FUNCTIONAL DERIVATIVES OF STERICALLY HINDERED AMINES. POLYALKYLPIPERIDINE DIESTERS

Frantisek VASS[a] and Jozef LUSTON[b,*]

[a] *VASACHEM Co., 851 01 Bratislava, Slovak Republic*
[b] *Polymer Institute, Slovak Academy of Sciences, 842 36 Bratislava, Slovak Republic*

Received June 16, 1995
Accepted July 26, 1995

Several diesters of dicarboxylic acids with pendant polyalkylpiperidine structural units were prepared from α-bromo and α,α′-dibromo substituted aliphatic dicarboxylic acid diesters by a nucleophilic replacement reaction with 2,2,6,6-tetramethyl-4-hydroxypiperidine, 1,2,2,6,6-pentamethyl-4-hydroxypiperidine, and 2,2,6,6-tetramethyl-4-aminopiperidine, by a nucleophilic addition of amino derivative to the α,β-unsaturated dicarboxylic acid diester and by an acid catalyzed condensation of 2,2,6,6-tetramethyl-4-oxopiperidine with diethyl bis(hydroxymethyl)malonate.

It has been reported previously[1] that besides of some utilization of sterically hindered amines as non-nucleophilic bases[2–5] and pharmaceutically active compounds[6–9] their main significance lays especially in commercial use as powerful hydrocarbon polymer light stabilizers[10–12]. Important is also their utilization as precursors of stable nitroxyl radicals which are useful as spin labels, spin probes, or radical scavengers in various biochemical and physico-chemical studies[13–17]. Among many possible structures of sterically hindered amines, the six-membered cyclic functional derivatives, mainly polyalkylpiperidines, are most frequent and important[18].

Sterically hindered amines are very useful and highly effective light stabilizers for commodity polymers, particularly for polyolefins[19,20]. They are several times as much effective as previously mostly used derivatives of 2-hydroxybenzophenone, 2-(2-hydroxyphenyl)benzotriazole, or chelates of transient metals[10–12]. Their incorporation into a polymer substrate extends its life-time many times.

The use of low molecular weight light stabilizers of polyalkylpiperidine type has many limitations, first of all, due to their physical loss from polymers[21–22]. The synthesis of functional polyalkylpiperidine derivatives opens a possibility for the prepara-

---

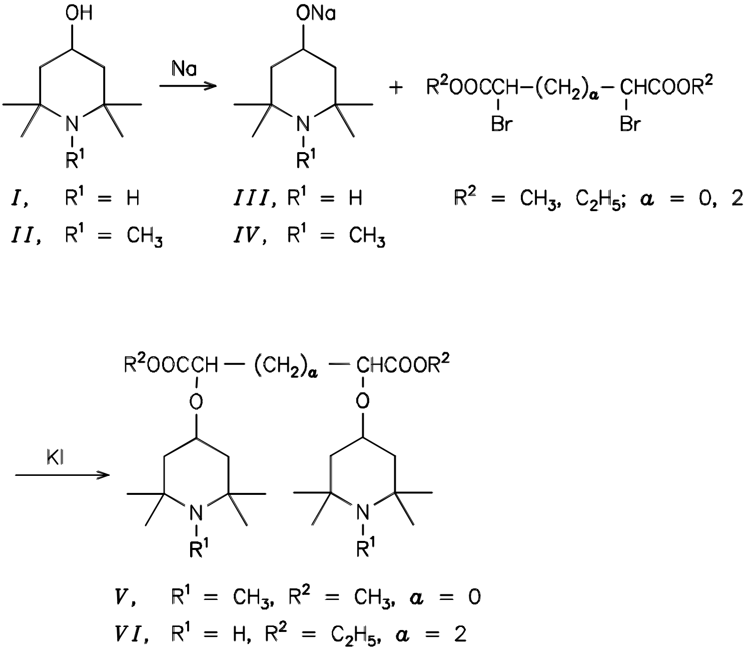
[*] The author to whom correspondence should be addressed.

tion of high-performance polymeric or oligomeric sterically hindered amine light stabilizers[20,23].

The objective of this work was to prepare several diesters of dicarboxylic acids with pendant polyalkylpiperidine structural units useful as polycondensation type monomers. These compounds in the form of stable nitroxyl radicals can be also used for spin labelling of various functional polymers containing amino and hydroxy groups.

The Williamson synthesis was used for the preparation of dimethyl ester of 2,3-bis(1,2,2,6,6-pentamethyl-4-piperidyloxy)butanedioic acid (*V*) and diethyl ester of 2,5-bis(2,2,6,6-tetramethyl-4-piperidyloxy)hexanedioic acid (*VI*) (Scheme 1).

In both cases, freshly prepared sodium salts of 2,2,6,6-tetramethyl-4-hydroxypiperidine (*III*) and sodium salt of 1,2,2,6,6-pentamethyl-4-hydroxypiperidine (*IV*) were used as the starting materials. These salts were reacted with the corresponding α,α′-dibromoalkane dicarboxylic acid esters in anhydrous toluene under nitrogen flow and catalytic effect of KI. The formation of solid NaBr enabled visual observation of the course of the nucleophilic replacement. At 80 °C and 24 h of reaction time, the yields of isolated products were slightly higher than 60%. Because of the considerably unstable sodium salts *III* and *IV*, the Williamson synthesis is very sensitive to the presence of moisture. Therefore, the use of anhydrous solvents, dried catalyst and anhydrous



SCHEME 1

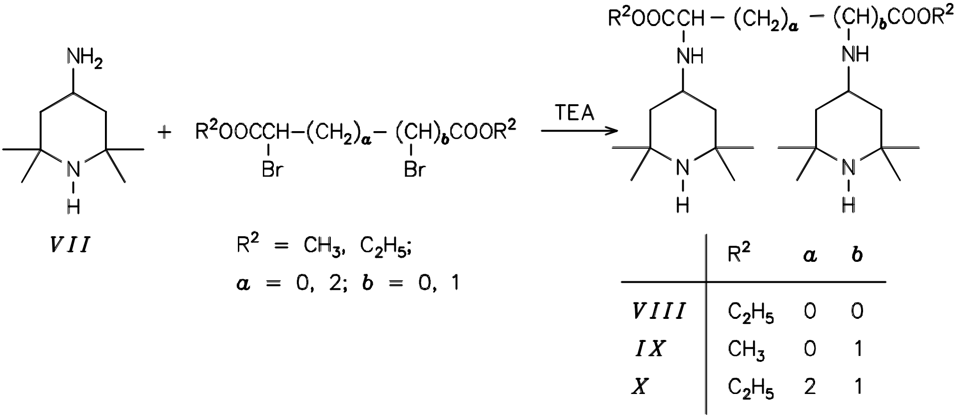
atmosphere is essential for the preparation of *V* and *VI*. In opposite case it means rapid decrease of yields.

Synthesis of diethyl ester of 2-(2,2,6,6-tetramethyl-4-piperidylamino)propanedioic acid (*VIII*), dimethyl ester of 2,3-bis(2,2,6,6-tetramethyl-4-piperidylamino)butanedioic acid (*IX*), and diethyl ester of 2,5-bis(2,2,6,6-tetramethyl-4-piperidylamino)hexanedioic acid (*X*) was carried out by the nucleophilic replacement of α-bromo, or α,α′-dibromo substituted aliphatic dicarboxylic acid esters with 2,2,6,6-tetramethyl-4-aminopiperidine (*VII*) in anhydrous benzene in the presence of triethylamine as base (Scheme 2).

The reaction between haloacid esters and amines proceeds according to expectation yielding the corresponding substituted aminoacid esters[24]. Bromine in the vicinity of carbonyl group is considerably reactive, and, therefore, it is better to perform the reaction under cooling or at lower temperatures and in non-polar solvents such as benzene or toluene what decreases the rate of the reaction. The formation of solid triethylamine hydrochloride enables visual detection of the course of the reaction. At 20 °C and reaction time 24 h the yields of isolated products were in the range between 50 and 60%. The presence of moisture has significant influence on the yields of the obtained substituted aminoacid esters. A considerable disadvantage of the prepared compounds is their hygroscopicity which decreases with the increase of the length of aliphatic part of dicarboxylic acid esters used.

The synthesis of dimethyl 2-(2,2,6,6-tetramethyl-4-piperidylamino)butanedioate (*XI*) was accomplished by the addition of *VII* to the double bond of dimethyl ester of *cis*-2-butenedioic acid (Scheme 3).

The nucleophilic addition of aliphatic amines to α,β-unsaturated dicarboxylic acid diesters in polar solvents proceeds very easily[25]. The synthesis was carried out in methanol at laboratory temperature under vigorous stirring for 10 h. This method provided



	R^2	*a*	*b*
VIII	C_2H_5	0	0
IX	CH_3	0	1
X	C_2H_5	2	1

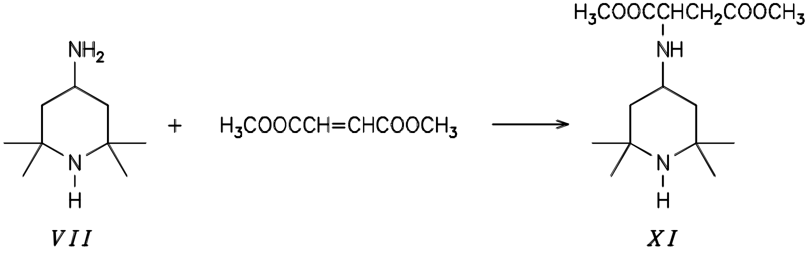
SCHEME 2

70–80% yields of the desired product what is in agreement with the previous results of the addition of amines to activated unsaturated bonds[26].

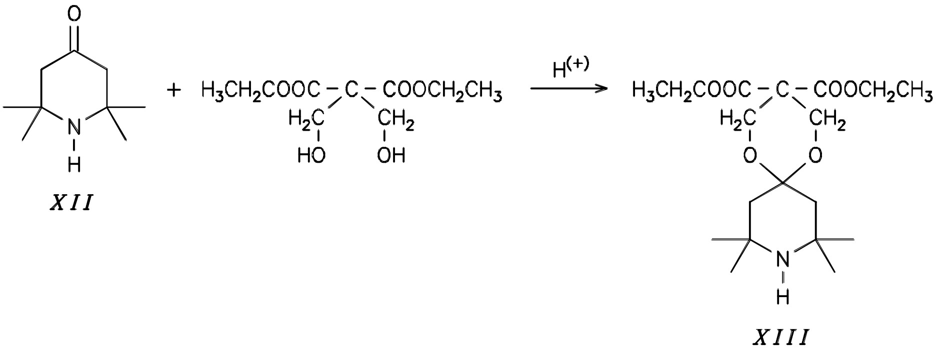
An exception in this series is the preparation of 1,5-dioxa-3,3-bis(ethoxycarbonyl)-8,8,10,10-tetramethyl-9-azaspiro[5.5]undecane (*XIII*) which was prepared by the acid catalyzed condensation of 2,2,6,6-tetramethyl-4-oxopiperidine (*XII*) with diethyl bis(hydroxymethyl)malonate (Scheme 4).

The condensation was performed in benzene what enables separation of the condensation water, and at more than equimolar amount of *p*-toluenesulfonic acid. The excess of the catalyst is necessary because of the formation of its salt with amine in the course of the reaction. Liberation of the product is performed by basification of the reaction mixture and the product is obtained in an excellent yield.

The newly prepared polyalkylpiperidine diesters have potential use for the preparation of new polymeric or oligomeric light stabilizers or they can be incorporated into commercial polyesters and polyamides during their polycondensation as permanent, polymer-bound stabilizers.



SCHEME 3



SCHEME 4

EXPERIMENTAL

Melting points were measured on a Koffler melting point apparatus (VEB Analytik, Germany) and are uncorrected. Microanalyses were done in the Microanalytical Laboratory of the Chemical Institute of the Slovak Academy of Sciences (Bratislava, Slovak Republic). Infrared spectra (ν, cm^{-1}) were recorded on a Specord IR-75 spectrophotometer (Zeiss, Jena, Germany) in chloroform. ^{1}H NMR spectra (δ, ppm; J, Hz) were measured on a BS-467 60 MHz (Tesla, Czechoslovakia) and FT JNM FX 100 (Jeol, Japan) spectrometers in deuteriochloroform using TMS as internal standard.

2,2,6,6-Tetramethyl-4-hydroxypiperidine (*I*, 98%, Aldrich) was used without purification. 1,2,2,6,6-Pentamethyl-4-hydroxypiperidine (*II*) was prepared from *I* according to Lutz[9]. 2,2,6,6-Tetramethyl-4-aminopiperidine (*VII*) was prepared from 2,2,6,6-tetramethyl-4-oxopiperidine according to Kurosaki[27]. Diethyl ester of 2-bromopropanedioic acid, dimethyl ester of 2,3-dibromobutanedioic acid and dimethyl ester of 2,5-dibromohexanedioic acid were prepared according to literature[28–30]. Dimethyl maleate and diethyl bis(hydroxymethyl)malonate (Aldrich) were used as received. Potassium iodide (Lachema, Czech Republic) was dried in a vacuum oven at 100 °C. Triethylamine (Lachema, Czech Republic) was dried by refluxing over potassium hydroxide pellets for 5 h and distilled under reduced pressure. Benzene and toluene (Lachema, Czech Republic) were purified and dried by standard methods[31].

Dimethyl Ester of 2,3-Bis(1,2,2,6,6-pentamethyl-4-piperidyloxy)butanedioic Acid (*V*)

Sodium salt of 1,2,2,6,6-pentamethyl-4-hydroxypiperidine (*IV*) was prepared by dissolution of sodium (0.46 g, 0.02 mol) in a solution of *II* (3.42 g, 0.02 mol) in anhydrous toluene (70 ml) by 10 h reflux under vigorous stirring in dry nitrogen atmosphere. To the freshly prepared solution of *IV*, KI (0.02 g) was added followed by slow addition of dimethyl ester of 2,3-dibromobutanedioic acid (3.04 g, 0.01 mol) in anhydrous toluene (30 ml) at the temperature between 85 to 90 °C. The reaction time was 24 h. After cooling, the reaction mixture was washed three times with distilled water and brine, and dried over anhydrous sodium sulfate. Toluene was removed in a rotary evaporator and 3.35 g (67.1%) of yellow oil with n_D^{20} 1.4983 was obtained. The column chromatography (silica gel, methanol–NH_3) afforded pale-yellow oil with n_D^{20} 1.4972. For $C_{26}H_{28}N_2O_6$ (464.5) calculated: 63.43% C, 9.98% H, 5.78% N; found: 63.97% C, 9.61% H, 5.59% N. IR spectrum: 1 745 (C=O); 1 390, 1 370 (gem. CH_3); 1 280, 1 255 (C–O, ester). ^{1}H NMR spectrum: 1.01 and 1.1 brd, 24 H (gem. CH_3); 1.45 and 1.72 2 × d, 8 H (–CH_2–); 2.18 s, 6 H (N–CH_3); 3.25 q, 2 H (C–H); 3.32 s, 6 H (O–CH_3); 5.01 m, 2 H (α-H).

Diethyl Ester of 2,5-Bis(2,2,6,6-tetramethyl-4-piperidyloxy)hexanedioic Acid (*VI*)

The sodium salt of 2,2,6,6-tetramethyl-4-hydroxypiperidine (1.79 g, 0.01 mol) and diethyl ester of 2,5-dibromohexanedioic acid (1.8 g, 0.005 mol) were used for the reaction. The synthesis followed the same procedure as described for the synthesis of *V*. The yield was 1.58 g (61.9%) white crystals with m.p. 78–81 °C. For $C_{28}H_{52}N_2O_6$ (512.7) calculated: 65.58% C, 10.22% H, 5.46% N; found: 66.02% C, 9.92% H, 5.35% N. IR spectrum: 1 740 (C=O); 1 380, 1 360 (gem. CH_3); 1 270, 1 240 (C–O, ester).

Diethyl Ester of 2-(2,2,6,6-Tetramethyl-4-piperidylamino)propanedioic Acid (*VIII*)

To a solution of *VII* (1.56 g, 0.01 mol) and triethylamine (1.4 ml, 0.01 mol) in anhydrous benzene (40 ml), the solution of diethyl ester of 2-bromopropanedioic acid (2.39 g, 0.01 mol) in anhydrous benzene (10 ml) was slowly added at room temperature. The reaction mixture was vigorously stirred overnight. The white solid precipitate of triethylamine hydrochloride was filtered off, dissolved in the concentrated solution of potassium carbonate and thoroughly extracted with ether. The combined organic solutions were washed with distilled water and brine, and dried over anhydrous sodium sulfate. The solvents were evaporated in the rotary evaporator and to the sticky residue petrolether (20 ml) was added what resulted in solidification of the product. After filtration, 1.66 g (52.8%) of yellowish, easily powderable, strongly hygroscopic product was isolated, m.p. 93–96 °C. For $C_{16}H_{30}N_2O_4$ (314.4) calculated: 61.32% C, 9.62% H, 8.94% N; found: 61.10% C, 9.51% H, 8.72% N. IR spectrum: 1 730 (C=0); 1 390, 1 375 (gem. CH_3); 1 240 (C–O, ester). ^1H NMR spectrum: 0.92 s, 1 H (NH); 1.07 brs, 12 H (gem. CH_3); 1.15 t, 6 H (CH_3); 1.44 and 1.57 2 × d, 4 H (CH_2); 3.20 m, 5 H (CH_2, CH); 5.45 s, 1 H (CH).

Dimethyl Ester of 2,3-Bis(2,2,6,6-tetramethyl-4-piperidylamino)butanedioic Acid (*IX*)

2,2,6,6-Tetramethyl-4-aminopiperidine (3.13 g, 0.02 mol), dimethyl ester of 2,3-dibromobutanedioic acid (3.04 g, 0.01 mol), and triethylamine (2.8 ml, 0.02 mol) were used for the reaction. The synthesis of *IX* was carried out in the same manner as described for the synthesis of *VIII*. The yield was 2.14 g (47.1%) of yellowish, easily powderable and hygroscopic product, m.p. 83–85 °C. For $C_{24}H_{46}N_4O_4$ (454.6) calculated: 63.40% C, 10.20% H, 12.32% N; found: 63.10% C, 10.33% H, 12.16% N. IR spectrum: 1 740 (C=O); 1 390, 1 370 (gem. CH_3); 1 226 (C–O, ester).

Diethyl Ester of 2,5-Bis(2,2,6,6-tetramethyl-4-piperidylamino)hexanedioic Acid (*X*)

2,2,6,6-Tetramethyl-4-aminopiperidine (1.56 g, 0.01 mol), diethyl ester of 2,5-dibromohexanedioic acid (1.8 g, 0.005 mol) and triethylamine (1.4 ml, 0.01 mol) were used for the reaction. The synthesis was performed as described for the synthesis of *VIII*, and yielded 1.57 g (61.4%) of yellowish, easily powderable, slightly hygroscopic product, m.p. 131–133 °C. For $C_{28}H_{54}N_4O_4$ (510.7) calculated: 65.84% C, 10.66% H, 10.97% N; found: 65.75% C, 10.81% H, 10.70% N. IR spectrum: 1 720 (C=O); 1 390, 1 370 (gem. CH_3); 1 230 (C–O, ester).

Dimethyl Ester of 2-(2,2,6,6-Tetramethyl-4-piperidylamino)butanedioic Acid (*XI*)

To a solution of *VII* (1.56 g, 0.01 mol) in methanol (10 ml), dimethyl ester of *cis*-2-butenedioic acid (1.76 g, 0.01 mol) was slowly added. The reaction mixture was vigorously stirred at laboratory temperature for 10 h. Methanol was removed on a rotary evaporator. The residue was dissolved in chloroform (20 ml), washed three times with distilled water and brine, and dried over anhydrous sodium sulfate. Solvent was evaporated, and product was crystallized from petrolether. The yield was 1.93 g (76.5%) of white transparent needles, m.p. 101–102.5 °C. For $C_{15}H_{28}N_2O_4$ (300.4) calculated: 60.20% C, 9.03% H, 9.36% N; found: 60.57% C, 9.22% H, 9.10% N. IR spectrum: 1 720 (C=O); 1 380, 1 360 (gem. CH_3); 1 280 (C–O, ester).

1,5-Dioxa-3,3-bis(ethoxycarbonyl)-8,8,10,10-tetramethyl-9-azaspiro[5.5]undecane (*XIII*)

To a flask equipped with a Dean–Stark trap, a condensor, and a stirring bar, benzene (80 ml), 2,2,6,6-tetramethyl-4-oxopiperidine *XII* (6.21 g, 0.04 mol), and *p*-tolenesulfonic acid monohydrate (8.37 g, 0.044 mol) were charged. The reaction mixture was stirred under reflux for 0.5 h, while crystal water and moisture from the system were eliminated. Simultaneously, the acid salt of piperidine derivative was formed. Then, diethyl bis(hydroxymethyl) malonate (8.81 g, 0.04 mol) was added and the reaction mixture was refluxed while theoretical amount of water was separated in Dean–Stark trap (14 h). After cooling, the reaction mixture was poured into 20% NaOH solution (100 ml). The organic layer was washed three times with water and brine, and dried over anhydrous sodium sulfate. Benzene was removed in a rotary evaporator, and yellowish liquid was obtained (13 g, 91%) which was distilled at reduced pressure. The colorless fraction distilling at 150–157 °C at 80 Pa was collected (11.7 g, 81.9%). For $C_{18}H_{31}NO_6$ (357.4) calculated: 60.43% C, 8.74% H, 3.92% N; found: 59.62% C, 9.03% H, 3.77% N. ^1H NMR spectrum: 1.20 s, 12 H (CH_3); 1.28 t, 6 H, J = 1.5 (CH_3); 1.68 s, 4 H (CH_2); 4.24 q, 4 H, J = 1.5 (CH_2O); 4.29 s, 4 H (CH_2O).

REFERENCES

1. Luston J., Vass F.: Makromol. Chem., Macromol. Symp. *27*, 231 (1989).
2. Hamell M., Levine R.: J. Org. Chem. *15*, 162 (1950).
3. Barton D. H. R., Hesse R. H., Tarzin G., Pechet M. M.: J. Chem. Soc., Chem. Commun. *1969*, 1497.
4. Olofson R. A., Dougherty C. M.: J. Am. Chem. Soc. *92*, 581 (1973).
5. Olofson R. A., Lotts K. D., Barber G. N.: Tetrahedron Lett. *1976*, 3779.
6. Craig L. E.: Chem. Rev. *42*, 285 (1948).
7. Spinks A., Young E. H. P.: Nature *181*, 1397 (1958).
8. Corne S. J., Edge N. D.: Br. J. Pharmacol. *13*, 339 (1958).
9. Lutz W. B., Lazarus S., Meltzer R. I.: J. Org. Chem. *27*, 1695 (1962).
10. Usilton J. J., Patel A. R. in: *Stabilization and Degradation of Polymers* (D. L. Allara and W. L. Hawkins, Eds), p. 116. Am. Chem. Soc., Washington 1978.
11. Gugumus F. in: *Developments in Polymer Stabilisation – 1* (G. Scott, Ed.), p. 293. Applied Science, London 1979.
12. Gachter R., Muller H.: *Taschenbuch der Kunststoff-Additive*, p. 129. Carl Hauser, Munchen 1979.
13. Berliner L. J.: *Spin Labelling – Theory and Applications*. Academic Press, New York 1974.
14. Lichtenstein G. I.: *Methods of Spin Labelling in Molecular Biology*. Nauka, Moscow 1974.
15. Kuznetsov A. N.: *Methods of Spin Probing*. Nauka, Moscow 1976.
16. Rozantsev E. G.: *Free Iminoxyl Radicals*. Khimiya, Moscow 1976.
17. Rozantsev E. G., Sholle V. D.: *Organic Chemistry of Free Radicals*. Khimiya, Moscow 1979.
18. Vass F.: *Thesis*. Polymer Institute, Slovak Academy of Sciences, Bratislava 1986.
19. Usilton J. J., Patel A. R.: Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.) *18* (1), 393 (1977).
20. Tozzi A., Cantattore G., Masina F.: Text. Res. J. *48*, 433 (1978).
21. Luston J. in: *Developments in Polymer Stabilisation – 2* (G. Scott, Ed.), Chap. 5. Applied Science Publishers, London 1980.
22. Billingham N. C., Calvert P. D. in: *Developments in Polymer Stabilisation – 3* (G. Scott, Ed.), Chap. 5. Applied Science Publishers, London 1980.
23. Karrer F. E.: Makromol. Chem. *181*, 595 (1980).
24. Ernest I., Hermanek S.: *Preparative Reactions in Organic Chemistry*, Vol. 4, p. 214. CSAV, Prague 1959.
25. Buehler C. A., Pearson D. E.: *Survey of Organic Synthesis*, Vol. 1, Chap. 8. Wiley-Interscience, New York 1970.
26. Houben–Weyl: *Methoden der organischen Chemie*, Vol. 8, p. 590. Thieme Verlag, Stuttgart 1952.
27. Kurosaki T., Lee K. W., Okawara M.: J. Polym. Sci., A-1 *10*, 3295 (1972).
28. Gilman H. (Ed.): Org. Synth., Coll. Vol. *I*, 245 (1948).
29. Schwetlick K. (Ed.): *Organikum*, p. 322. VEB Deutscher Verlag der Wissenschaften, Berlin 1981.
30. Gilman H. (Ed.): Org. Synth., Coll. Vol. *III*, 623 (1955).
31. Riddick J. A., Bunger W. B.: *Organic Solvents*. Wiley-Interscience, New York 1970.