3. W. Seibert, Chem. Ber., 80, 494 (1947).
4. R. O. Hutchins, D. Kandasamy, F. Dux, and C. A. Mryanoff, J. Org. Chem., 43, 2259 (1978).
5. W. G. Dauben and G. A. Boswell, J. Am. Chem. Chem. Soc., 83, 5003 (1961).
6. A. K. Sheinkman, S. I. Suminov, and A. N. Kost, Usp. Khim., 42, 1415 (1973).
7. A. V. Chudinov, V. D. Sholle, and É. G. Rozantsev, Izv. Akad. Nauk SSSR, Ser. Khim., 476 (1981).
8. É. G. Rozantsev, V. A. Golubev, and M. B. Neiman, Izv. Akad. Nauk SSSR, Ser. Khim., 391 (1965).

HALOGEN-CONTAINING NITROXYL RADICALS.

COMMUNICATION 5.* THE SYNTHESIS AND REACTIONS OF 2,2,5,5-TETRAMETHYL-Δ^3-PYRROLIN-1-OXYL

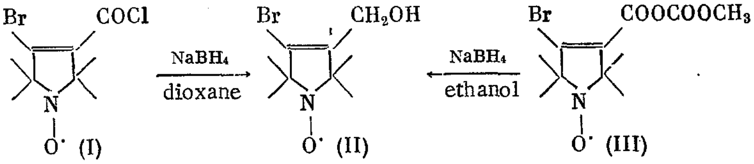
A. V. Chudinov, É. G. Rozantsev,
and B. V. Rozynov

UDC 542.91:547.743.4

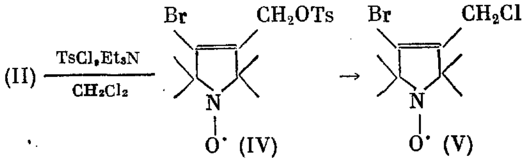
The use of spin labels and probes, synthesis of complexones, and many other applications of nitroxyl radicals have encouraged the search for convenient methods for the synthesis of simple functionally-substituted nitroxyls. 3-Bromo-4-carboxy-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl obtained by the reaction of 2,2,6,6-tetramethyl-4-oxopiperidin-1-oxyl with sodium hypobromite served as the starting material for the synthesis of a considerable number of representatives of a new series of nitroxyl radicals, namely, bromopyrrolinoxyls [1, 2].

In the present work, we extended our study of the chemical transformations of this series of nitroxyl radicals.

The reaction of $NaBH_4$ with acid chloride (I) in dioxane and with anhydride (III) in ethanol yielded alcohol (II). The treatment of anhydride (III) with $NaBH_4$ in ethanol at low temperature minimized the acylation of ethanol and gave alcohol (II) in good yield



The tosylation of alcohol (II) in CH_2Cl_2 in the presence of triethylamine leads to tosylate (IV) is about 50% yield

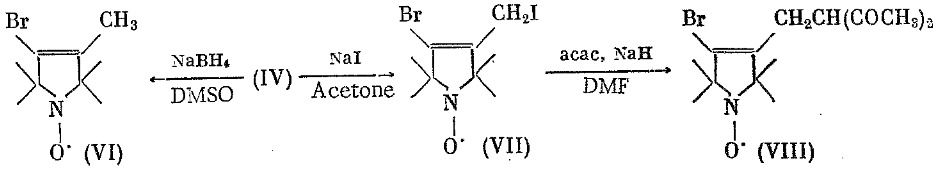


A byproduct is chloride (V) which is the product of the reaction of tosylate (IV) with $(C_2H_5)_3N \cdot HCl$ dissolved in CH_2Cl_2. The tosylation of alcohol (II) in benzene in the presence of $(C_2H_5)_3N$ decreases this undesired process and increases the yield of tosylate (IV) up to ∿73%. This product was reduced with $NaBH_4$ in DMSO according to Hutchins et al. [3] to yield bromopyrroline (VI) and was converted to iodide (VII) by treatment with NaI in acetone This iodide readily alkylates acetylacetone in the presence of NaH in DMF to yield diketone (VIII)

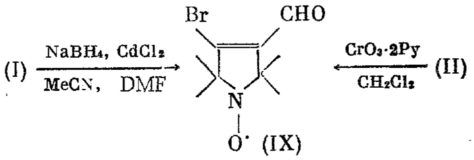
---

*Communication 4, see [1].

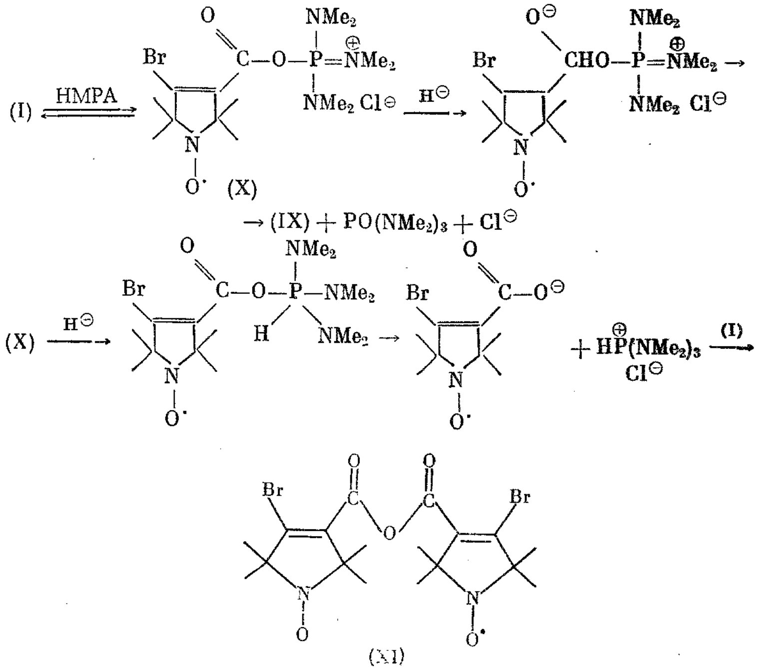
Institute of Chemical Physics, Academy of Sciences of the USSR, Moscow. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 2, pp. 409-413, February, 1983. Original article submitted May 5, 1982.



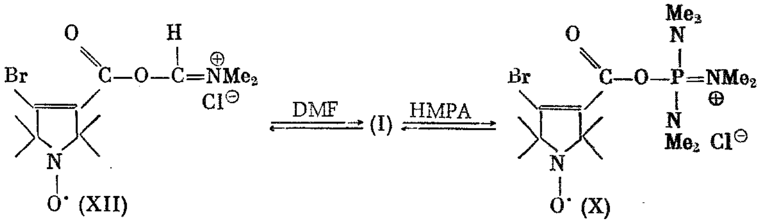
Acid chloride (I) is reduced by $Cd(BH_4)_2$ obtained in situ in acetonitrile in the presence of DMF as catalyst according to Entwistle et al. [4] to yield aldehyde (IX) in 32% yield and anhydride (XI) as the major product



This reaction is also catalyzed by tetramethylurea, N-methylpyrrolidone, and, more effectively, hexamethylphosphorotriamide (HMPTA) and the yield of aldehyde (IX) is increased to 81%. The reduction presumably proceeds as follows:

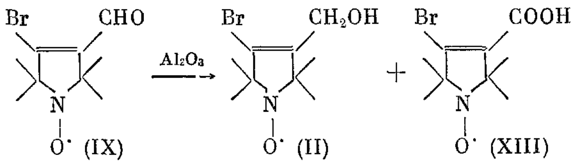


The significant difference in the yields of aldehyde (IX) using HMPTA instead of DMF is attributed to the formation of different intermediates (X) and (XI) in the reactions of these catalyst with (I)



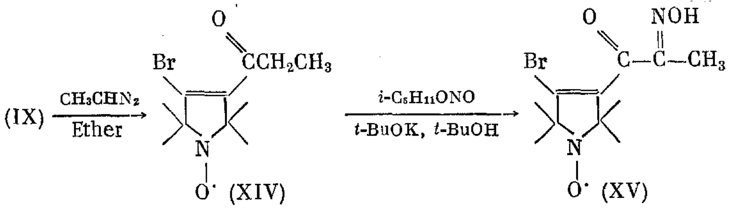
The carbonyl group carbon atom in (X) is most favorable for attack of the hydride anion. The competing attack of the anhydride anion of the carbon atom attached to the amide group is also possible in (XII) due to reduced steric hindrance and, thus, the yield of anhydride (XI) increases and the yield of aldehyde (IX) decreases. This aldehyde was also obtained by the oxidation of alcohol (II) by the complex $CrO_3 \cdot 2Py$ in CH_2Cl_2 according to Ratcliffe and Rodehorst [5].

Aldehyde (IX) is a crystalline compound which is stable upon storage. In solution, (IX) is stable in weakly acidic and neutral media. In alkaline media in the presence of Al_2O_3, (IX) undergoes the oxidation-reduction Cannizzaro reaction with the formation of alcohol (II) and acid (XIII). The nitroxyl group is not affected in this case



We should note that reduction of the nitroxyl group to hydroxylamine occurs in nitroxyl radicals of the imidazoline aldehyde series in alkaline media [6].

The action of diazoethane on aldehyde (IX) in ether gives ketone (XIV) and treatment of (XIV) by isoamyl nitrite in t-BuOH in the presence of t-BuOK gives oximinoketone (XV)



EXPERIMENTAL

Samples of starting 3-bromo-4-chloroformyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (II) and anhydride (III) were obtained by procedures given in our previous work [2]. The IR spectra were taken on a UR-20 spectrometer in KBr pellets. The mass spectra were taken on an RMU-6D mass spectrometer. The ESR spectra were taken on an EPRB-IKhF spectrometer in dilute toluene solution at 25°C. The experimental error was a_N ± 0.01 mT and g ± 0.0001.

3-Bromo-4-hydroxymethyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (II). a) Samples of 0.01 mole $NaHCO_3$ and 0.025 mole $NaBH_4$ were added in portions over 5 min to a solution of 0.005 mole acid chloride (I) in 20 ml dioxane with stirring and ice cooling. The mixture was then stirred for 4 h at 20°C. Upon cooling, 5 ml saturated aq. Na_2CO_3 was added and the mixture was poured into 60 ml water and extracted with chloroform. The chloroform extracts were washed with aq. NaCl, dried over $MgSO_4$, evaporated in vacuum, and filtered through a 100 × 16-mm alumina column. Removal of chloroform gave 1.10 g (88%) (II) as yellow crystals with mp 152-153°C (from chloroform—hexane). Found: C, 43.54; H, 6.06; N, 5.72%, mol. mass 248 (M^+), 250 (M^+), mass spectroscopically. Calculated for $C_9H_{15}BrNO_2$: C, 43.39; H, 6.07; N, 5.62%, mol. mass 249.134. IR spectrum (ν, cm^{-1}): 1650 (C=C), 3330-3520 (OH). The ESR spectrum was a triplet with a_N = 1.39 mT and g = 2.0055.

b) A sample of 0.02 mole $NaBH_4$ was added in portions over 5 min with stirring to a suspension of 0.01 mole anhydride (III) in 40 ml ethanol at from —30° to —40°C. Then the mixture was placed in an ice bath and stirred for 2 h. The solvent was removed and 70 ml water was added. The mixture was extracted with chloroform. The chloroform extract was washed with water and aq. NaCl and dried over $MgSO_4$. Removal of the solvent and recrystallization from toluene gave 1.87 g (75.2%) pure (II).

3-Bromo-p-toluenesulfonyloxymethyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (IV). a) A sample of 0.02 mole triethylamine and, with stirring and chilled-water cooling, a solution of 0.011 mole p-toluenesulfonyl chloride (TsCl) in 20 ml dry benzene were added consecutively to a suspension of 0.01 mole (II) in 20 ml dry benzene. The mixture was maintained at ∼20°C for 24 h. The solution was then filtered and evaporated to dryness. Recrystallization of the residue from hexane gave 2.96 g (73.5%) (IV) as shiny yellow crystals with mp 95-97°C (from hexane). Found: C, 47.50; H, 5.41; N, 3.57%, mol. mass 402 (M^+), 404 (M^+). Calculated for $C_{16}H_{21}BrNO_4S$: C, 47.64; H, 5.25; N, 3.47%, mol. mass 403.320. IR spectrum (ν, cm^{-1}): 1175, 1190 (SO_2), 1500 (phenyl C=C), 1600 (phenyl C=C), 1660 (C=C). The ESR spectrum was a triplet with a_N = 1.40 mT and g = 2.0055.

b) A solution of 0.0165 mole TsCl in 15 ml CH_2Cl_2 was added dropwise over 5 min with stirring and ice cooling to a solution of 0.015 mole (II) and 0.03 mole triethylamine in

30 ml dry CH_2Cl_2. The reaction mixture was maintained at ∿20°C for 24 h, washed with water, and dried over $MgSO_4$. The solvent was removed and the residue was recrystallized from hexane to yield 3.20 g (53%) (IV). The mother liquor was evaporated to dryness and subjected to chromatography on a 250 × 16-mm column packed with LS 40/100 silica gel using benzene as eluent. The first colored band was taken. Solvent removal gave 1.29 g (32%) (V) as yellow crystals with mp 71.5-72°C (sublimate). Found: C, 40.45; H, 5.43; N, 5.31%, mol. mass 266 (M^+), 268 (M^+), 270 (M^+). Calculated for $C_9H_{14}BrClNO$: C, 40.39; H, 5.27; N, 5.23%, mol. mass 267.588. IR spectrum (ν, cm^{-1}): 1650 (C=C). The ESR spectrum was a triplet with a_N = 1.40 mT and g = 2.0055.

3-Bromo-2,2,5,5-pentamethyl-Δ^3-pyrrolin-1-oxyl (VI). A sample of 0.02 mole was added in portions over 5 min with stirring at ∿20°C to a solution of 0.01 mole tosylate (IV) in 40 ml dry DMSO. The mixture was stirred for 15 min at 20°C and then for 2 h at 90-95°C. After cooling, the reaction mass was poured into 200 ml water and extracted with hexane. The extract was washed with water and aq. NaCl and dried over $MgSO_4$. Removal of the solvent and recrystallization from pentane gave 1.80 g (77%) (VI) as yellow crystals with a camphor aroma and mp 58-59°C (sublimate). Found: C, 46.25; H, 6.55; N, 6.09%, mol. mass 232 (M^+), 234 (M^+). Calculated for $C_9H_{15}BrNO$: C, 46.36; H, 6.48; N, 6.01%, mol. mass 233.134. IR spectrum (ν, cm^{-1}): 1660 (C=C). The ESR spectrum was a triplet with a_N = 1.33 mT and g = 2.0055.

3-Bromo-4-iodomethyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (VII). A sample of 0.01 mole tosylate (IV) was added over 5 min to a solution of 0.015 mole NaI (dried for 40 h at 120°C) in 40 ml dry acetone with stirring at 20°C. The mixture was stirred for an additional 1 h. The solvent was removed in vacuum. A sample of 20 ml 10% aq. $Na_2S_2O_3$ was added to the residue and the mixture was extracted with ether. The extract was washed with water and aq. NaCl, dried over $MgSO_4$, and the solvent was removed. Recrystallization from hexane gave 3.52 g (98%) (VII) as yellow crystals with mp 83.5-84.5°C (sublimate). Found: C, 30.23; H, 4.02; N, 3.90%, mol. mass 358 (M^+), 360 (M^+). $C_9H_{14}BrINO$: C, 30.11; H, 3.93; N, 3.90, mol. mass 359.034. IR spectrum (ν, cm^{-1}): 1635 (C=C). The ESR spectrum was a triplet with a_N = 1.38 mT and g = 2.0057.

3-Bromo-4-(2,2-diacetylethyl)-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (VIII). A solution of 0.02 mole acetylacetone in 5 ml dry DMF was added dropwise over 5 min to a suspension of 0.01 mole NaH in 5 ml DMF with stirring at from –10° to –15°C. The mixture was stirred for an additional 10 min. Then, a solution of 5 mmoles in 10 ml DMF was added dropwise at this temperature over 5 min. The mixture was stirred for 3 h in an ice bath and for 1 h at ∿20°C. The reaction mass was poured into 120 ml water, acidified with 5% HCl to pH 2-3, and extracted with ether. The ethereal extracts were washed with aq. NaCl and evaporated to dryness. The residue was dissolved in 5 ml methanol and a solution of 1 g $(CH_3CO_2)_2Cu \cdot H_2O$ in 10 ml water was added. After completion of the separation of the copper complex precipitate (30 ml), it was filtered off, washed with water and hexane, and then, the complex was added to a mixture of 50 ml ether and 10 ml 2 N H_2SO_4. This mixture was stirred in an ice bath until the complex was completely dissolved (∿1 h). The ethereal solution was separated, washed with aq. $NaHCO_3$ and aq. NaCl, and dried over $MgSO_4$. Removal of the solvent and recrystallization from hexane gave 1 g (60.5%) (VIII) as yellow-orange crystals. This compound does not have a distinct melting point and melts from 88° to 106°C depending on the heating rate. Found: C, 50.91; H, 6.46; N, 4.33%, mol. mass 330 (M^+), 332 (M^+). Calculated for $C_{14}H_{21}BrNO_3$: C, 50.76; H, 6.39; N, 4.23%, mol. mass 331.234. IR spectrum (ν, cm^{-1}): 1550-1630. The ESP spectrum was a triplet with a_N = 1.35 mT and g = 2.005.

3-Bromo-4-formyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (IX). A sample of dry 2 ml HMPTA and 3.8 mmole finely ground $CdCl_2$ (dried for 5 h at 120°C) were added with stirring to a suspension of 5 mmoles $NaBH_4$ in 15 ml dry acetonitrile in an ice bath and the mixture was stirred for 15 min. Then, a solution of 5 mmoles acid chloride (I) in 5 ml dry acetonitrile was added dropwise rapidly and stirred in an ice bath for 40 min. The reaction mass was poured into a mixture of 100 ml ice water and 4 ml 5% HCl and extracted with ether. The extract was washed with aq. NaCl and dried over $MgSO_4$. The solvent was evaporated. The residue was treated with hot hexane and filtered. The insoluble portion was a sample of 0.12 g (9.6%) (II) which had mp 152-153°C after recrystallization from hexane–chloroform. The hexane solution was evaporated to dryness and subjected to chromatography on a 250 × 16-mm column packed with LS 40/100 silica gel using 1:2 ether–hexane as eluent. The first colored band was collected. Removal of the solvent gave 1 g (81%) (IX) as yellow crystals with mp 123-124°C (from hexane). Found: C, 44.01; H, 5.25; N, 5.69%, mol. mass 246 (M^+), 248 (M^+). Calculated for $C_9H_{13}BrNO_2$: C, 43.74; H, 5.30; N, 5.67%, mol. mass 247.114. IR spectrum (ν, cm^{-1}): 1605

(C=C), 1680 (C=O). The ESR spectrum was a triplet with a_N = 1.38 mT and g = 2.0057.

b) A sample of 0.06 mole CrO_3 was added in portions with stirring and ice cooling to a solution of 0.12 mole pyridine in 30 ml dry CH_2Cl_2. The cooling was terminated and the stirring was continued for an additional 15 min. A solution of 0.01 mole (II) in 15 ml CH_2Cl_2 was added to the mixture obtained and stirring was continued for 20 min. Then, 50 ml ether was added and the organic layer was separated. The precipitate was washed with ether. The combined organic layer was washed consecutively with 5% HCl, water, aq. $NaHCO_3$, and aq. NaCl, and dried over $MgSO_4$. After removal of the solvent, the residue was dissolved in benzene and filtered through a 75 × 16-mm column packed with LS 40/100 silica gel. Solvent removal gave 2.22 g (90%) pure (IX).

Reaction of 3-Bromo-4-formyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (IX) with Al_2O_3. A sample of 25 g neutral Al_2O_3 with grade II activity was added to a solution of 2 mmoles aldehyde (IX) in 10 ml benzene, carefully stirred, and maintained at ∿20°C for 5 h. Then, the mixture was washed with 5% acetic acid in $CHCl_3$. The chloroform solution was washed with 1 N NaOH. The aqueous layer was acidified with concentrated HCl to pH 2-3 and extracted with chloroform. Removal of the solvent from the extract gave 0.12 g (22.8%) pure acid (XIII). The chloroform solution was evaporated to dryness and the residue was subjected to chromatography on a 200 × 10-mm column packed with LS 40/100 silica gel using 1:1 ether–hexane as eluent. The first colored band gave 0.20 g (40.5%) aldehyde (IX) and the second colored band gave 0.11 g (22.1%) alcohol (II). All the characteristics of the compounds obtained were completely identical to those of authentic samples.

3-Bromo-4-propionyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (XIV). A sample of 25 ml of a cooled, dry solution of diazoethane obtained by the reaction of 0.015 mole N-nitrosoethylurea with 6 ml 40% aq. KOH was added with stirring to a suspension of 5 mmoles (IX) in 5 ml dry ether on an ice bath and then the mixture was maintained at about 20°C. Gas liberation and dissolution of the precipitate were noted. After 8 h, the solvent was removed and the residue was subjected to chromatography on a 150 × 16-mm column packed with LS 40/100 silica gel with 100:3 benzene–ether as eluent. The first colored band was taken. Solvent removal gave 1.33 g (97%) (IXV) as yellow crystals with mp 49-50°C (sublimate). Found: C, 48.19; H, 6.20; N, 5.19%, mol. mass 274 (M^+), 276 (M^+). Calculated for $C_{11}H_{17}BrNO_2$: C, 48.01; H, 6.23; N, 5.09%, mol. mass 275.174. IR spectrum (ν, cm^{-1}): 1590 (C=C), 1675 (C=O). The ESR spectrum was a triplet with a_N = 1.36 mT and g = 2.0055.

3-Bromo-4-(3-oximinopropionyl)-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl (XV). A sample of 5 mmoles ketone (XIV) was added to a solution of 0.01 mole t-BuOK in 20 ml t-BuOH with stirring in an argon atmosphere and stirring was continued for 30 min. A solution of 6.25 mmoles isoamyl nitrite was added dropwise with chilled-water cooling to the solution obtained and stirring was continued for an additional 2 h. Then, the mixture was maintained for 24 h at 20°C in an argon atmosphere. A sample of 10 ml water was added and the t-BuOH was removed in vacuum at 30-40°C bat temperature. A sample of 5 ml 1 N NaOH was added and the mixture was washed with chloroform. The aqueous solution was acidified with acetic acid and extracted with chloroform. The chloroform extract was washed with aq. NaCl and dried over $MgSO_4$. Removal of the solvent and recrystallization from heptane gave 0.67 g (44%) (XV) as yellow crystals with mp 132-133°C (from cyclohexane). Found: C, 43.52; H, 5.25; N, 9.24%, mol. mass 303 (M^+), 305 (M^+). Calculated for $C_{11}H_{16}N_2O_3$: C, 43.43; H, 5.30; N, 9.21%, mol. mass 304.176. IR spectrum (ν, cm^{-1}): 1630 (C=C), 1670 (C=C–C=N), 3190-3260 (OH). The ESR spectrum was a triplet with a_N = 1.40 mT and g = 2.0057.

CONCLUSIONS

1. Syntheses were reported for a series of stable nitroxyl radicals, namely, 4-substituted 3-bromo-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyls containing hydroxymethyl, tosyloxymethyl, chloromethyl, iodomethyl, methyl, formyl, propionyl, 2-oximinopropionyl, and 2,2-diacetylethyl groups as the substituents.

2. The nitroxyl group of 3-bromo-4-formyl-2,2,5,5-tetramethyl-Δ^3-pyrrolin-1-oxyl was not affected in the Cannizzaro oxidation–reduction reaction.

LITERATURE CITED

1. A. V. Chudinov, É. G. Rozantsev, and B. V. Rozynov, Izv. Akad. Nauk SSSR, Ser. Khim., 403 (1983).

2. A. V. Chudinov and É. G. Rozantsev, Izv. Akad. Nauk SSSR, Ser. Khim., 400 (1983).
3. R. O. Hutchins, D. Kandasamy, F. Dux, and C. A. Mryanoff, J. Org. Chem., 43, 2259 (1978).
4. J. D. Entwistle, P. Boehm, R. A. Johnstone, and R. P. Telford, J. Chem. Soc., Perkin Trans. 1, 27 (1980).
5. R. Ratcliffe and R. Rodehurst, J. Org. Chem., 35, 4000 (1970).
6. I. A. Grigor'ev and L. B. Volodarskii, Izv. Akad. Nauk SSSR, Ser. Khim., 208 (1978).

THE ROLE OF FULLY SUBSTITUTED ORGANOMAGNESIUM COMPOUNDS IN THE REACTION OF ALIPHATIC SULFOXIDES WITH GRIGNARD REAGENTS

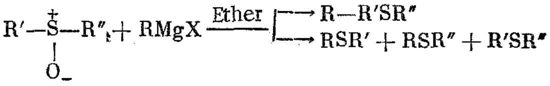
N. A. Nesmeyanov, V. A. Kalyavin,
and O. A. Reutov

UDC 541.124:542.957.2:547.279.52

Reaction of aliphatic sulfoxides R'S(O)R" with Grignard reagents RMgX usually results in the formation of a mixture of sulfides containing all the possible combinations of the radicals of the starting materials (R'SR", R'SR, and R"SR), together with the sulfide formally derived from R'SR" by replacement of the α-hydrogen atom in R' or R" by the radical R from the Grignard reagent, which may be formally represented as R—R'SR" [1]. The latter is usually the main reaction product.

In order to elucidate the mechanism of this reaction, we have studied the effects of adding various compounds (RLi, Et_2NLi, $MgBr_2$, LiBr, and dioxane) on the reactions of dimethylsulfoxide (DMSO) and ethyl methyl sulfoxide (EMSO) with RMgX (R = Me, Et, and Ph, X = Br and I). The results are shown in Table 1. The following facts are immediately apparent: a) the effect of the additive (we shall term this the third component) was observed in all cases except LiBr; b) the third component affects only the ratios of the reaction products and not their composition, c) the third components themselves, except for RLi, do not react with the sulfoxides, d) in the absence of the Grignard reagent organolithium compounds, although they react with the sulfoxides, do not give rise to sulfides R—R'SR". An exception is the reaction of DMSO with EtLi, in which a small amount (7%) of methyl n-propyl sulfide is formed, and e) the third component has different effects on the yields of the different products. The amounts of RSR', RSR", and R'SR" formed in the reactions do not vary to any great extent depending on the nature of the third component, and it was not possible to arrive at any regularities in this respect. The yields of the sulfides R—R'SR" did however vary considerably. Thus, in the reaction of EMSO with EtMgBr and PhMgBr, the yields of MeSEt, Et_2S, MeSPh, and EtSPh varied between 4-15, 2-4, 6-14, and 1-3%, respectively. However, the yields of EtSPr-p and $EtSCH_2Ph$, which are compounds of the R—R'SR" type, varied from 0 to 75 and 0 to 71%, respectively (experiments 2, 5, 6, 9, 10, 12, 17, 20-23, and 25, Table 1). Similar behavior was observed in the reaction of DMSO with EtMgBr (experiments 28-32).

These findings probably indicate the independence or the slight dependence of the reactions leading to the formation of the sulfides RSR', RSR", and R'SR" on the one hand, and R—R'SR" on the other hand. It is therefore possible to postulate main (1) and side (2) reactions of sulfoxides with Grignard reagents:



$$R'\!-\!\underset{\underset{O_-}{|}}{\overset{+}{S}}\!-\!R'' + RMgX \xrightarrow{\text{Ether}} \begin{cases} R\!-\!R'SR'' & (1) \\ RSR' + RSR'' + R'SR'' & (2) \end{cases}$$

Several routes might be suggested for the formation of the main product R—R'SR". The most rational, in our view, is given below for the reaction of DMSO.

We suggest that R_2Mg and RMgX are involved in the reaction, these being, as is well known, in equilibrium*

---

*We have not dealt with the role of the extent of association of the organomagnesium compounds. It may, however, be noted that according to the data presented in [2], under the conditions of our experiments it is close to unity.

M. V. Lomonosov Moscow State University. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 2, pp. 414-418, February, 1983. Original article submitted April 14, 1982.

0568-5230/83/3202-0375$07.50