QUANTUM-CHEMICAL STUDY OF SUBSTITUENT EFFECTS IN *meta* AND *para* SUBSTITUTED PHENYL ISOTHIOCYANATES IN π-ELECTRONIC APPROXIMATION

Ivan Danihel[a], Pavol Kristian[a], Josef Kuthan[b] and Mária Minčíková[a]

[a] *Department of Organic Chemistry and Biochemistry, Šafárik University, 041 67 Košice and*
[b] *Department of Organic Chemistry*
Prague Institute of Chemical Technology, 166 28 Prague 6

HMO and PPP calculations of a series of *meta* and *para* substituted phenyl isothiocyanates have been carried out with the aim of study of the substituent effects on the reaction centre of these compounds. The transition state of nucleophilic addition reaction of phenyl isothiocyanates has been approximated by two models, and the calculated localization energies at the carbon atom of NCS group have been investigated with respect to logarithms of rate constants of the nucleophilic reaction and to σ constants. Whereas in the former relation (*i.e.* localization energies *vs* log *k*) rough trends only have been found, the latter one (*i.e.* localization energies or π-electron densities *vs* σ) shows statistically significant linear correlations.

Substituent effects on reaction rate of nucleophilic addition reactions of phenyl isothiocyanates (alcohol, glycine) were studied in previous works[1] from the viewpoint of macroscopical approach. Linear correlation between logarithm of rate constants of these reactions and the Hammett σ constants was found[2-5]. From the substituent effects on the rate of the mentioned reaction or *e.g.* from intensity changes of the band of NCS group in IR spectra[6,7] importance of mesomeric structures of the NCS group was deduced[1-8]. This approach to study of electronic structure of NCS group was recently supplemented[9-17] by the quantum-chemical approach.

The present paper deals with the substituent effect on the reaction rate of the nucleophilic addition reaction of *meta* and *para* substituted phenyl isothiocyanates by means of simple Hückel method (HMO) and the Pariser–Parr–Pople (PPP) method, *i.e.* in π-electronic approximation.
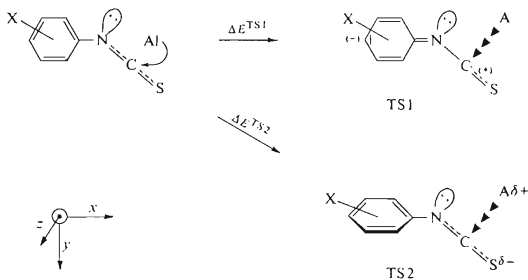
CALCULATIONS

The HMO calculations of *meta* and *para* substituted phenyl isothiocyanates (X = $N(CH_3)_2$, NH_2, OH, OCH_3, CH_3, H, F, Cl, Br, I, CN, NO_2) were carried out with the same parametrization of coulombic and resonance integrals as that used in refs[9,18]. For calculation of π-electronic energies of the activated complexes TS1: $\alpha_N + 0.5\beta_{CC}$; $\beta_{C\theta-N} = 1.0\beta_{CC}$* and for TS2: $\alpha_N = \alpha_C + 1.5\beta_{CC}$; $\beta_{C\theta-N} = 0.8\beta_{CC}$. The calculations were carried out with a Tesla 220 computer.

* The symbol C_θ denotes the benzene ring carbon atom carrying the NCS groups.

The PPP calculations of the studied compounds (X = N(CH$_3$)$_2$, NH$_2$, OH, OCH$_3$, CH$_3$, C$_6$H$_5$, H, SCH$_3$, F, SH, Cl, Br, I, COOH, CHO, CN, NO$_2$) were carried out according to the standard SCF-LCI theory[19,20] (20 monoexcited configurations) with approximation of bicentric repulsion integrals $\gamma_{\mu\nu}$ according to Mataga and Nishimoto[21]. The substituents geometry and parametrization are the same as in ref.[18]. The parametrization used for NCS group is given in Table I along with that for nitrogen atom in TS1 and TS2. For parametrization of atomic centres and bonds the currently recommended values were used. The parameters for sulphur and C—S bond are taken from ref.[22]. Geometry of phenyl isothiocyanate was considered according to the authors[15]. Linear arrangement of NCS group was considered (the calculated[16] deviation from linear arrangement of HNCS is 3·9°). Adequacy of the used parametrization of NCS group was verified[23] by comparison of theoretical and experimental characteristics of UV spectra of phenyl isothiocyanate, 1-naphthyl isothiocyanate, 2-naphthyl isothiocyanate, 2-anthracenyl isothiocyanate and 6-chrysenyl isothiocyanate. The PPP calculations were carried out with an IBM 370 model 145.

RESULTS AND DISCUSSION

The nucleophilic additions to aromatic isothiocyanates known so far appear to be irreversible[1], and, hence, kinetically controlled A_N course can be anticipated. Under these conditions a suitable quantum-chemical criterion of reactivity can be the difference in π-electron energies between the corresponding MO models of transitions state TS and that of the starting isothiocyanate. Scheme 1 gives two situations with different transition states TS1 and TS2, the both formed by attack of the substrate by nucleophile A in perpendicular direction to the xy plane,* *i.e.* in direction

SCHEME 1

---

* This presumption is considered justifiable on the basis of the fact that LUMO of the more extended π-electronic system of isothiocyanate has substantially lower energy (according to both HMO and PPP calculations) than LUMO of the orthogonal π-system of NCS symmetrical with respect to plane of the molecule xy. From the PPP calculations the $\varepsilon_{\text{LUMO}}$ for NCS and phenyl isothiocyanate equals —0·06 and —1·15 eV, respectively.

of p_z atomic orbitals of the aromatic ring. The structure TS1 is characterized by maintained coplanarity of aryl and the atomic centres N—C—S, due to which the free electron pair at nitrogen is not conjugated with the aromatic system. On the contrary, formation of the TS2 structure involves rotation of the aromatic ring to the xz plane bringing it into conjugation with the above mentioned electron pair. The π-electron MO models of the both transition states were, therefore, approximated by taking out the fragment A$\cdots$C—S from the π-electronic system of the substrate and by approximating the nitrogen atomic centre in TS1 and TS2 through "pyridine" type and a type with conjugated electron pair, respectively. Adequacy of the both models was then verified by correlation of experimental and theoretical substituent effect in the studied compound series. The former was represented by empirical substituent constants $\sigma_{m,p}$ or $\sigma_{m,p}^-$, the latter was calculated from the relation

$$\Delta \Delta E^{TS1(2)} = \Delta E_X^{TS1(2)} - \Delta E_H^{TS1(2)}, \tag{1}$$

where the quantities at the right-hand side are differences of π-electron energies between the given transition state and the starting isothiocyanate for the X-substituted and non-substituted starting derivative. That transition state was then considered "better" for which the linear correlation

$$\Delta \Delta E^{TS1(2)} = a\sigma_{m,p} + b \tag{2}$$

was closer from the viewpoint of the chosen correlation criteria.

From Table II it is obvious that the correlation criteria are satisfied (in the sense of Eq. (2)) always better by the transition state TS1, i.e. that one which is obviously closer in structure to products of A_N reaction. Closer examination of the correlation

TABLE I

Parametrization of NCS Group and Nitrogen for Transition States Used in PPP Calculations

Atomic centre	$-I_\mu$, eV	$\gamma_{\mu\nu}$, eV	Bond	$-\beta_{\mu\nu}$, eV	$R_{\mu\nu}$, nm	Z_μ
N	14·12	12·34	$C_\varnothing$—N	2·386	0·140	1
C	11·19	11·09	N—C	2·782	0·124	1
S	18·22	10·00	C—S	1·920	0·156	2
N_{TS1}	14·12	12·34	$C_\varnothing$—N	2·386	0·135	2
N_{TS2}	22·60	14·45	$C_\varnothing$—N	2·090	0·142	2

TABLE II

The Correlation Relations Type $y = ax + b$ Obtained on Basis of PPP Calculations

y	x	$a \cdot 10^2$	$b \cdot 10^3$	$\|r\|$	$t_{p=.01}$	n
$\Delta \Delta E_p^{TS1a}$	$\sigma_p(\sigma_p^-)$	1·23	− 5·6	0·963	11·3	12
$\Delta \Delta E_m^{TS1a}$	σ_m	− 0·10	0·5	0·808	4·3	12
$\Delta \Delta E_p^{TS2a}$	$\sigma_p(\sigma_p^-)$	3·77	− 1·1	0·980	15·7	12
$\Delta \Delta E_{m,p}^{TS1}$	$\sigma_{m,p}(\sigma_p^-)$	−32·87	56·9	0·929	14·0	33
$\Delta \Delta E_p^{TS2}$	$\sigma_p(\sigma_p^-)$	− 3·16	9·9	0·930	9·8	17
$\Delta \Delta E_m^{TS2}$	σ_m	4·23	−11·9	0·775	4·8	17
$\Delta \Delta E_{m,p}^{TS1}$	$\Delta \varepsilon_{HOMO}$	42·47	−59·9	0·792	7·2	33
$\Delta \varepsilon_{HOMO}$	$\sigma_{m,p}$	−76·10	219·0	0·912	12·3	23
Δq_N	$\Delta \Delta E_{m,p}^{TS1}$	− 2·35	− 0·6	0·851	9·0	33
Δq_C	$\Delta \Delta E_{m,p}^{TS1}$	3·83	1·3	0·941	15·5	33
Δq_S	$\Delta \Delta E_{m,p}^{TS1}$	4·22	0·6	0·949	16·8	33
Δq_N	$\sigma_{m,p}(\sigma_p^-)$	0·86	− 2·1	0·881	10·4	33
Δq_C	$\sigma_{m,p}(\sigma_p^-)$	− 1·34	3·6	0·933	14·5	33
Δq_S	$\sigma_{m,p}(\sigma_p^-)$	− 1·47	3·2	0·932	14·2	33
$\Delta q_{C\alpha}$	$\sigma_p(\sigma_p^-)$	− 3·59	11·9	0·949	11·6	17

[a] HMO calculation; the HMO energies are in β units, and the PPP energies are in eV; meaning of the symbols: r correlation coefficient, t the Student test, p the correlation significance level, n number of points, $\sigma_{m,p}(\sigma_p^-)$ means that σ_p values were substituted by σ_p^- for electronacceptor substituents. Note: the values $\sigma_{m,p}$ and σ_p^- were taken from refs[26,27,29].
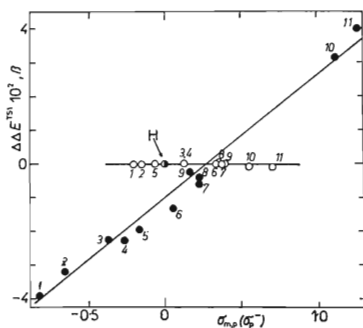

FIG. 1

Dependence of Relative π-Electron Energies $\Delta \Delta E^{TS1}$ of HMO Models of *m,p*-Substituted Phenyl Isothiocyanates *vs* $\sigma_{m,p}(\sigma_p^-)$

Numbering of points: 1 $N(CH_3)_2$, 2 NH_2, 3 OH, 4 OCH_3, 5 CH_3, 6 F, 7 Cl, 8 Br, 9 I, 10 CN, 11 NO_2.

field describing the relation (2) gives some further information about influence of π-electrons of the substituent X on reactivity of the reaction centre in NCS group towards a nucleophilic attack. From Fig. 1 it is seen that HMO model is insensitive to changes in *meta* X substituents. This phenomenon resembles ionization of *meta* substituted benzoic acids[18,24] and has obviously analogous reasons, *i.e.* neglection of repulsion part of the π-electron energy. According to expectation the desintegration of the correlation field disappears with the corresponding π-SCF models (Fig. 2), and, therefore, the theoretical *meta* substituent effect is most variable in the repulsion part of π-electron energy[25].

Negative slope of the regression line (2) in Fig. 2 is physically reasonable, as it implicates that the X-substituted derivatives with higher π-components of theoretical activation energy ($\Delta \Delta E^{TS1} > 0$) will tend to belong to cases with negative parameters $\sigma_{m,p}$ and *vice versa*. Thus here the π-electron contribution to the activation energy changes proportionally to the overall activation energy of the reaction under consideration. From Fig. 3 it is seen that in case of π-SCF model of the transition state TS2 a similar situation only is among the *para* derivatives. The slope in the relation (2) for *meta* derivatives is positive and, hence, disagrees with the above interpretation. This circumstance is considered further argument against adequacy of the TS2 structure.

It was also found that the orbital energies $\Delta \varepsilon_{HOMO} = \varepsilon_{HOMO}^X - \varepsilon_{HOMO}^H$ calculated by the PPP method for X substituted phenyl isothiocyanates show linear correlation with $\Delta \Delta E_{m,p}^{TS1}$ (Table II) and, hence, express well the substituent effect, too. On the contrary, $\Delta \varepsilon_{LUMO}$ do not express the substituent effect in spite of nucleophilic character of the reaction.
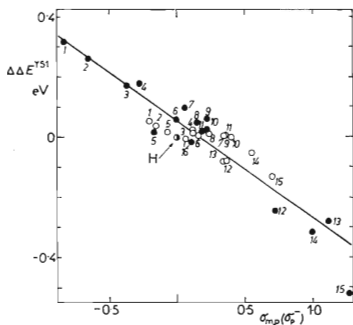

FIG. 2

Dependence of Relative π-Electron Energies $\Delta \Delta E^{TS1}$ of SCF Models (PPP) of *m,p*-Substituted Phenyl Isothiocyanates *vs* $\sigma_{m,p}(\sigma_p^-)$

Numbering of points: *1* N(CH$_3$)$_2$, *2* NH$_2$, *3* OH, *4* OCH$_3$, *5* CH$_3$, *6* SCH$_3$, *7* F, *8* SH, *9* Cl, *10* Br, *11* I, *12* COOH, *13* CHO, *14* CN, *15* NO$_2$, *16* C$_6$H$_5$. The points of the *para* and *meta* series are denoted by full and empty circles, respectively.

On basis of separation of inductive and resonance effect of substituents[28] the relation of $\Delta \Delta E^{TS1}$ to the resonance parameters $\bar{\sigma}_R$ should give information about contribution of π-electrons of the studied compound set to transmission of the substituent effect. It was found that the relative localization energy $\Delta \Delta E^{TS1}$ shows significant linear correlation (3) with the resonance parameters σ_R^0 substituted by the parameters σ_R^- for the electronacceptor substituents

$$\Delta \Delta E_{m,p}^{TS1} = a\alpha\sigma_R^0 + b \, , \tag{3}$$

where α equals 1 and 0·35 for *para* and *meta* series, respectively. The relation (3) is also fulfilled by σ_R constants, but the correlations thus obtained are statistically less significant as compared with those using σ_R^0 constants. Higher statistical significance of the correlations according to Eq. (3) as compared with those according to Eq. (2) as well as higher magnitude of the slope of the regression straight line indicate significant part of π-electrons in transmission of substituent effect (Tables II and III).

Furthermore, we investigated changes of π-electron densities $\Delta q = q_X - q_H$ at individual centres of NCS group and at the carbon atom carrying NCS group due to substitution. As we found close linear correlation between π-electron densities at the individual centres of NCS group and $\Delta \Delta E^{TS1}$ energies (Table II), we can investigate the theoretical substitution effect by means of π-electron densities, too.

Fɪɢ. 3
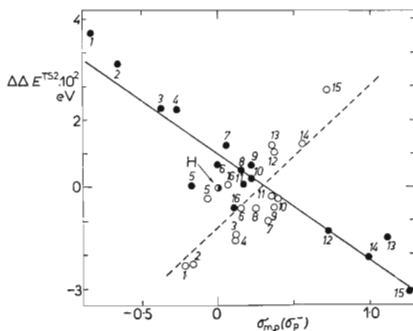
Dependence of Relative π-Electron Energies $\Delta \Delta E^{TS1}$ of SCF (PPP) Models of *m,p*-Substituted Phenyl Isothiocyanates *vs* $\sigma_{m,p}(\sigma_p^-)$

For numbering of points see Fig. 2.

In this case again the carbon atom of NCS group is of primary importance because of nucleophilic attacks occurring here. Relation between π-electron densities and σ constants (or $\log k$) enables a clearer interpretation of substituent effects in the studied compounds set. The π-electronic component of activation energy decreases, and, hence, rate of nucleophilic addition in the studied series increases with decreasing

TABLE III

Linear Correlation between the Theoretical Quantities Calculated by PPP Method and Resonance Parameters σ_R^0

For meaning of the symbols see Table II; for *para* and *meta* series $\alpha = 1$ and 0·35, respectively; $\sigma_R^0(\sigma_R^-)$ means that the σ_R^0 values were substituted by σ_R^- for electron-acceptor substituents; the σ_R^0 and σ_R^- values were taken from ref.[28].

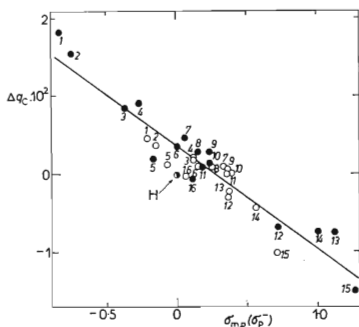| y	x	$a \cdot 10^2$	$b \cdot 10^3$	$\lvert r \rvert$	$t_{p=,01}$	n
$\Delta \Delta E_{m,p}^{TS1}$	$\alpha\sigma_R^0(\sigma_R^-)$	−68·69	−69·64	0·962	19·0	31
Δq_N^p	$\sigma_R^0(\sigma_R^-)$	1·46	0·62	0·954	12·0	16
Δq_N^m	$\sigma_R^0(\sigma_R^-)$	1·59	2·72	0·882	7·0	16
Δq_C^p	$\sigma_R^0(\sigma_R^-)$	− 2·62	− 0·80	0·949	11·3	16
Δq_C^m	$\sigma_R^0(\sigma_R^-)$	− 1·39	− 2·61	0·885	7·1	16
Δq_S^p	$\sigma_R^0(\sigma_R^-)$	− 2·79	− 2·29	0·964	13·6	16
Δq_S^m	$\sigma_R^0(\sigma_R^-)$	− 1·85	− 3·19	0·871	6·6	16
$\Delta q_{C_8}^p$	$\sigma_R^0(\sigma_R^-)$	− 7·00	− 1·51	0·958	12·5	16

FIG. 4

Dependence of Relative π-Electron Densities Δq at the NCS Carbon Atom of m,p-Substituted Phenyl Isothiocyanates Obtained by PPP Method *vs* $\sigma_{m,p}(\sigma_p^-)$

For numbering of points see Fig. 2.

π-electron density at NCS carbon atom (Fig. 4). The reaction rate increase also corresponds to π-electron density decrease and increase at NCS sulphur and nitrogen atoms, respectively. In the *para* series the increase in log k is accompanied by decrease of π-electron density at the carbon atom carrying NCS group. In the *meta* series no linear dependence between $\Delta \Delta E^{TS1}$ and $\Delta q_{C\emptyset}$ values was found due to relative large deviations of the points for electronacceptor substituents, the π-electron densities at this centre being but slightly changed by substitution. Therefore, π-electron density $\Delta q_{C\emptyset}$ is not a suitable characteristic of substituent effect in *meta* series, neither is it an adequate reactivity index for the studied nucleophilic attack of *meta* substituted phenyl isothiocyanates.

According to the concepts proposed in refs[30,31], analysis of the relation

$$\Delta q_i = a\sigma_1 + b\bar{\sigma}_R \tag{4}$$

can create an idea about magnitude of π-inductive effect of the substituent on a centre i, its measure being $\lambda = a/b$. From Table IV it follows that the π-inductive effect viewed in this way is substantially greater and has an opposite sense for the carbon atom carrying NCS group than that for the *meta* series of the studied compounds. This finding corresponds qualitatively to the situation found with monosubstituted benzenes[30–32]. Furthermore, from Table IV it follows that the π-inductive effect in the side chain (the NCS group) is greater for the *meta* substituted compounds

TABLE IV

The Correlations Type $y = ax_1 + bx_2 + c$ Obtained from PPP Calculations

y	x_1	x_2	$a \cdot 10^3$	$b \cdot 10^2$	r	$|\lambda|$	n
Δq_N^p	σ_1	$\sigma_R^0(\sigma_R^-)$	4·22	1·35	0·972	0·313	16
Δq_N^m	σ_1	σ_R^0	6·86	1·37	0·940	0·501	16
Δq_C^p	σ_1	$\sigma_R^0(\sigma_R^-)$	— 7·57	—2·40	0·965	0·315	16
Δq_C^m	σ_1	σ_R^0	— 6·51	—1·08	0·917	0·603	16
Δq_S^p	σ_1	$\sigma_R^0(\sigma_R^-)$	— 8·79	—2·55	0·982	0·345	16
Δq_S^m	σ_1	σ_R^0	— 8·42	—1·57	0·934	0·536	16
$\Delta q_{C\emptyset}^p$	σ_1	$\sigma_R^0(\sigma_R^-)$	—15·61	—6·57	0·967	0·238	16
$\Delta q_{C\emptyset}^m$	σ_1	σ_R^0	— 0·04	1·03	0·957	0·004	12[a]

[a] Values for electronacceptor substituents are not involved in the correlation. Note: the values σ_1, σ_R^0 and σ_R^- were taken from ref.[28].

as compared with that of the *para* series. This fact is not changed even by use of σ_R^0 or σ_R constants for the *para* substituted series and for electronacceptor substituents. This result can indicate that theoretical evidence of π-inductive effect by means of Eq. (4) is not quite justifiable for transmission of this effect into a side chain.

REFERENCES

1. Drobnica Ľ., Kristian P., Augustín J. in the book: *The Chemistry of Cyanates and their Thio Derivatives* (S. Patai, Ed.), Chap. 12. Wiley — Interscience, New York 1977.
2. Vlachová D., Zahradník R., Antoš K., Kristian P., Hulka A.: This Journal 27, 2826 (1962).
3. Rao C. N. R., Venkataraghavan R.: Tetrahedron 18, 531 (1962).
4. Drobnica Ľ., Augustín J.: This Journal 30, 99 (1965).
5. Kristian P., Drobnica Ľ.: This Journal 31, 1333 (1966).
6. Caldow G. L., Thompson H. W.: Spectrochim. Acta 13, 212 (1958).
7. Katritzky A. R., Keogh H. J., Ohlenrott S., Topsom R. D.: J. Amer. Chem. Soc. 92, 6855 (1970).
8. Rao C. N. R.: *Chemical Applications of Infrared Spectroscopy*, Chap. XII, p. 575, 576. Academic Press, New York 1963.
9. Zahradník R., Vlachová D., Koutecký J.: This Journal 27, 2336 (1962).
10. Wagner E. L.: J. Chem. Phys. 43, 2728 (1965).
11. Zabrodin V. B., Bagaturyanc A. A., Entelis S. G.: Zh. Fiz. Khim. 42, 2324 (1968).
12. Zabrodin V. B.: Zh. Fiz. Khim. 45, 682 (1971).
13. Matsui T., Nagano M.: Chem. Pharm. Bull. 22, 2123 (1974).
14. Kobayashi T., Nagakura S.: J. Electron. Spectrosc. Relat. Phenom. 7, 488 (1975).
15. Higgins R. J., Combs L., Malloy T. B. jr, Cook R. L.: J. Mol. Struct. 28, 121 (1975).
16. Bak B., Christiansen J. J., Nielsen O. J., Svanholt H.: Acta Chem. Scand. A31, 666 (1977).
17. Wittel K., Meeks J. L., McGlynn S. P. in the book: *The Chemistry of the Cyanates and their Thio Derivatives* (S. Patai, Ed.), Chap. 1. Wiley - Interscience, New York 1977.
18. Kuthan J., Danihel I., Skála V.: This Journal 43, 447 (1978).
19. Pople J. A.: Trans. Faraday Soc. 49, 1375 (1953).
20. Pariser R., Parr R. G.: J. Chem. Phys. 21, 466, 767 (1953).
21. Mataga N., Nishimoto K.: Z. Phys. Chem. (Frankfurt am Main) 13, 140 (1957).
22. Bock H., Wagner G., Kroner J.: Chem. Ber. 105, 3857 (1972).
23. Danihel I.: Unpublished results.
24. Kuthan J., Skála V.: Z. Chem. 8, 340 (1968).
25. Kuthan J., Danihel I.: The Fourth International Symposium on Physical Organic Chemistry. York, England 1978.
26. McDaniel D. H., Brown H. C.: J. Org. Chem. 23, 420 (1958).
27. Jaffé H. H.: Chem. Rev. 53, 191 (1953).
28. Ehrenson S., Brownlee R. T. C., Taft R. W.: Progr. Phys. Org. Chem. 10, 1 (1973).
29. Laurence C., Wojtkowiak B.: Ann. Chim. (Paris) 5, 163 (1970).
30. Topsom R. D.: Progr. Phys. Org. Chem. 12, 1 (1976).
31. Hehre W. J., Taft R. W., Topsom R. D.: Progr. Phys. Org. Chem. 12, 159 (1976).
32. Danihel I., Kuthan J.: This Journal 44, 873 (1979).

Translated by J. Panchartek.