

LETTERS TO THE EDITOR

Noncatalytic Alkylation of Phenol with 1,3,5-Trimethyl-1*H*-pyrazol-4-ylmethanol

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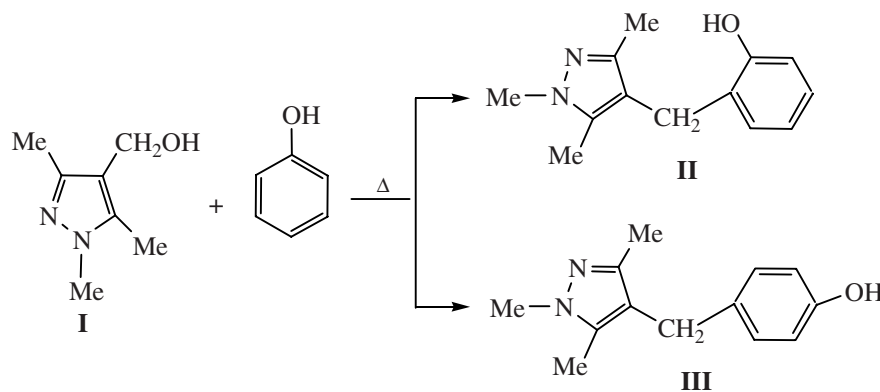
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We previously showed that heating of 1,3,5-trimethylpyrazol-4-ylmethanol (**I**) in the presence of benzyl and hexyl alcohols leads mainly to the formation of mixed trimethylpyrazolylmethyl ethers. While studying the scope of application of this transformation we examined the reaction of compound **I** with phenol. We found that, instead of the expected pyrazolylmethyl phenyl ether, the reaction gave isomeric products **II** and **III** via alkylation of the

aromatic ring in phenol. At a **I**-to-PhOH ratio of 1:5 the yield of the alkylation products (a mixture of *ortho* and *para* isomers) attained 67%. According to the ¹H NMR data, the ratio of isomeric phenols was 3:2. The signal from the hydroxy proton of isomer **II** was located in a weaker field (δ 8.91 ppm) than the corresponding signal of isomer **III** (δ 8.62 ppm). Isomer **II** was isolated by fractional crystallization.



We failed to interpret the observed behavior of alcohol **I** on the basis of generally accepted views [2–4], for the presence of pyrazole heteroring should hinder heterolytic dissociation of the C–OH bond and formation of C–O–C ether bond or C–H alkylation in the absence of acid catalyst. A reasonable explanation

may be given in terms of the new generalized theory of acids and bases [5].

2- and 4-(1,3,5-Trimethyl-1*H*-pyrazol-4-ylmethyl)phenols (II) and (III). A mixture of 1.4 g of 4-hydroxymethyl-1,3,5-trimethyl-1*H*-pyrazole (**I**) and

9.5 g of phenol was heated for 5 h under reflux. Excess phenol was removed, and the residue (dark crystals) was treated with 10 ml of water and with sodium hydroxide. The aqueous phase was extracted with chloroform and neutralized with hydrochloric acid, and the precipitate was filtered off. Yield 1.45 g (67%), mp 152–201°C. IR spectrum, ν , cm^{-1} : 1510 (pyrazole), 1590 ($\text{C}-\text{C}_{\text{arom}}$), 3200–3500 (OH). ^1H NMR spectrum, δ , ppm (J , Hz): 1.98 s (3H, 3- CH_3), 2.11 s (3H, 5- CH_3), 3.52 s (2H, CH_2), 3.64 s (3H, NCH_3), 6.58 m (2H, $m\text{-H}$), 6.80 m (2H, $o\text{-H}$), 8.66 s (1H, OH).

Recrystallization of the product from ethanol gave pure isomer **II**. mp 195°C. ^1H NMR spectrum ($\text{DMSO}-d_6$), δ , ppm (J , Hz): 2.00 s (3H, CH_3), 2.12 s (3H, CH_3), 3.53 s (2H, CH_2), 3.65 s (3H, NCH_3), 6.57 t. d (1H, H_{arom} , $J_1 = 7.4$, $J_2 = 1.4$), 6.70 d. d (1H, H_{arom} , $J_1 = 7.5$, $J_2 = 1.9$), 6.72 d. d (1H, H_{arom} , $J_1 = 7.8$, $J_2 = 1.4$), 6.88 d. d. d (1H, H_{arom} , $J_1 = 7.8$, $J_2 = 7.5$, $J_3 = 1.9$), 8.90 s (1H, OH). Found, %: C 69.94; H 7.21; N 11.85. $\text{C}_{13}\text{H}_{16}\text{N}_2\text{O}$. Calculated, %: C 72.22; H 7.41; N 12.96.

The ^1H NMR spectra were recorded on a Varian

Mercury-300 instrument at 300 MHz. The IR spectra were measured on a Specord 75-IR spectrometer from thin films.

REFERENCES

1. Attaryan, O.S., Gevorkyan, A.A., Antanosyan, S.K., Martirosyan, S.S., Panosyan, G.A., and Matsoyan, S.G., *Russ. J. Gen. Chem.*, 2005, vol. 75, no. 9, p. 1500.
2. Becker, H., *Einführung in die Elektronentheorie organisch-chemischer Reaktionen*, Berlin: Wissenschaften, 1974, 3rd ed.
3. Dneprovskii, A.S. and Temnikova, T.I., *Teoreticheskie osnovy organicheskoi khimii* (Theoretical Foundations of Organic Chemistry), Moscow: Khimiya, 1979.
4. Sykes, P., *A Guidebook to Mechanism in Organic Chemistry*, Harlow, Essex, England: Longman, 1986, 6th ed.
5. Gevorkyan, A.A., *Obobshchennaya teoriya kislot i osnovanii. Novoe vozzrenie na reaktivnost' atomov i molekul* (Generalized Theory of Acids and Bases. Novel Concepts of the Reactivity of Atoms and Molecules), Erevan: Gitutyun, 2006.