ISSN 1070-4280, Russian Journal of Organic Chemistry, 2006, Vol. 42, No. 7, pp. 1087–1088. © Pleiades Publishing, Inc., 2006.
Original Russian Text © B.F. Kukharev, V.K. Stankevich, E.Kh. Sadykov, N.A. Lobanova, V.A. Kukhareva, 2006, published in Zhurnal Organicheskoi Khimii, 2006, Vol. 42, No. 7, pp. 1103–1104.

SHORT COMMUNICATIONS

Ketone *O*-(3,5,5-Trimethyl-4,5-dihydro-1*H*-pyrazol-1-ylmethyl)oximes

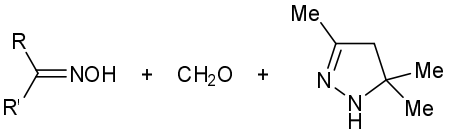
B. F. Kukharev, V. K. Stankevich, E. Kh. Sadykov, N. A. Lobanova, and V. A. Kukhareva

Favorskii Irkutsk Institute of Chemistry, Siberian Division, Russian Academy of Sciences, ul. Favorskogo 1, Irkutsk, 664033 Russia
e-mail: irk_inst_chem@irioch.irk.ru

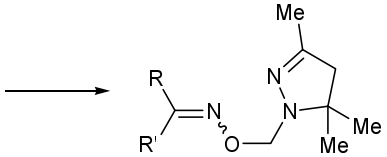
Received February 28, 2005

DOI: 10.1134/S1070428006070293

Like common alcohols, ketone oximes are capable of forming mixed and symmetric acetals [1]. With a view to obtain potential biologically active compounds, we made an attempt to synthesize oxime ethers **Ia**–**Ic** from ketone oximes **IIa**–**IIc** and 3,5,5-trimethyl-4,5-dihydro-1*H*-pyrazole (**III**). The reactions of ketone oximes **IIa**–**IIc** with dihydropyrazole **III** and paraformaldehyde were carried out by heating an equimolar mixture of the reactants in boiling benzene with simultaneous removal of water by azeotropic distillation; the products were isolated by subsequent vacuum distillation. The yields of oxime ethers **Ia**–**Ic** were not high (36–54%), while the main by-product was symmetric aminal **IV**. In all cases, the yield of the latter ranged from 20 to 30%.

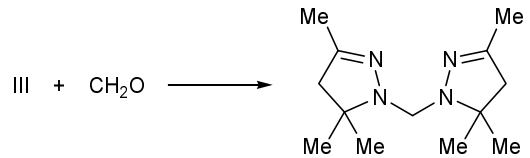


IIa–IIc III



Ia–Ic

R = R' = Me (**a**); RR' = $(CH_2)_5$ (**b**); R = Me, R' = Ph (**c**).



IV

The IR spectra of compounds **Ia**–**Ic** contained absorption bands in the regions 1615–1640 and 1620–1665 cm^{-1} due to stretching vibrations of the dihydropyrazole and oxime C=N bonds, respectively. No amino or hydroxy group absorption was observed in the region 3200–3500 cm^{-1}.

Compounds **Ia**–**Ic** showed in the ^1H NMR spectra a singlet at δ 5.11–5.33 ppm due to protons of the methylene group (NCH_2ON). In addition, signals from protons in the pyrazole and oxime fragments were present. Judging by the ^1H NMR data, oxime ether **Ic** was formed as a single isomer. Taking into account the chemical shift of the methyl protons in the acetophenone fragment (δ 2.21 ppm) and published data for various acetophenone oxime derivatives [2], compound **Ic** is *E* isomer.

General procedure for the synthesis of ketone *O*-(3,5,5-trimethyl-4,5-dihydro-1*H*-pyrazol-1-ylmethyl)oximes Ia–Ic. A mixture of 0.1 mol of compound **III**, 0.1 mol of ketone oxime **IIa**–**IIc**, and 0.1 mol of paraformaldehyde in 100 ml of benzene was heated under reflux in a flask equipped with a Dean–Stark trap until water no longer separated. The solvent was distilled off, and the residue was distilled under reduced pressure to isolate compounds **Ia**–**Ic** and **IV**.

Acetone *O*-(3,5,5-trimethyl-4,5-dihydro-1*H*-pyrazol-1-ylmethyl)oxime (Ia). Yield 36%, bp 122–125°C (14 mm), d_4^{20} = 1.000, n_D^{20} = 1.4759. IR spectrum, ν, cm^{-1}: 465, 550, 600, 660, 720, 805, 930, 1050, 1090, 1130, 1115, 1220, 1250, 1320, 1350, 1375, 1420, 1450, 1615, 1665, 2930, 2960. ^1H NMR spectrum, δ, ppm: 1.22 s (6H, CMe_2), 1.81 s (3H, N=CMe), 1.84 s and 1.90 s (3H each, Me_2C=NO), 2.47 s (2H, CCH_2C), 5.11 s (2H, NCH_2O). Found, %: C 60.88; H 10.03;

N 21.24. $C_{10}H_{19}N_3O$. Calculated, %: C 60.88; H 9.71; N 21.30.

Cyclohexanone *O*-(3,5,5-trimethyl-4,5-dihydro-1*H*-pyrazol-1-ylmethyl)oxime (Ib). Yield 54%, bp 126–129°C (1 mm), d_4^{20} = 1.001, n_D^{20} = 1.4995. IR spectrum, ν, cm^{-1}: 475, 530, 560, 595, 645, 670, 730, 775, 835, 890, 910, 940, 990, 1100, 1135, 1170, 1265, 1335, 1365, 1390, 1450, 1640, 1655, 2865, 2940. ^1H NMR spectrum, δ, ppm: 1.24 s (6H, CMe_2), 1.56–1.64 m (6H, $3CH_2$, cyclohexane), 1.91 s (3H, N=CMe), 2.21–2.49 m (6H, $2CH_2$, cyclohexane, CCH_2C), 5.14 s (2H, NCH_2O). Found, %: C 65.82; H 9.89; N 17.10. $C_{13}H_{23}N_3O$. Calculated, %: C 65.79; H 9.77; N 17.70.

Acetophenone *O*-(3,5,5-trimethyl-4,5-dihydro-1*H*-pyrazol-1-ylmethyl)oxime (Ic). Yield 48%, bp 159–162°C (3 mm), d_4^{20} = 1.051, n_D^{20} = 1.4995. IR spectrum, ν, cm^{-1}: 445, 545, 630, 660, 685, 730, 750, 830, 915, 985, 1075, 1110, 1160, 1230, 1255, 1300, 1325, 1360, 1380, 1430, 1455, 1485, 1565, 1590, 1605, 1620, 2930, 2970, 3055. ^1H NMR spectrum, δ, ppm: 1.28 s (6H, CMe_2), 1.94 s (3H, N=CMe), 2.21 s (3H, MeC=NO), 2.44 s (2H, CCH_2C), 5.33 s (2H, NCH_2O), 7.30–7.36 m (3H, *o*-H, *p*-H), 7.60–7.65 m (2H, *m*-H). Found, %: C 69.93; H 8.41; N 16.25. $C_{15}H_{21}N_3O$. Calculated, %: C 69.47; H 8.16; N 16.20.

Bis(3,5,5-trimethyl-4,5-dihydro-1*H*-pyrazol-1-yl)methane (IV). Yield 20–30%, bp 152–154°C (22 mm), d_4^{20} = 0.965, n_D^{20} = 1.4921. IR spectrum, ν, cm^{-1}: 470, 530, 555, 630, 640, 675, 705, 740, 770, 815, 850, 890, 910, 915, 940, 975, 1000, 1015, 1085, 1125, 1155, 1210, 1230, 1310, 1345, 1355, 1375, 1420, 1450, 1545, 1610, 1700, 2740, 2825, 2860, 2875, 2900, 2925, 2955. ^1H NMR spectrum, δ, ppm: 1.24 s (12H, $2CMe_2$), 1.91 s (6H, 2N=CMe), 2.43 s (4H, $2CH_2$), 4.18 s (2H, NCH_2N). Found, %: C 66.63; H 10.44; N 23.22. $C_{13}H_{24}N_4$. Calculated, %: C 66.06; H 10.23; N 23.70.

The ^1H NMR spectra were recorded on a Bruker DPX-400 instrument (400 MHz) at 26°C using $CDCl_3$ as solvent and HMDS as internal reference. The IR spectra were obtained on a Specord 75IR spectrometer from samples prepared as thin films. The purity of the initial compounds and reaction products was checked by GLC on an LKhM-80 chromatograph equipped with a thermal conductivity detector and a steel column (3×3000 mm) packed with 3% of OV-17 on Inerton Super (0.160–0.200 mm); oven temperature programming from 60 to 280°C at a rate of 4 deg/min; carrier gas helium.

Commercial ketone oximes **IIa**–**IIc** were distilled before use. 3,5,5-Trimethyl-4,5-dihydro-1*H*-pyrazole (**III**) was freshly prepared according to the procedure described in [3]; according to the GLC data, it contained no less than 99% of the main substance. Commercial paraformaldehyde with a purity of 95% was used.

REFERENCES

1. Voronkov, M.G., Keiko, N.A., Kalikhman, I.D., Korostova, S.E., Mikhaleva, A.I., Chuvashev, E.A., and Trofimov, B.A., *Zh. Org. Khim*., 1985, vol. 21, p. 766.
2. Tarasova, O.A., Korostova, S.E., Mikhaleva, A.I., Sobenina, L.N., Nesterenko, R.N., Shevchenko, S.G., and Trofimov, B.A., *Zh. Org. Khim*., 1994, vol. 30, p. 810; Krivdin, L.B., Shcherbakov, V.V., Korostova, S.E., and Shevchenko, S.G., *Izv. Akad. Nauk SSSR, Ser. Khim*., 1987, p. 766.
3. Kost, A.N. and Grandberg, I.I., *Zh. Obshch. Khim*., 1956, vol. 26, p. 1717.