methanol, and recrystallized from a suitable solvent.

The compounds thus obtained are listed in Table I.

NMR: **17**, δ 4.88 (CH_2), 6.40-7.82 (ArH and NH).

IR (cm^{-1}): **1**, 3230 (NH), 3040 (CH_2); **3**, 3050 (NH), 2800 (CH_2); **6**, 3350 (NH), 3000 (CH_2); **20**, 3300 (NH), 3000 (CH_2).

CNS Activity

Compounds **2**, **6**, **9**, **16**, and **19** were administered intraperitoneally at different dosages such as 200, 400, and 1000 mg to groups of 5, 4, and 4 mice, respectively. During gross observation, it was found that spontaneous motor activity and reactivity of the animals were increased.

ALD_{50} of compounds **2**, **16**, and **19** was >1000 mg/kg and for **6** and **9** it was 681 mg/kg.

The compounds did not show any protection against maximum electric shock (MES).

Antiviral Activity

Compounds **1**, **9**, **10**, **13**, **20**, and **21** were tested against the strains of vaccinia and Ranikhet disease viruses in vitro by a method reported earlier. The system taken was CAM culture of chick embryo; compound **10** showed an inhibition of 40% whereas the remaining compounds were inactive against these strains.

Antibacterial Activity

All the compounds (except **4**) of Table I were tested against the strains of *Bacillus subtilis* and *Sarcina lutea* by the Agar diffusion method (*12*). The results are recorded in Table I. Fifteen compounds showed inhibition against *B. subtilis* while six compounds were effective against *S. lutea*.

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Literature Cited

(1) Varma, R. S.; Nobles, W. L. *J. Pharm. Sci.* **1973**, *62*, 140.
(2) Varma, R. S.; Imam, S. A. *Indian J. Microbiol.* **1973**, *13*, 43.
(3) Varma, R. S.; Imam, S. A. *Def. Sci. J.* **1975**, *67*, 25.
(4) Gujral, M. L.; Saxena, P. N.; Tiwari, R. S. *Indian J. Med. Res.* **1955**, *43*, 637.
(5) Kacker, I. K.; Zaheer, S. H. *J. Indian Chem. Soc.* **1951**, *38*, 344.
(6) Zaheer, S. H.; Sidhu, G. S.; Sattur, P. B.; Seth, U. K. Symposium on CNS drugs. CSIR: New Delhi, 1966; 170.
(7) Jamamoto, M.; Morooka, S. *Japan Kokai Tokkyo Koho* **1974**, *110*, 681.
(8) Furman, R. H.; Howard, R. P.; Keaty, C. E. *Am. J. Med.* **1958**, *24*, 80.
(9) Kurihava Tonaburo et al. *Annu. Rep. Tokoku Coll. Pharm.* **1970**, *17*, 43; *Chem. Abstr.* **1971**, *75*, 110246r.
(10) Ram, V. J.; Pande, H. N. *J. Indian Chem. Soc.* **1974**, *51*, 634.
(11) Kapoor, Anup Ph.D. Thesis, 1978, Lucknow University.
(12) Varma, R. S.; Nobles, W. L. *J. Pharm. Sci.* **1968**, *57*, 1801.

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Selective Reaction of Isocyanates with the Amino Group of 2-Amino-2-methyl-1,3-propanediol

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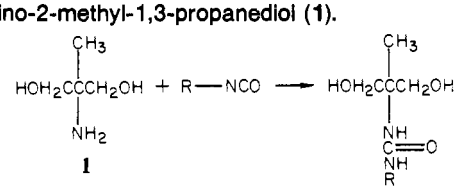
Isocyanates react very specifically with the amino group of 2-amino-2-methyl-1,3-propanediol. Five model compounds were made and identified with elemental analysis and IR, NMR, and mass spectra.

On the basis of information available from the literature,[1-3] a number of new urea derivatives have been synthesized by reacting model isocyanates very selectively with the amino group of 2-amino-2-methyl-1,3-propanediol (**1**).



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Analytical and proton chemical shift data of all the urea derivatives are listed in Table I. Infrared spectra of these compounds have no absorption at 5.8-5.9 μm characteristic of the urethane carbonyl and all of them have urea carbonyl absorption at 5.98-6.02 μm. C, H, and N analyses and the $(M + 1)^+$ peaks for all five compounds were as calculated.

Experimental Section

General Procedure. Isocyanates and 2-amino-2-methyl-1,3-propanediol were obtained from Eastman and Aldrich Chemical Co. Isocyanates were used as received. The diol was recrystallized twice from acetone.[4] Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded by using a Perkin-Elmer 521. Nuclear magnetic resonance spectra were obtained with a Varian EM 390 instrument, using tetramethylsilane as an internal standard and Me_2SO-d_6. Molecular weights were determined by chemical ionization mass spectrometer (Biospect) using methane as a reagent gas. Microanalysis were performed at American Cyanamid Co. of Bound Brook, N.J..

Synthesis of 2-Substituted-2-methyl-1,3-propanediol. Aqueous 2-propanol as Solvent. A 13-g sample (0.12 mol) of 2-amino-2-methyl-1,3-propanediol was dissolved in 40 mL of 70% aqueous 2-propanol and heated to gentle reflux. Isocyanate (0.10 mol) was added dropwise and then the mixture was refluxed for 30 min. Upon cooling of the mixture, the urea derivative precipitated, which was removed by filtration and recrystallized twice from aqueous 2-propanol.

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Table I. Urea Reaction Products of RNCO and 2-Amino-2-methyl-1,3-propanediol

$RNHCONHC(CH_2OH)_2$ (CH₃ on the central C)

R	reaction solvent	% yield	mp, °C	proton chemical shift data (δ)[a] RNHC=O	O=CNHC	CH₃C(CH₂OH)
n-dodecyl	2-PrOH(aq)	86	63	6.20 t	5.65 s	5.10 t
n-octadecyl	$CHCl_3$	81	85	6.18 t	5.65 s	5.13 t
cyclohexyl	2-PrOH(aq)	63	155	6.10–6.20 d	5.65 s	5.13 t
phenyl	$CHCl_3$	63	133–135	8.70 s	6.00 s	4.90 t
naphthyl	$CHCl_3$	95	176	8.75 s	6.55 s	4.93 t

[a] Key: s = singlet; d = doublet; t = triplet.

Chloroform as Solvent. A 13-g sample (0.12 mol) of 2-amino-2-methyl-1,3-propanediol was slurried into 100 mL of chloroform and heated to gentle reflux. Isocyanate (0.10 mol) was added dropwise and then finished as above.

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Literature Cited

(1) J. S. Pierce, C. D. Luneford, R. W. Raiford, J. I. Rush, and D. W. Riley, *J. Am. Chem. Soc.*, **73**, 2595 (1951).
(2) Roy G. Neville, *J. Org. Chem.*, **23**, 750–751 (1958).
(3) S. Glasstone and A. Schram, *J. Am. Chem. Soc.*, **69**, 1213 (1947).
(4) B. N. Vanderbilt and H. B. Haas, *Ind. Eng. Chem.*, **32**, 34 (1940).

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Studies on Cycloimmonium Ylides: Synthesis of Some New 2,4,6-Trisubstituted Pyridines. 2

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A wide range of 2,6-di(2-thienyl)-4-arylpyridines, 2-(4-biphenyl)-4-aryl-6-(2-thienyl)pyridines, and 2-(4-biphenyl)-4-aryl-6-(2-naphthyl)pyridines have been synthesized by the interaction of 1-(2-thiophenoylmethyl)pyridinium iodide, 1-(4-phenylphenacyl)pyridinium bromide, and 1-(2-naphthoylmethyl)pyridinium bromide with a variety of α,β-unsaturated ketones. Ammonium acetate in glacial acetic acid was used as cyclization agent. The structures of the resulting products were confirmed by IR and NMR spectral analyses.

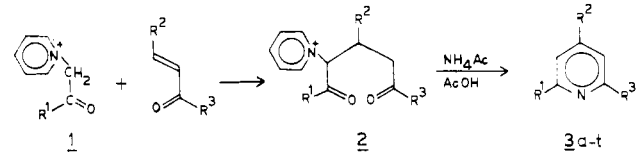
Introduction

Continuing our previous studies on the reactivity of cycloimmonium ylides,[1] we wish to report herein the reactivity of (2-thionylmethylene)pyridinium ylide, (4-phenylphenacyl)pyridinium ylide, and (2-naphthoylmethylene)pyridinium ylide with a variety of α,β-unsaturated ketones, leading to the formation of some new substituted 2,4,6-triarylpyridines.

Results and Discussion

(2-Thiophenoylmethyl)pyridinium iodide (**1a**) was prepared by the Ortoleva–King reaction[2] which involved the reaction of pyridine with 2-acetylthiophene and iodine at reflux. Treatment of the salt (**1a**) with α,β-unsaturated ketones, i.e., subsituted benzylidene-2-acetothiophene, in the presence of ammonium acetate and glacial acetic acid at reflux temperature afforded 2,6-di(2-thienyl)-4-(substituted phenyl)pyridine (**3a–f**). However, the salt **1a** when treated with substituted benzylidene-4-acetobiphenyl under similar reaction conditions gave 2-(4-biphenyl)-4-(substituted phenyl)-6-(2-thienyl)pyridines (**3g–j**) (Scheme I).

Scheme I



1 2 3a-t

The reaction of (2-naphthoylmethyl)pyridinium bromide (**1b**), prepared by the quaternization of pyridine with ω-bromo-2-acetonaphthone with substituted benzylidene-4-acetobiphenyl in the presence of ammonium acetate and glacial acetic acid gave 2-(4-biphenyl)-4-(substituted phenyl)-6-(2-naphthyl)pyridines (**3k–t**) (Scheme I).

The synthesis of pyridines **3k–t** has also been achieved by an alternative route which involved the reaction of (4-phenylphenacyl)pyridinium bromide **1c** with substituted benzylidene-2-acetonaphthone. Ammonium acetate in glacial acetic acid was used for bringing about aza ring closure of the intermediate (**2**), formed by the nucleophilic attack of the ylide carbanion on the β-carbon atom of α,β-unsaturated ketones.

Various 2,4,6-trisubstituted pyridines synthesized above are listed in Table I. All the pyridines **3a–t** gave satisfactory elemental analyses. The spectral data for the resulting pyridines were also consistent with the proposed structures. The IR[3,4] spectra showed a characteristic absorption band in the region 3090–3000 cm^{-1} which may be assigned to the C–H stretching mode of the pyridine ring. Two bands in the region 1600 cm^{-1}

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