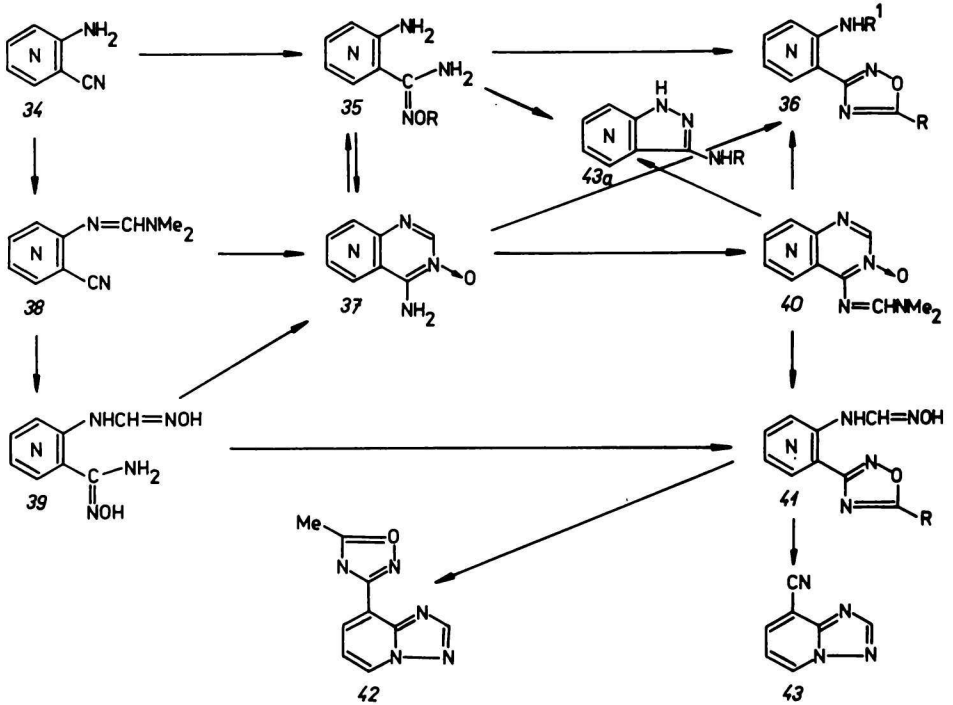
Scheme 4

4-hydrazinopyrimidine (*31*) which was cyclized either with triethylorthoformate or *N*,*N*-dimethylformamide dimethyl acetal to give first *s*-triazolo[4,3-*c*]pyrimidine (*33*) followed by a Dimroth rearrangement into *s*-triazolo[1,5-*c*]pyrimidine (*30*) [27]. The intermediate *33* was isolated under mild reaction conditions [28].

Azinopyrimidines and their 3-oxides

Heterocyclic *ortho* amino-cyano compounds can be used as starting compounds for the preparation of azino-pyrimidines and their 3-oxides. These can be further converted into 1,2,4-oxadiazolylazines, *s*-triazolo[1,5-*x*]azines, pyrazolo[3,4-*x*]-azines, and some other products.

Usually, amino-cyanoazines *34* (Scheme 5) were transformed with hydroxylamine into the corresponding amide oximes *35*, and with triethyl *ortho*-formate into 4-amino-azino-pyrimidine 3-oxides *37*. The latter could be prepared also by treatment of *ortho* amino-cyanoazines *34* with *N*,*N*-dimethylformamide dimethyl acetal to give first the corresponding amidines *38*. These were transformed with hydroxylamine into 4-amino-azino-pyrimidine 3-oxides (*37*) directly or through *o*-(hydroxyimino)methyleneamino-azinocarboxamide oximes *39*.

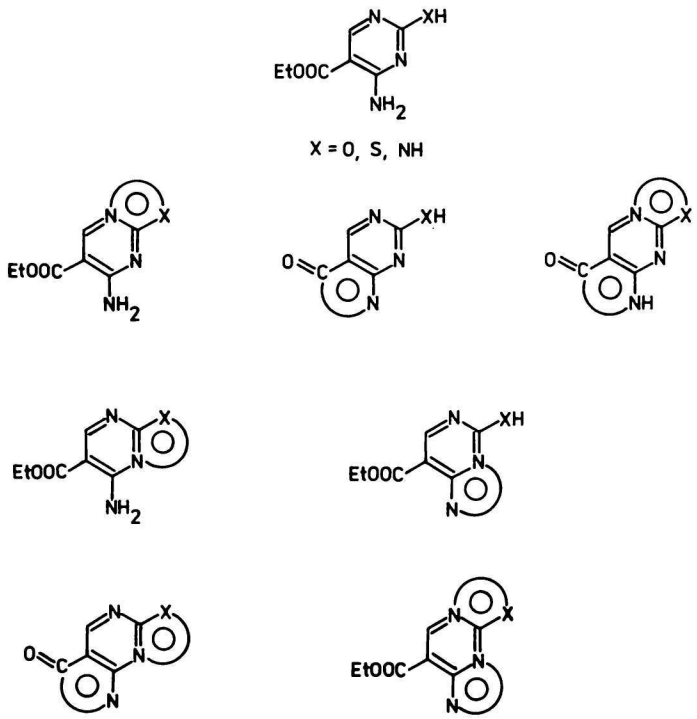


Scheme 5

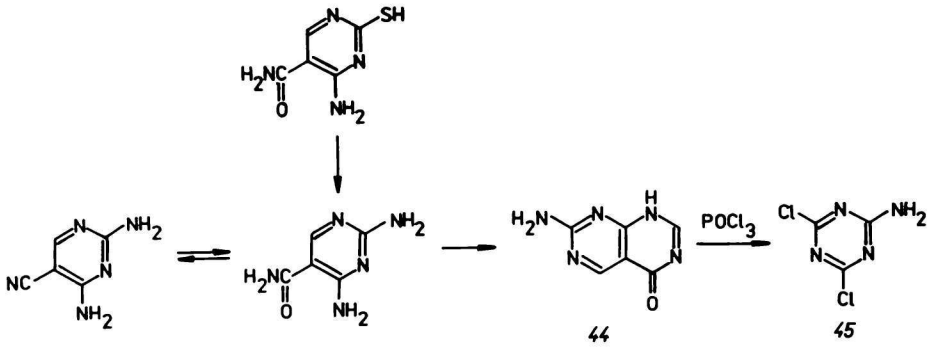
Carboxamide oximes *39* or 4-(*N*,*N*-dimethylaminomethyleneamino)-azino--pyrimidine 3-oxides *40* could be transformed into 2-(hydroxyiminomethyleneamino)-1′,2′,4′-oxadiazol-3′-yl)azines *41*. The latter compound was in pyridine series in polyphosphoric acid transformed into 8-(5′-methyl-1′,2′,4′-oxadiazol-3′-yl)-*s*-triazolo[1,5-*a*]pyridine (*42*) and 8-cyano-*s*-triazolo[1,5-*a*]pyridine (*43*). Pyrazolo[3,4-*x*]azines *43a* were formed either from *40* or from *o*-aminoazinecarboxamide oximes *35* [29—31].

These transformations were recently extended also to pyrimido-pyrimidines [32], pyridazino-pyrimidines [33], pteridines and their *N*-oxides [34].

With these methods some new bi- and polycyclic heterocyclic systems, or new derivatives of old systems by new methods, can be prepared, as is schematically shown in the case of three-substituted pyrimidines as starting compounds [32] (Scheme 6). In some instances, very unusual rearrangements were observed during these transformations. For example, 2-amino-8*H*-pyrimido[4,5-*d*]pyrimid-5-one (*44*) rearranges by treatment with phosphorous oxychloride into 2-amino--4,6-dichloro-1,3,5-triazine (*45*) [35] (Scheme 7).



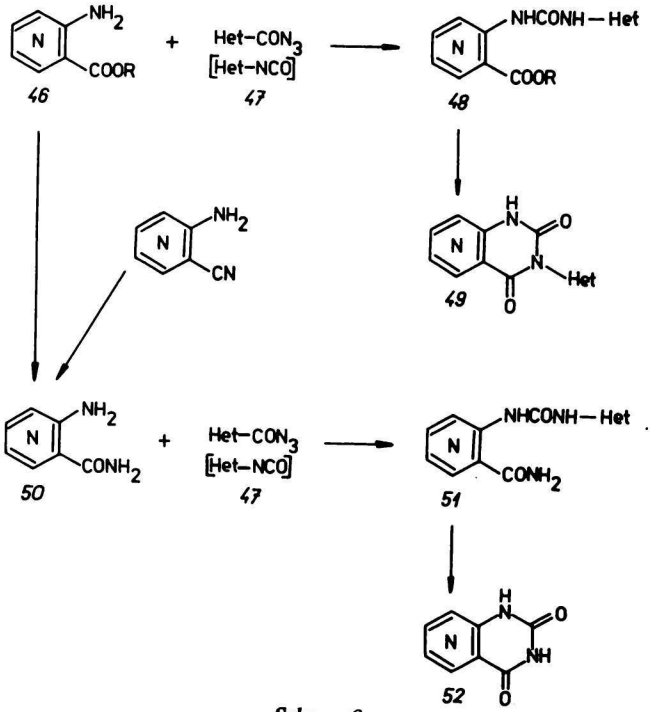
Scheme 6



Scheme 7

Azaquinazolines and azino-s-triazines

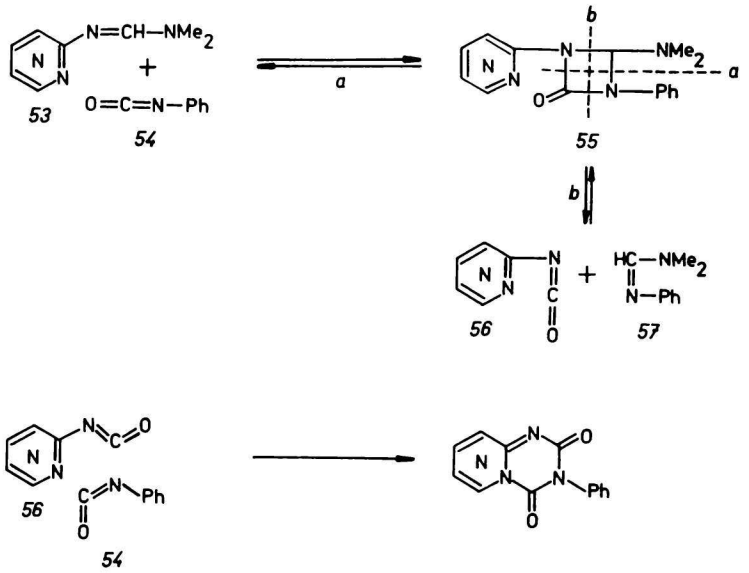
There are various methods for the synthesis of 1*H*,3*H*-quinazolin-2,4-diones described in the literature [36]. In the course of our investigations of substituted heterocyclic amines with heteroacylazides we found that substituted heterocyclic



Scheme 8

amides and *N,N*-disubstituted ureas were formed, in dependence on the reaction conditions and the relative reactivity of both components [37]. However, in ureas *48* (Scheme 8) with a carbethoxy group at *ortho* position a cyclization occurred to give azolo- and azino-pyrimidines *49* with *N*-heteroaryl substituted at position 3 in pyrimidine ring. On the other hand, when a carboxamido group was attached at *ortho* position to amino group, the intermediate urea cyclized into azolo- and 1*H*,3*H*-azino-pyrimidin-2,4-diones *52* by elimination of a heterocyclic amine [38]. In this reaction a heterocyclic isocyanate is formed *in situ*, which reacts with an amino group of a heterocyclic amine. This reaction is therefore similar to that of anthranilic acid derivatives with alkyl or aryl isocyanates in which 3-alkyl or 3-aryl substituted quinazolines are formed [36].

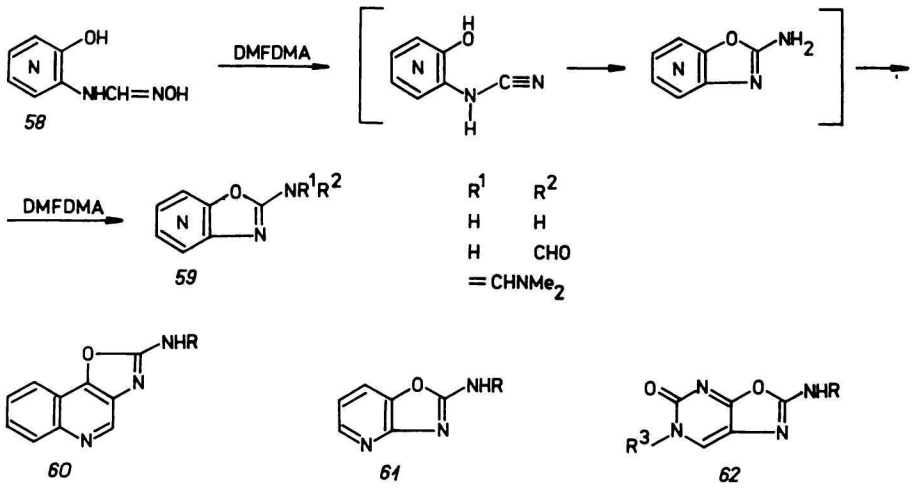
There was found another evidence for the existence of the intermediate heterocyclic isocyanate. Namely, in the reaction of *N,N*-dimethyl-*N'*-(pyridazin-3-yl)formamidine, and some of its derivatives, with phenyl isocyanate pyridazino[2,3-*a*]-[1,3,5]-triazines were obtained [39]. Recently, (2+2) cycloadducts *55* (Scheme 9) were isolated in some instances at room temperature [40]. They decompose at elevated temperatures in two different ways to give either *53* and *54*, or *56* and *57*. In subsequent (2+4) cycloaddition of heterocyclic isocyanate *56* and phenyl isocyanate *54* 3-phenyl-azino-1,3,5-triazine-2,4-diones are formed [40].



Scheme 9

Substituted 2-aminooxazoloazines

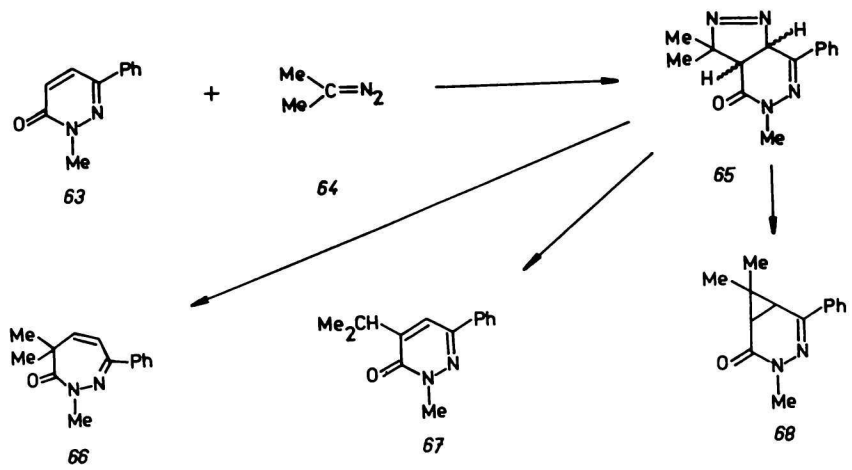
Another application of *N*-heteroarylformamide oximes is the synthesis of substituted aminooxazoloazines. The reaction of *o*-aminohydroxy substituted aromatic compounds with cyanogen bromide can be used only for the preparation of 2-aminobenzoxazoles [41], while in heteroaromatic series the intermediate *N*-cyanoamino derivatives do not cyclize into oxazolo-azines [42]. On the other hand, 2-aminooxazoloazines *59* (Scheme 10) can be easily obtained from *o*-hydroxy substituted *N*-heteroarylformamide oximes *58* by treatment with *N,N*-dimethylformamide dimethyl acetal. For example, 3-amino-1*H*--quinolin-4-one was converted into *N,N*-dimethylaminomethyleneamino derivative and subsequently transformed into oxime, which cyclodehydrated in the presence of DMFDMA into *60*. Similarly, substituted 2-aminooxazolo[2,3-*d*]pyridines (*61*) and 2-aminooxazolo[5,4-*d*]pyrimidines (*62*) [43] were obtained.



Scheme 10

Synthesis of pyrazolo[4,4-c]pyridazines

So far, only the reaction between 1-methyl-3-phenyl-1*H*-pyridazin-6-one (*63*) and 2-diazopropane (*64*) has been described in the literature, to give a mixture of products *66*, *67*, and *68* formed from the unstable cycloadduct *65* [44] (Scheme 11).



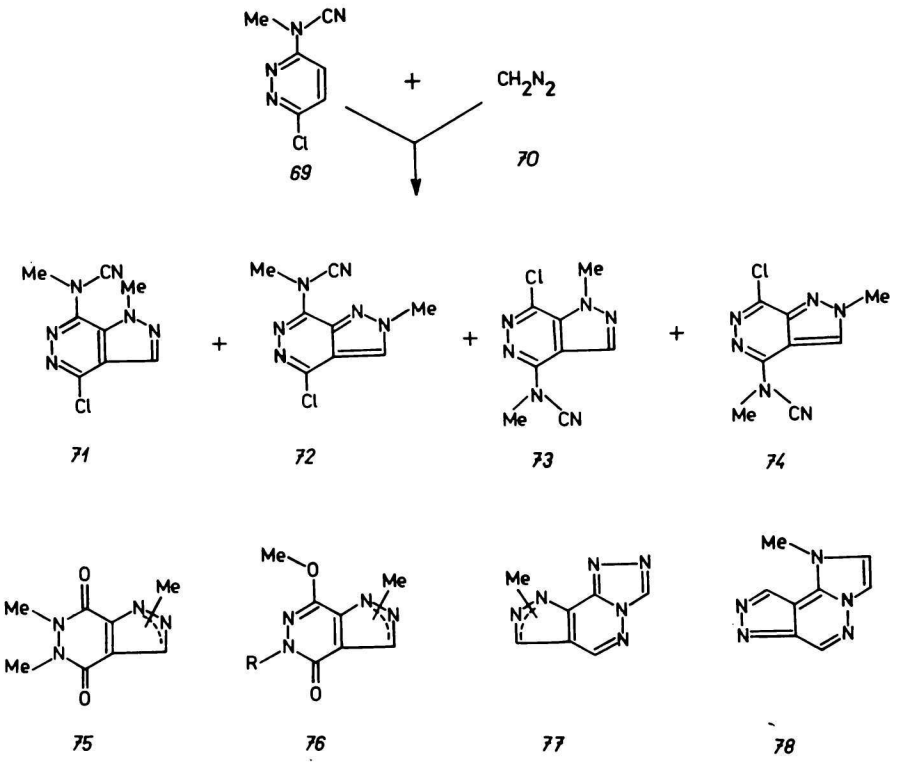
Scheme 11

An unusual reaction between pyridazine derivatives and diazomethane was observed during our studies. The reaction was observed first to take place between 3-chloro-6-(*N*-methylcyanoamino)pyridazine (*69*) and diazo methane (*70*, Scheme 12). The reaction is a 1,3-dipolar cycloaddition of diazomethane to a localized double bond followed by dehydrogenation, a 1,3-sigmatropic hydrogen shift and *N*-methylation of the pyrazole part of the bicyclic system. All four possible isomers *71*, *72*, *73*, and *74* were isolated and identified [45].

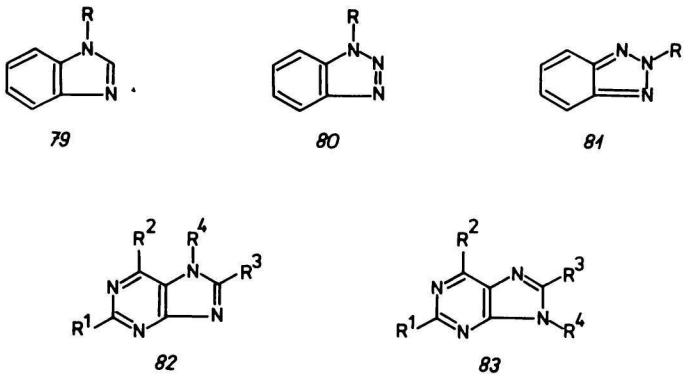
The reaction was extended also to some other monocyclic and bicyclic pyridazine derivatives, such as 1,2-dimethyl-1*H*,3*H*-pyridazine-3,6-dione and 1-substituted 3-methoxy-1*H*-pyridazin-6-ones to give *75* and *76*. In bicyclic series, *s*-triazolo[4,3-*b*]pyridazine and tetrazolo[1,5-*b*]pyridazines gave the corresponding pyrazolo-*s*-triazolo-pyridazines *77* and pyrazolo-tetrazolo-pyridazines. Imidazo[1,2-*b*]pyridazine did not react with diazomethane. However, the reactivity can be increased by quaternization and the corresponding pyrazolo-imidazo-pyridazine *78* was isolated [45].

N,S- and/or O-methylations with DMFDMA

N,N-Dimethylformamide alkyl acetals have been used frequently as alkylating agents for the preparation of ethers and thioethers from phenols and thiophenols and some *S*-methylated heterocycles, especially in pyridine, pyrimidine, and benzoxazole series [46, 47]. On the other hand, *N*-methylation occurred in uracil derivatives [48, 49], in nucleosides [50, 51], and in uridine [52]. Recently, the methylation has been extended to a series of heterocyclic compounds containing



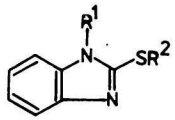
Scheme 12



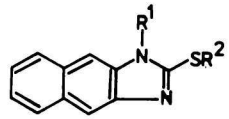
Scheme 13

	R^1	R^2	R^3	R^4
a	H	H	H	H
b	H	H	H	Me
c	SH	H	H	H
d	H	SH	H	H
e	SH	H	Me	H
f	H	H	SH	H
g	SH	SH	H	H
h	SMe	H	H	Me
i	H	SMe	H	Me
j	SMe	H	Me	Me
k	H	H	SMe	Me
l	SMe	SMe	H	Me
m	H	NH_2	H	H
n	H	N=CHNMe	H	Me
o	SMe	H	Me	H

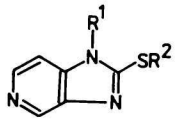
Scheme 13 (Continued)



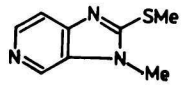
84



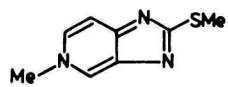
85



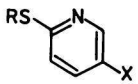
86



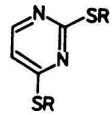
87



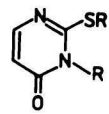
88



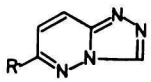
89



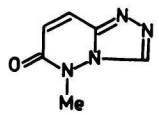
90



91



92



93

Scheme 14

NH, OH, and SH (or potential SH), and NH and OH (or potential OH) groups [53]. In this respect, *N*-methylated benzimidazoles *79*, 1-methyl- (*80*) and 2-methylbenzotriazoles (*81*), 7-methyl- *82b* and 9-methylpurines (*83b*) were isolated (Scheme 13). The compounds with NH and SH (or potential SH) groups, such as 1*H*,3*H*-benzimidazole-2-thione and 1*H*,3*H*-naphth[2,3-*d*]imidazole--2-thione underwent selective *S*-methylation to give first the corresponding *S*-methylated products *84* ($R^1 = H$, $R^2 = CH_3$) and *85* ($R^1 = H$, $R^2 = CH_3$) and on prolonged reaction the *N*,*S*-dimethyl derivatives *84* ($R^1 = R^2 = CH_3$), while methylation of purinethiones gave a mixture of *S*,7- and *S*,9-dimethyl derivatives *82h—l* and *83h—l*; *N*-methylation thus taking place exclusively on the imidazole ring. Adenine methylated at *N*-7 and *N*-9, and in addition, 6-amino group was transformed into *N*,*N*-dimethylaminomethyleneamino group to give *82n* and *83n*. With 1*H*,3*H*-imidazo[4,5-*c*]pyrimidine-2-thione selective *S*-methylation was achieved only when the reaction was stopped immediately after the solid starting material dissolved. On prolonged heating a mixture of 1-methyl-2-methylthio *86* ($R^1 = R^2 = CH_3$), 3-methyl-2-methylthio *87*, and 5-methyl-2-methylthio derivative *88* was isolated (Scheme 14). This system is the only exception in which *N*-methylation was observed to take place also in the six-membered ring. Other thiones and dithiones methylated exclusively at sulfur affording *S*-methylated and bis-*S*-methylated products *89* and *90*. Thiouracil methylated at sulfur and nitrogen to give 3-methyl-2-methylthio-3*H*-pyrimid-4-one (*91*) [53], contrary to the results obtained recently with trimethyl phosphate in the presence of triethylamine [54].

The compounds with the OH (or potential OH) group attached to the heterocyclic ring methylated usually at nitrogen. An exception was 5-hydroxy--*s*-triazolo[3,4-*b*]pyridazine (*92*, R = OH), which methylated at oxygen to give the corresponding 6-methoxy derivative *92* ($R = OCH_3$), and not *N*-methyl product *93* [53].

Acknowledgements. I would like to express my gratitude to my colleagues for continuous criticism and to all coworkers and students for their enthusiastic collaboration in this research program. Their names appear as the names of coauthors in literature references. Financial support of the Research Council of Slovenia, Chemical and Pharmaceutical Works LEK, Ljubljana, and, in part, Chemical and Pharmaceutical Works KRKA, Novo mesto, is fully acknowledged.

References

1. Stanovnik, B., Žmitek, J., and Tišler, M., *Heterocycles 16*, 2173 (1981) and references cited therein.
2. Polanc, S., Verček, B., Stanovnik, B., and Tišler, M., *Tetrahedron Lett. 1973*, 1677.
3. Polanc, S., Verček, B., Šek, B., Stanovnik, B., and Tišler, M., *J. Org. Chem. 39*, 2143 (1974).

4. Challis, B. C. and Butler, A. R., in *The Chemistry of the Amino Group.* (Patai, S., Editor.) P. 277. J. Wiley, New York, 1970.
5. Beckwith, A. L. J., in *The Chemistry of Amides.* (Patai, Š., Editor.) P. 73. J. Wiley, New York, 1970.
6. Smolin, E. M. and Rapoport, L., in *The Chemistry of Heterocyclic Compounds.* (Weissberger, A., Editor.) P. 343. J. Wiley, New York, 1959.
7. Bredereck, H., Gompper, R., Schuh, H. G. v., and Theilig, G., in *Neuere Methoden der Präparativen Organischen Chemie,* Vol. *III.* (Foerst, W., Editor.) P. 163. Verlag Chemie, Weinheim, 1961.
8. Grundmann, Ch., in *Neuere Methoden der Präparativen Organischen Chemie*, Vol. *V.* (Foerst, W., Editor.) P. 156. Verlag Chemie, Weinheim, 1967.
9. Stanovnik, B., Štimac, A., Tišler, M., and Verček, B., *J. Heterocycl. Chem. 19,* 577 (1982).
10. Drobnič-Košorok, M., Polanc, S., Stanovnik, B., Tišler, M., and Verček, B., *J. Heterocycl. Chem. 15*, 1105 (1978).
11. Zupan, M., Pirc, V., Pollak, A., Stanovnik, B., and Tišler, M., *J. Heterocycl. Chem. 11*, 525 (1974).
12. Polanc, S., Verček, B., Stanovnik, B., and Tišler, M., *J. Heterocycl. Chem. 11*, 103 (1974).
13. Spickett, R. G. W. and Wright, S. H. B., *J. Chem. Soc. C1967*, 498.
14. Büllow, C. and Haas, K., *Ber. 42*, 4638 (1909).
15. Bagder, G. M., Nelson, P. J., and Potts, K. T., *J. Org. Chem. 29*, 2542 (1964).
16. Zupan, M., Stanovnik, B., and Tišler, M., *Tetrahedron Lett. 1972*, 4179.
17. Okamoto, T., Torigoe, Y., Sato, M., and Isogai, Y., *Chem. Pharm. Bull.* (Tokyo) *16*, 1154 (1968).
18. Tamura, Y., Hayashi, H., Kim, J. H., and Ikeda, M., *J. Heterocycl. Chem. 10*, 947 (1973).
19. Potts, K. T., Burton, H. R., and Bhattacharryya, J., *J. Org. Chem. 31*, 260 (1966).
20. Okamoto, T., Hirobe, M., Tamai, Y., and Yabe, E., *Chem. Pharm. Bull.* (Tokyo) *14*, 506 (1966).
21. Tamura, Y., Kim, J. H., and Ikeda, M., *J. Heterocycl. Chem. 12*, 107 (1975).
22. Gerchuk, M. P. and Taits, S. Z., *Zh. Obshch. Khim. 20*, 910 (1950); *Chem. Abstr. 44*, 9443 (1950).
23. Shriner, R. L. and Child, R. G., *J. Amer. Chem. Soc. 74*, 549 (1952).
24. Babič, K., Molan, Š., Polanc, S., Stanovnik, B., Stres-Bratoš, J., Tišler, M., and Verček, B., *J. Heterocycl. Chem. 13*, 487 (1976).
25. Verček, B., Stanovnik, B., Tišler, M., and Zrimšek, Z., *Org. Prep. Proced., Int. 10,* 293 (1978).
26. Bratoš-Stres, J., Polanc, S., Stanovnik, B., and Tišler, M., *Tetrahedron Lett. 1975*, 4429.
27. Jenko, B., Stanovnik, B., and Tišler, M., *Synthesis 1976*, 833.
28. Brown, D. J. and Nagamatsu, T., *Aust. J. Chem. 30*, 2515 (1977).
29. Verček, B., Leban, I., Stanovnik, B., and Tišler, M., *J. Org. Chem. 44*, 1695 (1979).
30. Verček, B., Leban, I., Stanovnik, B., and Tišler, M., *Heterocycles 9*, 1327 (1978).
31. Debeljak-Šuštar, M., Stanovnik, B., Tišler, M., and Zrimšek, Z., *J. Org. Chem. 43*, 393 (1978).
32. Stanovnik, B., Prhavc, M., Stibilj, V., Urleb, U., and Tišler, M., unpublished results.
33. Stanovnik, B., Stibilj, V., and Tišler, M., unpublished results.
34. Kočevar, M., Stanovnik, B., and Tišler, M., *Heterocycles 15*, 293 (1981).
35. Stanovnik, B., Koren, B., Šteblaj, M., Tišler, M., and Žmitek, J., *Vestn. Slov. Kem. Drus. 29,* 129 (1982).
36. Armarego, W. L. F., in *Fused Pyrimidines*, Part *I.* (Brown, D. J., Editor.) P. 116. J. Wiley, New York, 1967.
37. Stanovnik, B., Tišler, M., Golob, V., Hvala, I., and Nikolič, O., *J. Heterocycl. Chem. 17*, 733 (1980).
38. Stanovnik, B., Fatur, M., Smolej, A., and Tišler, M., unpublished results.
39. Zupan, M., Stanovnik, B., and Tišler, M., *J. Org. Chem. 37*, 2960 (1972).
40. Tišler, M. and Stanovnik, B., *J. Chem. Soc., Chem. Commun. 1980*, 313.

41. Cornforth, J. W., in *Heterocyclic Compounds*, Vol. *5*. (Elderfield, R. C., Editor.) P. 418. J. Wiley, New York, 1957.
42. Bachmann, G. B., Welton, D. E., Jenkins, G. L., and Christian, J. E., *J. Amer. Chem. Soc. 69*, 366 (1947).
43. Stanovnik, B., Štimac, A., Prhavc, M., Podergajs, S., and Tišler, M., unpublished results.
44. Georghiou, P. E. and Just, G., *J. Chem. Soc., Perkin Trans. 1, 1973*, 888.
45. Stanovnik, B., Štimac, A., Kermavnar, V., and Tišler, M., unpublished results.
46. Abdulla, R. F. and Brinkmeyer, R. S., *Tetrahedron 35*, 1675 (1979).
47. Holy, A., *Tetrahedron Lett. 1972*, 585.
48. Žemlička, J., *Collect. Czech. Chem. Commun. 28*, 1060 (1963).
49. Hirota, K., Watanabe, K., and Fox, J. J., *J. Heterocycl. Chem. 14*, 537 (1977) and references cited therein.
50. Žemlička, J., *Collect. Czech. Chem. Commun. 33*, 3796 (1968).
51. Žemlička, J., *J. Amer. Chem. Soc. 97*, 5896 (1975).
52. Phillips, K. D. and Horwitz, J. P., *J. Org. Chem. 40*, 1856 (1975).
53. Stanovnik, B., Tišler, M., Hribar, A., Barlin, G. B., and Brown, D. J., *Aust. J. Chem. 34*, 1729 (1981).
54. Hayashi, M., Hisanaga, Y., and Yamaguchi, K., *Syn. Commun. 10*, 791 (1980) and references cited therein.