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A novel synthesis of 2,5-diphenylpyrazine

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Abstract The compound $C_{16}H_{12}N_2$ (2,5-diphenylpyrazine) was obtained as the by-product of synthesizing 5H-Imidazol[2,3-b]isoquinoline-1-ethanol-5-one,1,2,3, 10b-tetrahydro-, $\beta(S)$-phenyl-3(S)-phenyl-(compound **2**), and its structure was determined by X-ray diffraction. The crystal is monoclinic, P2(1)/c, $a = 13.466(5)$ Å, $\alpha = 90.00^\circ$, $b = 5.758(2)$ Å, $\beta = 93.049(9)^\circ$, $c = 7.713(3)$ Å, $\gamma = 90.00^\circ$, $V = 597.2(4)$ Å^3, $Z = 2$, Dcalc. $= 1.292$ mg/m^3; the final R factor is $R_1 = 0.0592$, 771 for reflections with $I_0 > 2\sigma(I_0)$.

Keywords Crystal structure · $C_{16}H_{12}N_2$ · 2,5-Diphenylpyrazine · 5H-Imidazol[2,3-b]isoquinoline-1-ethanol-5-one · 1,2,3,10b-Tetrahydro- · $\beta(S)$-Phenyl-3(S)-phenyl-

Introduction

Pyrazine and derivatives are important medical products [1–3]; for example, they can be used for treating atherosclerosis, neurological, cardiovascular, and other diseases, and also used as intermediates for agrochemicals, pharmaceuticals and perfumes. They are easily prepared from reductive decyanation of pyrazinecarbonitriles, or from ethylenediamine on copper oxide/copper chromite catalysts [4, 5]. In this communication, we report on the crystal structure of 2,5-diphenylpyrazine.

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This compound was first reported in 1975 [6], and it was reported again in 1973 [7], Our original target was to synthesize the bis-oxazoline, but instead we got the two products, 5H-Imidazol[2,3-b]isoquinoline-1-ethanol-5-one,1,2,3,10b-tetrahydro-, β(*S*)-phenyl-3(*S*)-phenyl(compound **2**), and the by-products, 2,5-diphenylpyrazine (Scheme 1, Fig. 1).

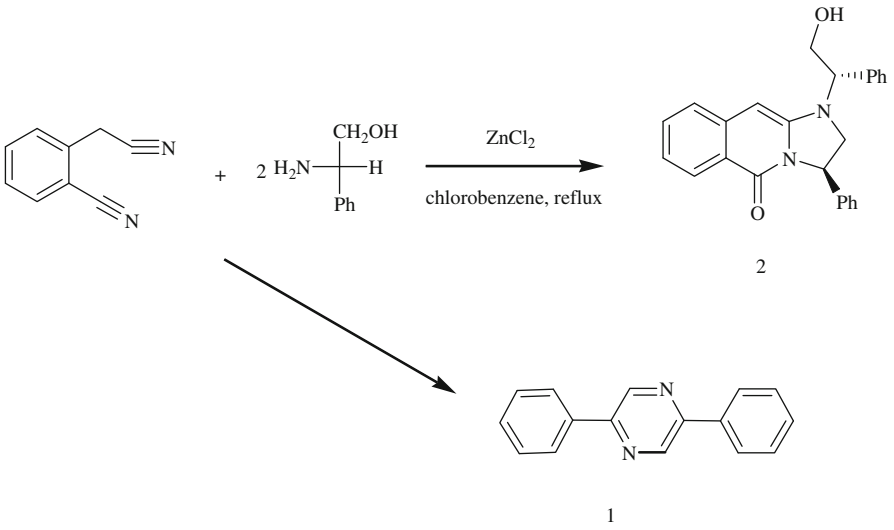
Experimental

Preparation of 2,5-diphenylpyrazine (**1**)

An amount of 60 mg of dry $ZnCl_2$, 2-cyanophenyacetonitrile (7.8 mmol) L-phenylalaninol (22.4 mmol) was added under anhydrous and oxygen-free condition in a dry 100-mL Schlenk flask. They were dissolved in 30 mL of dry chlorobenzene, the reaction mixture was refluxed for 72 h. The solvent was removed under reduced pressure and the residue was dissolved in 15 mL H_2O, extracted with 10 × 3 mL of dichloromethane, the solvent was removed under vacuum, to give the crude red oil. Further purification was performed by silica gel (petroleum ether/dichlormethane 4/1), the red crystals of **1** were obtained in the first component of the collection points.

Structure determination

A red block prismatic crystal of the title compound **1** of approximately 0.347 × 0.211 × 0.056 mm was selected for the data collection on a BRUKER SMART diffractometer with graphite monochromated MoKα radiation ($\lambda = 0.7103$ Å). A total of 1,103 reflections were collected in the range of $1.51 < \theta < 25.49°$ by using



Scheme 1 The synthetic route to the 2,5-diphenylpyrazine

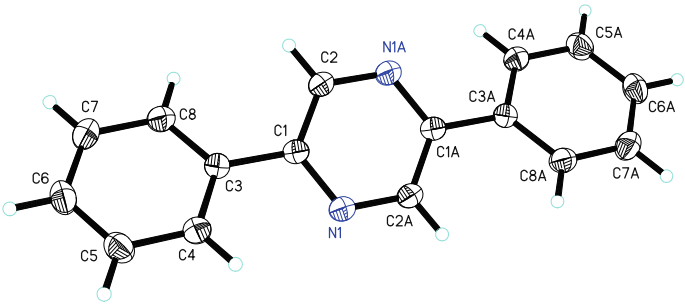


Fig. 1 Crystal structure of **1**

"phi and omega" scan techniques at 293(2) K, $C_{16}H_{12}N_2$, $M = 232.28$, monoclinic, P2(1)/c, $a = 13.466(5)$ Å, $\alpha = 90.00^\circ$, $b = 5.758(2)$ Å, $\beta = 93.049(9)^\circ$, $c = 7.713(3)$ Å, $\gamma = 90.00^\circ$, $V = 597.2(4)$ $Å^3$, $Z = 2$, Dcalc. $= 1.292$ mg/m^3, the final R factor is $R_1 = 0.0592$, 771 for reflections with $I_0 > 2\sigma(I_0)$, $R\omega = 0.1334$ for all data; largest peak and hole are 0.181 and $-0.175 eÅ^{-3}$ respectively. The structure were solved by full-matrix least-squares on F^2 using the SHELXTL PROGREM [8–10].

Results and discussion

The synthetic route can be summarized as follows (Scheme 1). We adopted an efficient, one-pot method to synthesize 5H-Imidazol[2,3-b]isoquinoline-1-ethanol-5-one,1,2,3,10b-tetrahydro-, $\beta(S)$-phenyl-3(S)-phenyl- (**2**). It was prepared from the reaction of 2-cyanophenylacetonitrile with L-phenylalaninol in chlorobenzene under dry, anaerobic conditions. $ZnCl_2$ was dried under vacuum and acted as the Lewis catalyst in this reaction, but interestingly, in the process of silical gel column chromatography, we were able to characterize the structure of 2,5-diphenylpyrazine.

From Fig. 1, several interesting observations can be made about the structure. Compound **1** was composed of two phenyl and 3,6-dihydropyrazine rings. The C(1), C(2), C(3), C(4), C(5), and C(6) atoms were all coplanar. The C–C distances ranged from 1.372(3) to 1.397(3) Å, and the C–C bond angles ranged from 118.5(2)° to 121.1(10)°. The aromatic ring in the molecule was in agreement with the literature without any unusual features. The two C=N bonds [N(1) ~C(1) = 1.340(3) Å, N(1) ~C(2) = 1.334(3) Å] were not equal, C(1), C(2), N(1), C(1A), C(2A), N(1A) atoms formed a pyrazine ring, they were also coplanar, and its bond angles were nearly 120°.

Conclusions

In summary, we report for the first time a novel method of synthesizing 2,5-diphenylpyrazine. It was obtained unexpectedly, and the next step of our research is to put forward a reasonable reaction mechanism.

References

1. A.E. Erickson, P.E. Spoerri, J. Am. Chem. Soc. **68**, 400–402 (1946)
2. C. Charalambos, N. Sotirios, C. Panayotis, J. Chem. Eng. Data **32**, 478–479 (1987)
3. B.M. Latha, V. Sadasivam, B. Sivasankar, Catal. Commun. **8**, 1070–1073 (2007)
4. J. Albaneze-Walker, M. Zhao, M.D. Baker, P.G. Dormer, J. McNamara, Tetrahedron Lett. **43**, 6747–6750 (2002)
5. B. George, G. Jose, J. Org. Chem. **56**, 2605–2606 (1991)
6. H. Alper, S. Wollowitz, J. Am. Chem. Soc. **97**, 3541–3543 (1975)
7. J. Daniel, D.N. Dhar, Synth. Commun. **23**, 2151–2157 (1993)
8. Sheldrick, G. M. *SHELXS-97, Program for X-ray Crystal Structure Solution* (Göttingen University, Germany, 1997)
9. Sheldrick, G. M. *SHELXL-97, Program for X-ray Crystal Structure Refinement* (Göttingen University, Germany, 1997)
10. G.H. Stout, L.H. Jensen, *X-Ray Structure Determination: A Practical Guide* (MacMillan, New York, 1968)