CYCLOADDITION REACTIONS OF METHYL 2-N-TRIFLUOROACETYLIMINOTRIFLUOROPROPIONATE

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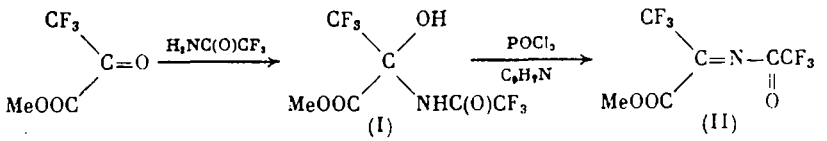
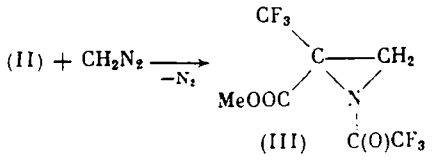
Acylimines of hexafluoroacetone form [1 + 4] cycloadducts with carbenes, their precursors, and carbenoids, and with unsaturated π-donating compounds they enter into "inverse" Diels–Alder reactions [1, 2], and only with active 1,3-dienes do they act as electron accepting 2π-systems [3]. These reactions are regiospecific and are accelerated by increased electron-accepting power of the acyl group. The properties of these types of transformations can be explained using the example of unsymmetrically substituted acylimines; therefore, we have studied cycloaddition reactions of the methyl ester of 2-(N-trifluoroacetylimino)trifluoropropionic acid (II) which was obtained by the following scheme in satisfactory yield

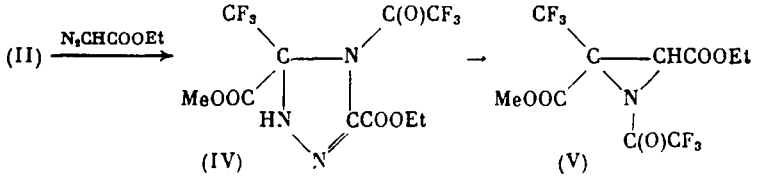


Judging from the spectral characteristics, compound (II) is distinguished by the high electron deficiency of the azomethine bond and facile Z/E-isomerization.

Reaction of (II) with diazomethane at −30°C is accompanied by elimination of nitrogen to give aziridine (III) and not [1 + 4]-cycloadduct, as in the same reaction of benzoylimine hexafluoroacetone [2]



Reaction of (II) with diazoacetic ester at 20°C leads to a mixture (2:1) of triazoline (IV), formed apparently as a result of a 1,3-hydride shift in the primary [3 + 2]-cycloadduct, and ethyleneimine (V). Thermolysis of (IV) at 150°C yields aziridine (V)



In the reactions of (II) with vinyl acetate and vinyl butyl ether, both containing substituents favoring endo-orientation of the reagents, one can expect formation of dihydrooxazines (VIa) and (VIIa) by the principle of cis-addition and endo-orientation. However, when the endo-orientation rule is not observed, which is often the case in cycloaddition of unsymmetric dienophiles to unsymmetric 1,3-dienes [4], dihydrooxazines (VIb) and (VIIb) can be formed (formula, top, following page).

It was found that under mild conditions (−30 to 20°C) these reactions are regiospecific and give dihydrooxazines (VI) and (VII) as mixtures of two isomers. According to the PMR spectra, in the reaction with vinyl acetate the main product (VIb) (84%) contains a pseudo-

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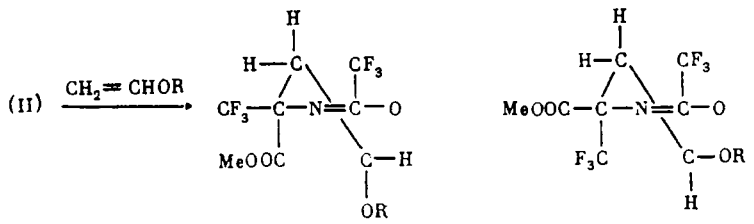
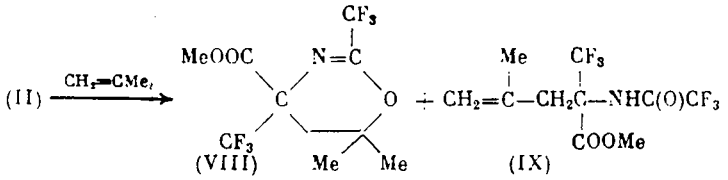


(VIa), (VIIa) (VIb), (VIIb)

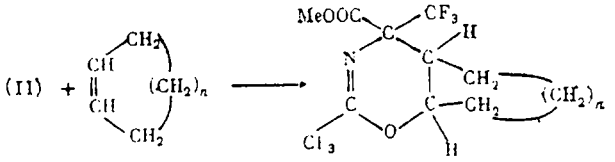
R = MeCO(VIa, b); C_4H_9(VIIa, b)

equatorial acetoxy group and with vinyl butyl ether dihydrooxazine (VIIa) is formed (>90%) with a pseudoaxial n.butoxy group, i.e., these reactions are stereoselective processes.

Similarly, the formation of dihydrooxazine (VIII) as the main product of reaction of (II) with 2-methylpropene, and formation of a minor amount of butene (IX) (25%) can be explained as a (2π + 2π)-reaction, accompanied by cationotropic transformations



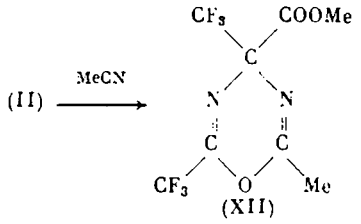
Unlike terminal akenes, cyclopentene and cyclohexene only under severe conditions (~150°C) form cycloadducts (X) and (XI) with (II)



(X), (XI)

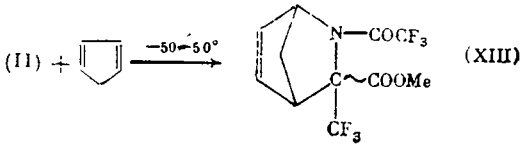
n = 1 (X); n = 2 (XI).

Similarly to hexafluoroacetone acylimines, compound (II) with acetonitrile at 20°C gives oxadiazine (XII)



(XII)

However, with cyclopentadienes compound (II) reacts only with moderate heating, forming (4 + 2)cycloadduct (XIII) as a mixture (1:1) of endo- and exo-isomers



(XIII)

From the obtained results it follows that (II) differs noticeably from hexafluoroacetone acylimines in its behavior in cycloaddition reactions. The 2π-system of the C=N bond is

strongly activated by exchange of one of the CF_3 groups on the hexafluoroisopropylidene fragment by a COOMe group, which is displayed in the $(2\pi + 2\pi)$ and $(4\pi + 2\pi)$-reactions of (II) with diazoalkanes. At the same time, compound (II), like hexafluoroacetone acylimines, resembles a conjugated 1,3-dipolar system in relation to electron donating unsaturated compounds, regio- and stereoselectively forming adducts which correspond to either exo- or endo-orientation of the reagents in the transition state.

Structure of the synthesized compounds was confirmed by elemental analysis and spectral methods. Particularly informative are the cycloadduct IR bands at 1730-1700 cm^{-1}, characteristic of oxazines, and at 3120-3010 cm^{-1} for aziridines. The (2 + 4)-cycloaddition stereochemistry was confirmed by the coupling constants of the vicinal ring protons.

EXPERIMENTAL

NMR spectra were taken on a Bruker WR-SV instrument (^1H 200, ^{19}F 188 MHz) with TMS (internal standard) and CF_3COOH (external standard). IR spectra were recorded on a UR-20 instrument.

Methyl-α-oxy-α-trifluoroacetamidotrifluoropropionate (I). A mixture of 15.6 g methyl trifluoropyruvate and 11.3 g trifluoroacetamide was kept for 24 h at 20°C until dissolution of the latter, and after distillation under vacuum of the excess methyl trifluoropyruvate 25.0 g (92%) of (I) was obtained with mp 78.0-78.5°C. PMR spectrum (d_6-acetone, δ, ppm): 7.98 s (1H, OH), 3.86 s (3H, MeO). ^{19}F NMR spectrum (acetone, δ, ppm): −0.8 s (CF_3). Found: C 26.68; H 1.91; N 4.98%. $C_6H_5F_6NO_4$. Calculated: C 26.72; H 1.85; N 5.20%.

Methyl Ester of 2-(N-Trifluoroacetylimino)trifluoropropionic Acid (II). To a solution of 10.0 g of (I) in 15 ml quinoline with stirring and water bath cooling 5.7 g $POCl_3$ was added dropwise, so that the temperature did not exceed 40°C. Then the mixture was slowly heated to 100°C with simultaneous distillation of the reaction product under vacuum. There was obtained 7.0 g (75%) of (II) with bp 57°C (30 mm), n_D^{24} 1.3500. ^{19}F NMR spectrum (δ, ppm): −5.8 s (CF_3), −1.5 s (CF_3). Found: C 28.74; H 2.02; F 45.19%. $C_6H_3F_6NO_3$. Calculated: C 28.68; H 1.19; F 45.42%.

N-Trifluoroacetyl-2-carbomethoxy-2-trifluoromethylaziridine (III). To a solution of 2.1 g imine (II) in 10 ml ether at −30°C a solution of 1.0 g diazomethane in 50 ml ether was added. The mixture was slowly heated and fractionated. There was obtained 1.5 g (60%) of (III) with bp 80°C (20 mm), n_D^{25} 1.3635. PMR spectrum (CCl_4, δ, ppm): 3.8 s (3H, OMe), 3.0 s and 2.8 s (2H, CH_2), ^{19}F NMR spectrum (CCl_4, δ, ppm): −5.5 s (CF_3), −1.9 s (CF_3). IR spectrum: 3120 (CH_2), 1775 (C=O), 1770 (C=O). Found: C 31.14; H 2.01; N 5.45%. Calculated: C 31.69; H 1.88; N 5.28%. $C_7H_5F_6NO_3$.

N-Trifluoroacetyl-3-carboethoxy-5-carbomethoxy-5-trifluoromethyl-4,5-dihydro-1,2,4-triazole (IV) and N-Trifluoroacetyl-2-carbomethoxy-2-trifluoromethyl-3-carboethoxyaziridine (V). To a solution of 5.6 g of (II) in 5 ml ether at −30°C 2.5 g diazoacetic ester in 5 ml of the same solvent was added. The mixture was heated to 20°C, kept at this temperature for 8 h, and fractionated. There was obtained 6.0 g of a mixture (2:1) of (IV) and (V) with bp 73-74°C (1 mm), n_D^{25} 1.3990. PMR spectrum of (IV) (CCl_4, δ, ppm, J, Hz): 4.32 broad s (1H, NH), 4.18 q (2H, CH_2, $^2J_{H-H}$ = 7.0), 3.81 s (3H, MeO), 1.15 t (3H, Me, $^2J_{H-H}$ = 7.0); ^{19}F NMR spectrum (CCl_4, δ, ppm): −5.4 s and −2.2 s ($2CF_3$, 1:1); IR spectrum (ν, cm^{-1}): 3370 (NH), 2130 (HN–N=), 1780 and 1760 (C=O), 1700 (C=N). PMR spectrum of (V) (CCl_4, δ, ppm, J, Hz): 4.20 q (2H, CH_2, $^2J_{H-H}$ = 7.0), 3.88 s (3H, MeO), 3.77 s (1H, CH), 1.20 t (3H, Me $^2J_{H-H}$ = 7.0). ^{19}F (CCl_4, δ, ppm): −10.3 s and −3.0 s ($2CF_3$, 1:1); IR spectrum (ν, cm^{-1}): 3010 (CH), 1780, 1775, and 1770 (C=O).

5.5 g of a mixture of (IV) and (V) was heated for 1 h at 150°C and fractionated. There was obtained 4.8 g (70.4%) of (V) with bp 104-105°C (6 mm), n_D^{25} 1.3840. Found: C 35.36; H 2.47; N 4.62%. $C_{10}H_9F_6NO_5$. Calculated: C 35.60; H 2.67; N 4.15%.

5,6-Dihydro-2,4-bis(trifluoromethyl)-4-carbomethoxy-6-acetoxy-1,3-oxazine (VI). To a solution of 2.1 g (II) in 5 ml khladon-113 at 0°C a solution of 0.8 g vinyl acetate in 5 ml of the same solvent was added. The mixture was heated to 20°C, kept at this temperature for 20 h, and fractionated. There was obtained 2.1 g (75%) of (VI) in the form of a mixture (1:5) of isomers with bp 81.5-82°C (1 mm), n_D^{26} 1.3900. IR spectrum (ν, cm^{-1}): 1785 and 1775 (C=O), 1710 (C=N). PMR spectrum of (VIa) (CCl_4, δ, ppm, J, Hz): 6.3 dd (1H, CH, $^3J_{H-H}$ = 3.0 and 1.0), 3.8 s (3H, MeO), 2.7 dd and 2.1 dd (2H, CH_2, $^2J_{H-H}$ = 10.0, $^3J_{H-H}$ = 3.0 and 1.0), 2.2 s (3H, Me). ^{19}F NMR spectrum (CCl_4): −4.2 s and 1.0 s ($2CF_3$, 1:1). PMR spectrum of (VIb)

(CCl_4, δ, ppm, J, Hz): 6.5 dd (1H, CH, $^3J_{H-H}$ = 11.0 and 4.0), 3.7 s (3H, MeO), 2.8 dd and 2.2 dd (2H, CH_2, $^2J_{H-H}$ = 10.0 and $^3J_{H-H}$ = 11.0 and 4.0), 2.05 s (3H, Me), ^{19}F spectrum (CCl_4, δ, ppm): −3.7 s and −0.5 s ($2CF_3$, 1:1). Found: C 35.33; H 2.63; N 4.20%. $C_{10}H_9F_6NO_4$. Calculated: C 35.61; H 2.67; N 4.15%.

5,6-Dihydro-2,4-bis(trifluoromethyl)-4-carbomethoxy-6-butoxy-1,3-oxazine (VII). To a solution of 2.1 g (II) in 5 ml khladon-113 at −30°C 0.8 g butyl vinyl ether in 5 ml of the same solvent was added. The mixture was slowly heated to 20°C, kept for 1 h, and fractionated. There was obtained 1.5 g (51%) of (VIIa) and an impurity (VIIb) with bp 85°C (1 mm), n_D^{25} 1.3910. PMR spectra (CCl_4, δ, ppm, J, Hz): 5.35 m (2H, CH), 3.80 s (3H, MeO), 3.55 m (4H, OCH_2), 2.80 dd (1H, CH_2, $^2J_{H-H}$ = 14.0, $^3J_{H-H}$ = 0.5), 2.10 dd (1H, CH_2, $^2J_{H-H}$ = 14.0, $^3J_{H-H}$ = 4.5), 1.40 m and 0.91 m (7H, C_3H_7). ^{19}F NMR spectrum (δ, ppm): −4.3 s (CF_3), −1.4 s (CF_3). IR spectrum (ν, cm^{-1}): 1765 (C=O), 1710 (C=N). Found: C 40.87; H 4.16; N 4.30%. $C_{12}H_{13}F_6NO_4$. Calculated: C 41.02; H 4.24; N 3.98%.

5,6-Dihydro-2,4-bis(trifluoromethyl)-4-carbomethoxy-6,6-dimethyl-1,3(4H)-0xazine (VIII) and 2-Methyl-4-carbomethoxy-4-trifluoromethyl-4-trifluoroacetylaminobut-1-ene (IX). To 4.5 g of (II) at −50°C 1.5 g 2-methylpropene was added. The mixture was shaken in an ampul for 4 h and fractionated. There was obtained 3.5 g of a mixture (3:1) of (VIII) and (IX) with bp 78-79°C (6 mm), n_D^{25} 1.3849. IR spectrum (ν, cm^{-1}): 1775 and 1765 (C=O), 1705 (C=N), 1650 (C=C). PMR spectra of (VIII) (CCl_4, δ, ppm, J, Hz): 3.80 s (3H, MeO), 2.75 d and 2.00 d (2H, CH_2, $^2J_{H-H}$ = 15.0), 1.49 s and 1.20 s (6H, 2Me). ^{19}F NMR spectrum (δ, ppm): −3.6 s (CF_3), −0.4 s (CF_3). PMR spectra of (IX) (CCl_4, δ, ppm, J, Hz): 7.50 br. s (1H, NH), 4.90 s and 4.75 s (2H, $=CH_2$), 3.89 s (3H, MeO), 3.65 d and 2.95 d (2H, CH_2, $^2J_{H-H}$ = 15.0), 1.70 s (3H, Me). ^{19}F NMR spectrum (δ, ppm): −4.2 s (CF_3), −1.7 (CF_3). Found: C 38.72; H 3.95; N 4.29%. $C_{10}H_{11}F_6NO_3$. Calculated: C 39.08; H 3.58; N 4.56%.

3,5-Bis(trifluoromethyl)-5-carbomethoxy-2-oxa-4-azabicyclo[4.3.0]non-3-ene (X). 4.1 g of (II) and 1.2 g cyclopentene were heated in an ampul for 4 h at 150°C and fractionated. There was obtained 2.0 g (50%) of (X) with bp 120°C (13 mm), n_D^{25} 1.4010. PMR spectra (CCl_4, δ, ppm): 4.50 m (1H, HC^1), 3.80 s (3H, MeO), 2.60 m (1H, HC^6), 1.90 m {6H, $(CH_2)_3$}. ^{19}F NMR (δ, ppm): −4.7 s (CF_3), −3.8 s (CF_3). IR spectrum (ν, cm^{-1}): 1760 and 1750 (C=O), 1710 (C=N). Found: C 41.37; H 3.34; N 4.46%. $C_{11}H_{11}F_6NO_3$. Calculated: C 41.37; H 3.44; N 4.38%.

3,5-Bis(trifluoromethyl)-5-carbomethoxy-2-oxa-4-azabicyclo[4.4.0]dec-3-ene (XI). To 5.0 g of (II) 1.6 g of cyclohexene was added and the mixture heated in an ampul for 4 h at 150°C and fractionated. There was obtained 4.7 g (70%) of (XI) with bp 90°C (1 mm), n_D^{23} 1.4118. PMR spectra (CCl_4, δ, ppm): 4.50 m (1H, HC^{-1}), 3.80 s (3H, MeO), 2.50 m (1H, HC^6), 1.65 m {8H, $(CH_2)_4$}. ^{19}F NMR spectrum (δ, ppm): −4.16 s (CF_3), −6.90 s (CF_3). IR spectrum (ν, cm^{-1}): 1770 (C=O), 1720 (C=N). Found: C 42.96; H 4.09; N 4.60%. $C_{12}H_{13}F_6NO_3$. Calculated: C 43.24; H 3.90; N 4.25%.

2-Methyl-4-carbomethoxy-4,6-bis(trifluoromethyl)-1,3,5-(4H)-oxadiazine (XII). To a solution of 5.0 g of (II) in 10 ml ether at −30°C a solution of 0.8 g acetonitrile in 5 ml of the same solvent was added. The mixture was slowly heated to 20°C, kept for 20 h, and fractionated. There was obtained 3.9 g (68%) of (XII) with bp 85°C (10 mm), n_D^{25} 1.3740. PMR spectrum (CCl_4, δ, ppm): 3.80 s (3H, MeO), 2.12 s (3H, Me). ^{19}F NMR spectrum (δ, ppm): −2.8 s (CF_3), −0.8 s (CF_3). IR spectrum (ν, cm^{-1}): 1760 (C=O), 1680 (C=N). Found: C 32.61; H 1.81; N 9.21%. $C_8H_6F_6N_2O_3$. Calculated: C 32.87; H 2.05; N 9.58%.

N-Trifluoroacetyl-2-aza-3-carbomethoxy-3-trifluoromethylbicyclo[2.2.1]heptene-5 (XIII). To a solution of 5.0 g of (II) in 10 ml ether at −50°C a solution of 1.3 g cyclopentadiene and 0.01 g hydroquinone in 10 ml of the same solvent was added. The mixture was slowly heated to 50°C, kept at this temperature for 2 h, and fractionated. There was obtained 3.8 g (60%) of (XIII) with bp 104-105°C (1 mm), n_D^{25} 1.4182 in the form of a mixture (1:1) of endo- and exo-isomers. PMR spectrum of exo-isomer (CCl_4, δ, ppm, J, Hz): 6.58 m and 6.21 m (2H, CH=CH), 5.01 m and 3.75 m (2H, 2CH), 3.79 s (3H, MeO), 2.10 d and 1.90 d (2H, CH_2, $^2J_{H-H}$ = 10), ^{19}F NMR spectrum (δ, ppm): −16.5 s (CF_3), −5.7 s (CF_3). PMR spectrum of endo-isomer (CCl_4, δ, ppm): 6.39 m and 5.90 m (2H, CH=CH), 5.01 m and 3.75 m (2H, CH), 3.83 s (3H, MeO), 1.65 and (2H, CH_2). ^{19}F NMR spectrum (δ, ppm): −14.62 s (CF_3), −5.69 s (CF_3). Found: C 41.38; H 2.41; N 4.82%. $C_{11}H_{12}F_6NO_3$. Calculated: C 41.64; H 2.83; N 4.41%.

CONCLUSIONS

The methyl ester of 2-(N-trifluoroacetylimino)trifluoropropionic acid reacts with diazoalkanes at the isolated C=N bond similarly to azomethines, forming [1 + 2]- and/or [3 + 2]-

cycloadducts, and with unsaturated donating type compounds as a 1,3-dipolar conjugated system to give products of [2 + 4]-cycloaddition regio- and stereo-selectively.

LITERATURE CITED

1. A. V. Fokin, A. F. Kolomiets, and N. V. Vasil'ev, Usp. Khim., 53, 398 (1984).
2. Yu. V. Zeifman, N. P. Gambaryan, L. A. Simonyan, et al., Zh. Obshch. Khim., 37, 2476 (1967).
3. L. N. Kryukov, L. Yu. Kryukova, and A. F. Kolomiets, Zh. Org. Khim., 18, 1873 (1982).
4. A. S. Onishchenko, Diene Synthesis [in Russian], Nauka, Moscow (1963), p. 38.

STUDIES IN THE CROWN ETHER SERIES.

3. CATALYTIC ACTIVITY OF CROWN ETHERS AND THEIR "HETEROGENATED" ANALOGS

N. I. Abakumova, I. P. Kolenko, L. A. Petrov, A. A. Novoselova, and L. M. Gus'kova

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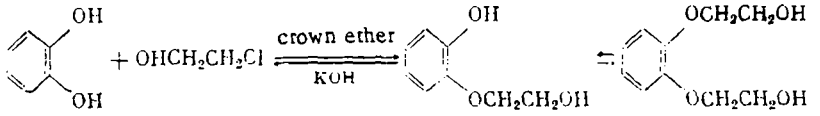
The immobilization of crown ethers on carriers is a method for preparing synthetic models of ionophoric and enzymatic systems with a prolonged and multiply repeated action [1]. Modeling the catalytic function of benzo-crown ethers and their heterogenated analogs in the nucleophilic substitution reaction has already been carried out in [2, 3].

In continuation of the investigation on these subjects, already commenced, we studied the influence of functionalization and immobilization factors of benzo-crown ethers on their catalytic activity in the synthesis of esters according to Williamson, in particular in the reaction of hydroxyethylation of pyrocatechol by ethylene chlorohydrin in the presence of an alkali



EXPERIMENTAL

For the investigation, we used dicyclohexyl-18-crown-6 (I) from the firm "Fluka," benzo-18-crown-6 (II) [4], dibenzo-18-crown-6 (III) and 18-crown-6 (VII), produced at the Scientific-Research Institute of General Chemistry of the Siberian Branch of the Academy of Sciences of the USSR, 4,4'-diaminodibenzo-18-crown-6 (IV) and 4,4'-dinitrodibenzo-18-crown-6 (VI) [5, 6], 4'-nitrobenzo-18-crown-6 (V), and 4-aminobenzo-18-crown-6 (VIII) [7]. The immobilized derivatives of crown ethers (IV) and (VIII) were obtained according to [2, 3].

The GLC was carried on a "Chrom-5" chromatograph in an isothermal regime, the flow rate of He, H_2 and air was 40, 40, 400 ml/min, respectively, using a 2.5 m × 4 mm glass column, a chromatone N-AW-HmDS carrier (0.2-0.25 mm) with 10% Lucoprene G-1000 as stationary phase, the temperature of the carrier 200°C, of the thermostat and the columns 170°C, and of the flame ionization detector 220°C.

Hydroxyethylation of Pyrocatechol. Potassium hydroxide (2 g, 0.035 mole) was added in portions in an inert atmosphere to a solution of 1.1 g (0.01 mole) of pyrocatechol and 0.002 mole of a crown ether in 15 ml of ethanol. Then, 2.5 g of ethylene chlorohydrin were added dropwise to the boiling mixture. The mixture was boiled for 2 h, then cooled, the KCl precipitate was filtered and washed with 10 ml of ethanol. In the filtrate, the content of 1,2-

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