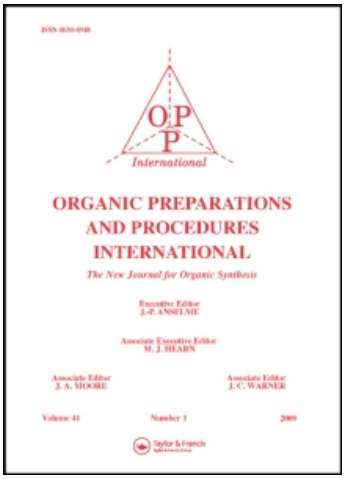

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SELECTIVE REACTIVITY OF THE BISENAMINE OF PIPERAZINE-CYCLOHEXANONE WITH BENZOYL CHLORIDE

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REFERENCES

1. T. Hisano, S. Yoshikawa and K. Muraoka, Org. Prep. Proced. Int., 5, 95 (1973); T. Hisano, T. Matsuoka and M. Ichikawa, Org. Prep. Proced. Int., 6, 243 (1974); T. Hisano, T. Matsuoka and M. Ichikawa, Heterocycles, 2, 163 (1974); R. A. Abramovitch, I. Shinkai and R. V. Dahn, J. Heterocycl. Chem., 13, 171 (1976); R. A. Abramovitch and I. Shinkai, Acc. of Chem. Res., 9, 192 (1976).

2. All the calculations were performed on the FACOM M-190 computer in the computer center of Kyushu University

3. P. Main, M. M. Woolfson and G. Germin, Acta Crist., B.26, 274 (1970); ibid., A.27, 368 (1971).

4. The universal Crystallographic Computation Program System UNICS II (Sakurai, Iwasaki, Watanabe, Kobayashi, Bando and Nakamichi, 1974).

5. The densities of I and II are measured by the floating method used a mixture of n-hexane and CCl_4.

SELECTIVE REACTIVITY OF THE BISENAMINE OF PIPERAZINE-CYCLOHEXANONE WITH BENZOYL CHLORIDE

Submitted by (9/19/78)

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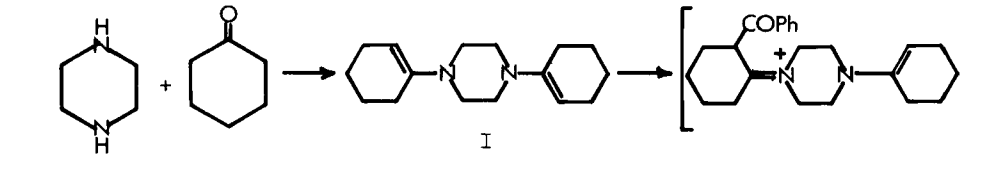
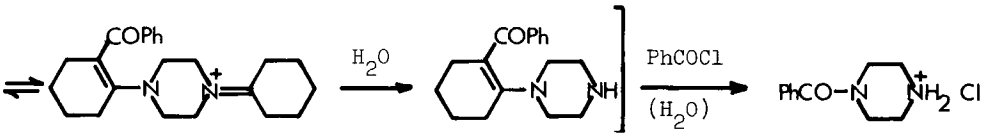
The selective benzoylation of bis-enamine I affords a novel path to N-benzoylpiperazine.[1,2]



I



EXPERIMENTAL

1,4-bis-[1-Cyclohexenyl]piperazine (I).- A solution of 11.28 g (0.13 mol) of piperazine in 150 ml of dry benzene was added to a stirred solution of 25.72 g (27.1 ml, 0.26 mol) of cyclohexanone in 150 ml of dry benzene in a 500 ml round-bottomed flask fitted with a Dean-Stark trap (half-filled with molecular sieves) and a reflux condenser. The system had been previously purged with N_2 and flame dried. A catalytic amound of p-toluenesulfonic acid monohydrate was added, and the mixture was heated under reflux for 24 hrs. The mixture was concentrated to 150 ml by distillation under reduced pressure and the product separated as white crystals on cooling which were collected. Further concentration of the filtrate in vacuo gave additional product which was filtered, washed with a small quantity of cold benzene and cold ether. After recrystallization from benzene-petroleum ether, the combined yield was 25.33 g (78%), mp. 119-120°; ^1H nmr [$(CH_3)_2CO$-d_6/TMS]: δ 1.5-1.9 (4H, broad), 1.9-2.2 (4H, broad), δ 2.8 (4H), δ 4.6 (2H, broad triplet). The bis-enamine is moderately stable to water and may be stored under N_2 in a desiccator.

Anal. Calcd. for $C_{16}H_{26}N$: C, 77.99; H, 10.65; N, 11.36.
Found: C, 77.84; H, 10.85; N, 11.35.

Monobenzoylpiperazine Hydrochloride (II).- To a stirred solution of 2.25 g (9.1 mmol) of I in 90 ml of anhydrous $CHCl_3$ was added a 2.5 molar equivalent (3.21 g, 2.65 ml, 22.75 mmol) of benzoyl chloride. The mixture was

stirred at room temperature, open to the atmosphere, for 18 hrs. Anhydrous ether (50 ml) was then added to precipitate a white solid (2.06 g), consisting of 75% N-benzoylpiperazine (II) and 25% piperazine as their hydrochlorides (nmr).

Treatment of the mixture with base followed by extraction with CH_2Cl_2 gave impure monobenzoylpiperazine (II), [picrate, mp. 239-240°, lit.[2a] mp. 240°]. This was converted to its hydrochloride by passing a stream of anhydrous HCl through an ethereal solution for a few minutes. The precipitate was separated by filtration to give 1.52 g (62%), mp. 260-265° (dec.), lit.[1] mp. 274°. The overall yield from piprazine was 50%.

^1H nmr (D_2O/acetone reference): δ 3.1-3.4 (4H, broad), δ 3.6-3.9 (4H, broad), δ 7.3 (5H, singlet).

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REFERENCES

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1. B. Dhawan and P. L. Southwick, Org. Prep. Proced. Int., 7, 85 (1975).
2. a) T. S. Moore, M. Boyle and V. M. Thorn, J. Chem. Soc., 42 (1929).
   b) M. Desai, J. W. H. Watthey and M. Zuckerman, Org. Prep. Proced. Int., 8, 85 (1976).