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Dedicated to Academician M. G. Voronkov on occasion of his 80th birthday

Transformations of 4,5-Substituted (4*S*,5*S*)-2,2-Dimethyl-1,3-dioxolanes

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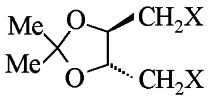
Abstract—(4*S*,5*S*)-4,5-Bis(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane treated with trifluoromethanesulfonyl chloride in pyridine undergoes tandem substitution of one hydroxy group by a triflate group, and the other by pyridinium moiety. In neutral solvents the (4*S*,5*S*)-4,5-bis(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane dilithium salt reacts with trifluoromethanesulfonyl chloride affording both triflates and chlorides and also suffers a cleavage of the dioxolane ring followed by transformations of acyclic products. A triflate cationic complex rhodium cyclooctadiene (4*S*,5*S*)-2,3-dihydroxy-1,4-bis(dimethylamino)-2,3-O-isopropylidenebutane was prepared and used as catalyst for hydrogenation of α-acetamidocinnamic and itaconic acids.

2,3-Dihydroxy-1,4-bis(diphenylphosphino)-2,3-*O*-isopropylidenebutane (DIOP) (**Ia**) is widely used as chelating ligand in catalysts for chiral hydrogenation. It is prepared by replacing the *p*-tolyenesulfonic group in tosylate Ib by Ph_2P moiety [1].



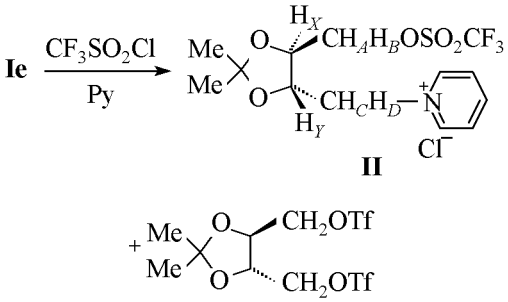
Ia–**f**

I, X = PPh_2 (**a**), OTs (**b**), NMe_2 (**c**), OTf (**d**), OH (**e**), Cl (**f**).

The nitrogen analogs of DIOP, optically active diamines of type **I** (X = NH_2, NR_2) are known as chiral catalysts for polymerization into highly regular polymers [2] and also as ligands for preparation of platinum(II) salts complexes possessing antitumor properties [3, 4]. Aiming at preparation and study of properties of chiral catalysts based on nitrogen analogs of DIOP we synthesized a rhodium complex of (4*S*,5*S*)-2,3-dihydroxy-1,4-bis(dimethylamino)-2,3-O-isopropylidenebutane (**Ic**) (DIODMA) and investigated hydrogenation of prochiral aminoacids catalyzed therewith. We also attempted to introduce into the molecule more nucleofugal group through a synthesis of the corresponding bistriflate **Id** in order to facilitate functionalization of compounds from **I** series.

The attempt to prepare bistriflate **Id** gave an unexpected result: in the reaction of (4*S*,5*S*)-4,5-bis-

Scheme 1.

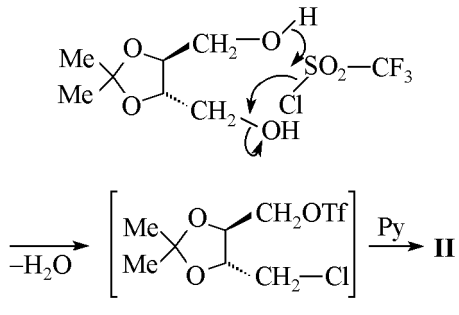


II

Id

(hydroxymethyl)-2,2-dimethyl-1,3-dioxolane (**Ie**) with trifluoromethanesulfonyl chloride in pyridine alongside the target compound **Id** formed as the main product a salt, (4*S*,5*S*)-1-(2,2-dimethyl-5-trifluoromethylsulfonyloxymethyl-1,3-dioxolan-4-yl)pyridinium chloride (**II**) (Scheme 1).

The assignment of signals in ^1H and ^{13}C NMR spectra was carried out with the use of two-dimen-



III

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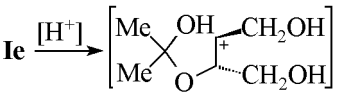
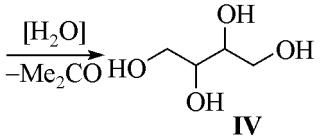
sional spectrum ^1H–^{13}C HETCOR. Since trifluoromethanesulfonyl chloride can operate both as sulfonating and chlorinating agent [5] the following scheme is presumable to rationalize formation of salt **II**: One hydroxy group is sulfonated, the other chlorinated, and then the intermediate chloride **III** is alkylated by pyridine.

Reaction product **II** arose also on performing reaction in THF when pyridine was used in equimolar amount just for scavenging liberating HCl. The chlorinating action of trifluorosulfonyl chloride was directly confirmed by isolation of (4*S*,5*S*)-2,2-dimethyl-4,5-bis(chloromethyl)-1,3-dioxolane (**If**) in reaction of diol **Ie** with an equimolar amount of pyridine in dioxane.

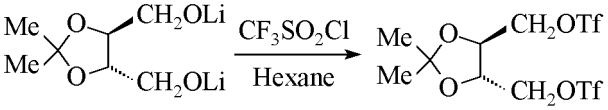
In reaction of diol **Ie** with trifluoromethanesulfonyl chloride in the absence of bases was obtained 1,2,3,4-butanetetrol (threitol) (**IV**) resulting from dioxolane ring cleavage with acetone elimination. The process is apparently catalyzed by HCl traces present in the acyl chloride or liberating at its reaction with diol **Ie**.





IV

The target bistriflate **Id** was obtained by reacting a dilithium salt of diol **Ie** with CF_3SO_2Cl in hexane.

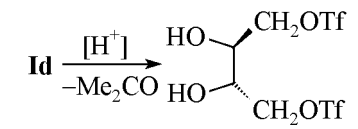


Id

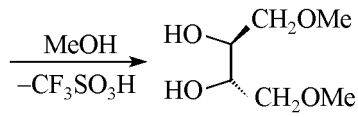
Note a considerable dependence of the chemical shifts of bis-triflate **Id** signals in the ^1H NMR spectrum on the solvent: all the signals suffer in benzene a strong upfield shift as compared to spectrum registered in chloroform: $\Delta\delta(CH_A)$ 0.85, $\Delta\delta(CH_B)$ 1.01, $\Delta\delta(CH)$ 0.89, $\Delta\delta(CH_3)$ 0.36 ppm. The corresponding shifts in the ^{13}C NMR spectrum do not exceed 0.5 ppm.

On storage of compound **Id** solution in chloroform for 3–4 days forms a new compound lacking in the ^1H NMR spectrum the signal from $C(CH_3)_2$ group; however are conserved the signals from the $CHCH_2$ fragment with diastereotopic protons of the methylene group: 4.46 ppm (CH) and 4.90 and 5.01 ppm (CH_AH_B). Also appears a broadened signal at 3.6–3.7 ppm (in deuteroacetone). The ^{13}C and ^{19}F spectra confirm the presence of triflate group. All this evidence suggests formation of 2,3-dihydroxybutane-1,4-bis(trifluoromethanesulfonate) (**V**) as a result of dioxolane ring opening effected by acid traces (HCl in CF_3SO_2Cl) (Scheme 2).

Scheme 2.



V



VI

In The ^1H NMR spectrum of compound **V** in CD_3OD the signals of the fragment CH–CH_2 are shifted upfield by ~0.4 ppm compared to its spectrum in acetone-d_6; in the course of time their intensity decreases, and appears and grows in intensity a new group of peaks. The transformation product **VI** isolated when the signals of compound **V** disappeared was a crystalline substance of low melting point with no signals in the ^{19}F NMR spectrum. The signals of diastereotopic protons from CH_2 group suffer a strong upfield shift o a region characteristic of CH_2 groups (3.37 and 3.44 ppm), and the signal from CH proton appears downfield from those of CH_2 (3.68 ppm) unlike the spectra of compounds **Id, V**. This spectral pattern is consistent with 1,4-dimethoxybytane-2,3-diol (**VI**) structure. The ^1H NMR spectrum published for this structure registered in D_2O [7] (mp 28°C [6]) has signals a little displaced (by 0.1 ppm) due to the solvent effect; however the relative chemical shifts and the coupling constants are in agreement with our data thus confirming the assumed structure. The formation of 2,3-dimethoxybutane-1,4-diol, isomer of compound **VI**, is excluded since in the ^1H NMR spectrum of this compound the resonance of methine protons appears upfield (3.54 ppm) from the methylene signal (3.78 ppm) [8]; we have not observed such signals in the spectrum of the reaction mixture under study.

Compound **V** can be obtained directly from lithium salt of diol **Ie** by treating it with CF_3SO_2Cl in dioxane. It should be noted that apart compounds **IV**–**VI** were formed also other transformation pro-

^{1}H NMR spectra of diamine **Ic** and its rhodium complex (δ, ppm, *J*, Hz)

Solvent	δ(CH), m	δ(CH_2) (H_A), d.d	δ(CH_2) (H_B)	δ(CH_3–N), s	δ(CH_3–C), s
Benzene-d_6	3.91	2.47, J_{AB} 12.99, J_{AC} 3.47	2.37 d.d, J_{BC} 5.86	2.13	1.35
Chloroform-*d*	3.77	2.49, J_{AB} 12.8, J_{AC} 6.77	2.38 d	2.28	1.39
Acetone-d_6	3.80	2.52, J_{AB} 12.99, J_{AC} 3.65	2.37 d.d, J_{BC} 6.20	2.21	1.29
Acetone-d_6[a]	4.10	3.02, J_{AB} 12.80, J_{AC} 7.10	2.96 d.d, J_{BC} 4.60	2.68	1.36

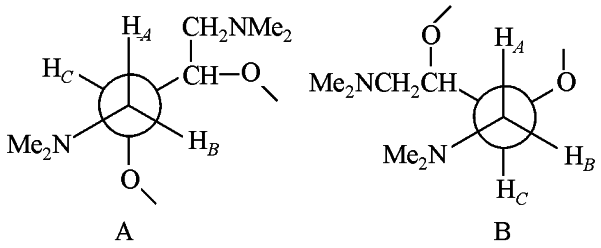
[a] Rhodium complex.

ducts containing in the ^{1}H NMR spectra signals from CH–CH_2 fragment with diastereotopic methylene protons. Their isolation and identification will be the subject of future studies.

The nitrogen analog of DIOP, DIODMA (**Ic**) was obtained by cyclization of (+)-tartaric acid diamide (**VII**) under the action of 2,2-dimethoxypropane followed by reduction of dicarboxamide **VIII** with lithium aluminum hydride along procedure [6].

Diamine **Ic** afforded a chelate cationic complex with rhodium that is supported by ^{1}H NMR spectrum where to the strongest downfield shift are subjected the protons of NMe groups (0.47 ppm) and the diastereotopic methylene protons (0.50 and 0.59 ppm). On going from the complex center the downfield shift decreases (0.3 ppm for CH protons and 0.07 ppm for CMe groups). The spectra of the free ligand and the complex were registered in the same solvent, acetone-d_6. In the ^{13}C NMR spectrum on the contrary the signals are shifted upfield: Δδ(CH) –1.73, Δδ(CH_2) –2.17, Δδ(NMe) –1.06, Δδ(CMe) –0.43 ppm. In the spectrum of the complex with diamine **Ic** are lacking the signals from cyclooctadiene that have appeared in the initial complex obtained by reaction of $[(COD)RhCl]_2$ with silver triflate. This means that ligand exchange occurred, and the diene molecule was displaced by diamine **Ic**.

The data in the table evidence that the prevailing conformation of diamine **Ic** changes on complexing. In the spectrum of free ligand **Ic** the downfield signal of the diastereotopic pair of protons CH_AH_B is split on H_C with a smaller coupling constant, the spectrum pattern in the complex is the opposite. We believe that this fact indicates a change in the conformation: that of the free ligand is apparently conformation A where the *gauche*-interactions of the bulky groups is minimal; at complexing both nitrogen atoms should be directed to the central rhodium atom, and this is possible only in B conformation. Taking into account the angular dependence of the coupling constants, in A conformation should be $^3J_{HA} < {}^3J_{HB}$ whereas in B conformation $^3J_{HA} > {}^3J_{HB}$. It is reasonable to assume that in both conformations the downfield signal corresponds to the same proton H_A, then the observed spectral changes are consistent with the change in conformation from A to B that are shown below in Newman projections:



Thus the rhodium complex containing one or two molecules of diamine Ic may be assigned the composition $\{Rh[(-)S,S\text{-DIODMA}]_n \times solv_m\}^+ CF_3SO_3^-$ (**IX**), where n = 1 or 2. Complex **IX** was tested in hydrogenation of prochiral substrates, itaconic and α-acetamidocinnamic acids. The hydrogenation was carried out with molecular hydrogen under mild conditions (p 1 at, 40°C); the conversion of itaconic and α-acetamidocinnamic acids into *R*(+)-α-methylsuccinic acid and *S*(+)-N-acetylphenylalanine was 70 and 15% respectively. The asymmetrization attained with complex **IX** was lower than at the use of the diphosphine analogs [9]: optical yields of the products of enantioselective hydrogenation of itaconic and α-acetamidocinnamic acids were 17.4 and 30% respectively. The moderate optical yield of the products may be ascribed to gradual decomposition of diamine complex **IX** under reductive conditions with liberation of metallic rhodium as is observed in the course of experiment.

EXPERIMENTAL

IR spectra were recorded on IKS-29 device from thin films. ^{1}H, ^{13}C, and ^{19} NMR spectra were registered on spectrometer Bruker DPX 400 at 400, 100, and 376 MHz respectively from solutions in

$CDCl_3$ using HMDS as internal reference. Chemical shifts are given relative to TMS. GC-MS analyses were carried out on LKB 2091 instrument. GLC was performed on a chromatograph LKhM-80 equipped with columns 1000 × 3 mm, stationary phase 5% SE-30 on Chromaton N-AW-DMCS, detector katharometer, carrier gas helium. Optical rotation was measured on Polamat A instrument at 546 nm wavelength and was recalculated to 589 nm wavelength with a factor 1.17543.

(4*S*,5*S*)-4,5-Bis(aminomethyl)-N^4,N^4,N^5,N^5,-2,2-hexamethyl-1,3-dioxolane (Ic) was obtained along procedure [6]. bp 41°C/1 mm Hg (publ. 54°C/0.8 mm Hg [6]). ^{1}H NMR spectrum, δ, ppm: 1.39 s (6H, Me_2C), 2.28 s (12H, NMe_2), 2.38 d (2H, H_A in CH_2), 2.50 d.d [2H, H_B in CH_2, $^2J(H_AH_B)$ 12.6, ^3J(HH) 6.8 Hz], 3.77 m (2H, CH) {publ. (in CCl_4): 1.32 s, 3.34* m, 3.50 m, 3.85 m [6]}. ^{13}C NMR spectrum, acetone-d_6, δ_C, ppm: 27.66 ($C\underline{C}H_3$), 46.74 (NCH_3), 62.77 (CH_2), 79.63 (CH), 109.11 ($\underline{C}CH_3$).

(4*S*,5*S*)-2,2-Dimethyl-4,5-bis(trifluoromethylsulfonyloxymethyl)-1,3-dioxolane (Id). To a dispersion of 0.53 g (3.05 mmol) of diol **Ie** bis-lithium salt in 8 ml of hexane was added dropwise at 5–10°C while stirring 0.65 ml (6 mmol) of CF_3SO_2Cl in 2 ml of hexane. The mixture was vigorously stirred for 2–3 h and then the precipitate of lithium salts (LiCl and CF_3SO_2Li) was filtered off. The hexane and excess acyl chloride was removed under reduced pressure without heating. The separated needle-like crystals were filtered off, washed with cold (–10°C) hexane, and dried in a vacuum. Yield 0.42 g (32%). mp 30°C. $[\alpha]_{546}$ –8.1° (*c* 2.2, hexane). ^{1}H NMR spectrum in $CDCl_3$, δ, ppm: 1.44 s (6H, Me_2C), 4.22 m (2H, CH), 4.56 d (2H, H_A in CH_2), 4.65 d [2H, H_B in CH_2, $^2J(H_AH_B)$ 11.0 Hz]. ^{13}C NMR spectrum, δ_C, ppm: 26.88 (CH_3), 73.52 (CH_2), 74.52 (CH), 112.21 (OCO), 118.82 q [CF_3, *J*(C–F) 319.4 Hz]. ^{19}F NMR spectrum (CCl_3F), δ_F, ppm: –75.14. Found, %: C 25.24; H 2.87; F 27.22; S 15.77. $C_9H_{12}F_6O_8S_2$. Calculated, %: C 25.36; H 2.84; F 26.74; S 15.04.

(4*S*,5*S*)-2,2-Dimethyl-4,5-bis(chloromethyl)-1.3-dioxolane (If). To a solution of 1.73 g (10.7 mmol) of diol **Ie** and 5 ml of pyridine in dioxane at 0°C was added dropwise with stirring within 1 h 1.5-fold excess of CF_3SO_2Cl. The mixture was left overnight, then solvents and excess acyl chloride were removed at reduces pressure. The oily substance obtained was separated from the precipitating crystals of pyridinium hydrochloride, was treated with water, three times with chloroform, the extract was filtered, the solvent was distilled off, and product **If** was purified by microdistillation. Yield 0.2 g (10%). ^{1}H NMR spectrum, δ, ppm: 1.43 s (6H, Me_2C), 3.68 m (4H, CH_2Cl), 4.15 m (2H, CH). ^{13}C NMR spectrum, δ_C, ppm: 27.20 q.q [CH_3, ^1J(H–^{13}C) 126.7, ^3J(H–^{13}C) 3.0 Hz], 44.42 t.m [4H, CH_2Cl, ^1J(H–^{13}C) 151.3 Hz], 78.58 d.m [CH, ^1J(H–^{13}C) 150.9 Hz], 110.57 m ($\underline{C}Me_2$).

(4*S*,5*S*)-1-(2,2-Dimethyl-5-trifluoromethylsulfonylmethyl-1,3-dioxolan-4-ylmethyl)pyridinium chloride (II). To a solution of 3.17 g (0.02 mol) of compound **Ie** in 20 ml of dry pyridine was added dropwise at –15°C 5.7 ml (0.06 mol) of CF_3SO_2Cl. The reaction mixture was stirred for 20 h at –25 ÷ –15°C and was then evaporated till dryness on a rotary evaporator. To remove pyridine completely the residue was treated with chloroform, acidified with HCl till pH ~3, heated to boiling, then cooled to 0°C, the separated colorless crystals of pyridine hydrochloride were filtered off, the filtrate was evaporated till dryness, the residue was dissolved in 20 ml of water, and compound **II** was extracted into dichloromethane. To isolate salt **II** the organic extract was washed with water, and the water layer was evaporated till dryness. Yield 1 g (15%), mp 99–100°C. $[\alpha]_{546}$ –37.8° (*c* 10.8, $CHCl_3$). ^{1}H NMR spectrum, δ, ppm: 1.36 and 1.41 s (6H, Me_2C), 3.81 m [2H, H_C+H_D, $^2J(H_CH_D)$ 12.0, $^3J(H_CH_Y)$ 5.0, $^3J(H_DH_Y$ 5.4 Hz], 4.11 m [1H, H_Y, $^2J(H_XH_Y)$ 8 Hz], 4.31 m [1H, H_X, $^3J(H_AH_X)$ 8.8, $^3J(H_BH_X)$ 2.2 Hz], 4.80 d.d [1H, H_A, $^2J(H_AH_B)$ 13.7 Hz], 5.11 d.d (1H, H_B), 8.07 t (2H, H_m, ^3J 7.0 Hz), 8.55 t (1H, H_p), 8.98 d (2H, H_o, ^3J 6.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 26.93 and 27.06 (CH_3), 43.68 (CH_2N), 63.42 (CH_2O), 77.39 ($\underline{C}CO$), 77.83 ($\underline{C}CN$), 111.73 (OCO), 120.70 q [CF_3, *J*(C–F) 319.6 Hz], 128.26 (C_m), 145.63 (C_o), 146.20 (C_p). ^{19}F NMR spectrum (CCl_3F), δ_F, ppm: –79.25 ppm Found, %: C 39.74; H 4.31; Cl 9.66; F 15.00; N 3.62; S 8.27. $C_{13}H_{17}ClF_3NO_5S$. Calculated, %: C 39.85; H 4.37; Cl 9.05; F 14.55; N 3.58; S 8.18. 1,2,3,4-Butanetetrol (IV). mp 89°C [10]. ^{1}H NMR spectrum, DMSO-d_6, δ, ppm: 3.33 m (2H, CH), 3.43 m (4H, CH_2), 4.20 br.s (4H, OH).

(2*S*,3*S*)-2,3-Dihydroxybutane-1,4-bis(trifluoromethanesulfonate) (V). To a dispersion of 0.53 g (3.3 mmol) of diol **Ie** bis-lithium salt in 8 ml of

* The figure is obviously wrong; apparently, the value is 22.34 ppm.

dioxane was added dropwise at 5–10°C while stirring 1.05 ml (10.9 mmol) of CF_3SO_2Cl in 2 ml of dioxane. The mixture was vigorously stirred for 2–3 h and then the precipitate of lithium salts was filtered off, and the filtrate was left standing for 24 h; the solution turned red. Dioxane was removed in a vacuum, to the residue was added 5–7 ml of hot chloroform and after stirring the mixture was cooled, and the separated crystals were filtered off. After the second treating with chloroform we obtained 0.64 g (50%) of compound V as colorless crystals. mp 97–99°C. $[\alpha]_{546}$ –14.8° (*c* 1.36, hexane–acetone, 1:1). ^{1}H NMR spectrum, acetone-d_6, δ, ppm: 3.64 br.s (2H, OH), 4.46 m (2H, CH), 4.90 m (2H, CH_A), 5.01 m [2H, CH_in, $^2J(H_AH_i$n) 11.1 Hz]. ^{13}C NMR spectrum, acetone-d_6, δ_C, ppm: 74.00 (CH_2), 75.34 (CH), 118.60 q [CF_3, ^1J(CF) 318.5 Hz]. ^{19}F NMR spectrum, acetone-d_6, δ_F, ppm: –71.67. Found, %: C 18.54; H 2.65; F 29.06; S 16.54. $C_6H_8F_6O_8S_2$. Calculated, %: C 18.66; H 2.09; F 29.51; S 16.60.

(4*R*,5*R*)-N^4,N^4,N^5,N^5,2,2-Hexamethyl-1,3-dioxolane-4,5-dicarboxamide VIII was obtained by procedure [6]. mp 82°C [6]. ^{1}H NMR spectrum, δ, ppm: 1.44 s (6H, Me_2C), 2.95 and 2.16 s (6H, NMe_2), 5.22 s (2H, CH) [publ. (in CCl_4): 1.38 s, 2.92 s, 3.16 s, 5.09 3s [6]).

Hydrogenation of itaconic and α-acetylaminocinnamic acids. Hydrogenation was carried out at constant temperature with vigorous shaking of a glass reactor connected to a manometer and a system of hydrogen input. The gas was purified and dried by standard procedure. Into the reactor in the hydrogen flow was charged 5 ml of methanol and about 1 mmol of substrate. Then the pressure was raised to 1.2–1.3 at, and with hypodermic syringe was added either solution of an individual complex or of catalyst prepared in situ in a separate flask under argon atmosphere in 5 ml of a mixture methanol–benzene (2:1). At this moment the shaking was switched on. The chemical yield of hydrogenated products was evaluated from the ^{1}H NMR spectra of the reaction mixtures by the ratio of the integral intensity of acetyl groups of the initial substrate at 2.08 ppm and of the hydrogenated product at 1.88 ppm (for α-acetamidocinnamic acid). With itaconic acid was used the ratio of intensities for the signals from the $=CH_2$ group of the initial substrate (6.27 ppm) and CH_3 group (1,19 d ppm) in the hydrogenated product.

REFERENCES

1. Murrer, B.A., Brown, J.M., Chaloner, P.A., Nicholson, P.N., and Parker, D., *Synthesis*, 1979, no. 5, pp. 350–352.
2. Okamoto, Y., Shohi, H., and Yuki, H., *J. Polym. Sci., Polym. Lett. Ed.*, 1983, vol. 21, no. 8, pp. 601–607.
3. US Patent, 5395947, 1993; *Chem. Abstr.*, 1993, vol. 118, P224389b.
4. Kim, D.K., Kim, G., Gam, J., Cho, Y.B., Kim, H.T., Tai, J.H., Kim, K.H., Hong, W.-S., and Park, J.G., *J. Med. Chem.*, 1994, vol. 37, no. 10, pp. 1471–1485.
5. Hakimelahi, G.H. and Just, G., *Tetrahedron Lett.*, 1979, no. 38, pp. 3643–3644.
6. Seebach, D., Kalinowski, H.O., Bastini, B., Crass, G., Daum, H., Doerr, H., DuPreez, N.P., Ehrig, V., and Langer, W., *Helv. Chim. Acta*, 1977, vol. 60, no. 1, pp. 301–325.
7. Potvin, P.G., Gau, R., Kwong, P.C.C., and Bianchet, S., *Canad. J. Chem.*, 1989, no. 10, pp. 1523–1537.
8. Cope, A.C. and Mehta, A.S., *J. Am. Chem. Soc.*, 1964, vol. 86, no. 24, pp. 5626–5630.
9. Nindakova, L.O., Shainyan, B.A., Albanov, A.I., and Ustinov, M.V., *Zh. Org. Khim.*, 2000, vol. 36, no. 11, pp. 1660–1665.
10. *Svoistva org. soed.* (Properties of Organic Compounds), Potekhin, A.A., Ed., Leningrad: Khimiya, 1984, p. 350.