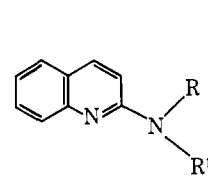
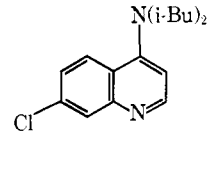
TABLE I: N,N-DISUBSTITUTED AMINOQUINOLINES




1–4




5

| Compd | Chloroquinoline + | Formamide | → | Product | Formula | Yield | Amine bp (mm) or mp, °C | Picrate mp, °C[a] |
|---|---|---|---|---|---|---|---|---|
| 1 | 2-Chloro | $HCON(n\text{-}Bu)_2$ | | R = R′ = *n*-Bu | $C_{17}H_{24}N_2$ | 88 | 130–133 (0.05) | 178.5–180 |
| 2 | 2-Chloro | $HCON(i\text{-}Bu)_2$ | | R = R′ = *i*-Bu | $C_{17}H_{24}N_2$ | 81 | 125–130 (0.1) | 159–160 |
| 3 | 2-Chloro | $HCONCH_3Ph$ | | R = $CH_3$, R′ = Ph | $C_{16}H_{14}N_2$ | 36 | 161–163 (0.05) | 172–174 |
| 4 | 2-Chloro | HCONHPh | | R = H, R′ = Ph | $C_{13}H_{12}N_2$ | 35 | 97–98[b] | |
| 5 | 4,7-Dichloro | $HCON(i\text{-}Bu)_2$ | | R = R′ = *i*-Bu | $C_{17}H_{23}ClN_2$ | 56 | 185–200 (0.2) | 203–204 |

[a] All liquid amines were analyzed as their crystalline monopicrates (from EtOH) for the elements C, H, and N. Analyses were within ±0.4% of theoretical values. [b] P. Friedlaender and H. Weinberg, *Ber.*, **18**, 1532 (1885), reported mp 98°.

supernatant. Similarly, when 1 g of 4,7-dichloroquinoline was refluxed with either formamide or N-*iso*-butylformamide, 7-chloro-4(1H)-quinolone could be isolated in 86 and 65% yields, respectively, mp 270–272°, lit.[3] mp 277–279°.

(3) A. R. Surrey and H. F. Hammer, *J. Amer. Chem. Soc.*, **68**, 113 (1946)

## Synthesis of 3-Bromo- and 3-Chloro-1-methyl-4-phenyl-4-propionoxypiperidines as Potential Analgetics

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Preparation of the title compounds was of interest to examine the effect of a halogen atom in the 3 position on the "reversed ester" of meperidine. Neither compound possessed analgetic activity.

### Experimental Section[1]

**3-Bromo-1-methyl-4-phenyl-4-propionoxypiperidine Hydrobromide.**—To a solution of 1-methyl-4-phenyl-1,2,5,6-tetrahydropyridine[2] (17.3 g, 0.1 mole) in 100 ml of ice–$H_2O$ and 5.2 ml of concentrated $H_2SO_4$ was added N-bromoacetamide (13.8 g, 0.1 mole) all at once with stirring. After the addition of the NBA, 0.5 ml of $H_2SO_4$ was added. The temperature rose to 29° during the next 5 min. After 0.5 hr, another 0.5 ml of $H_2SO_4$ was added.[3] Stirring was continued for 0.5 hr more at 35°, the solution was chilled in ice, basified with 35% NaOH solution, and extracted ($Et_2O$), and the extract was dried ($Na_2SO_4$) and treated with ethereal HBr. The $Et_2O$ was decanted and the residual white gum was treated with 75 ml of $Pr_2O$. The gum dissolved in 0.5 hr and the resulting solution was allowed to stand for several days. The crystalline solid was collected and recrystallized from MeOH–EtOAc to give 19.0 g (46.7%) product, mp 168–169°. *Anal.* ($C_{15}H_{21}Br_2NO_2$) C, H, Br.

**3-Chloro-1-methyl-5-phenyl-4-propionoxypiperidine Hydrochloride.**—Similar treatment of the ethereal epoxide solution with ethereal HBr and $(EtCO)_2O$ afforded 54.9% of product, mp 203–204° dec from EtOH. *Anal.* ($C_{15}H_{21}Cl_2NO_2$) C, H, Cl.

(1) Melting points were taken in open capillaries and are corrected. Where analyses are indicated by symbols of the elements, analytical results obtained for those elements were within 0.4% of the theoretical values.

(2) C. J. Schmidle and R. C. Mansfield, *J. Amer. Chem. Soc.*, **78**, 428 (1956).

(3) After this work had been completed, the epoxide was reported by R. E. Lyle and W. E. Krueger, *J. Org. Chem.*, **30**, 394 (1965).

# *Book Reviews*

**Modern Separation Methods of Macromolecules and Particles.** Edited by THEO GERRITSEN, with 19 contributors. Wiley-Interscience, New York, N. Y. 1969. xi + 250 pp. 15.7 × 23.4 cm. $14.95.

Advances in macrobiochemicals and synthetic polymers depend on the methodology of separating fractions, and ultimately compounds, of similar but not equal molecular weights and sizes. As we immerse ourselves more deeply in factors that may play a role in immunological disorders, the adequacy of separation methods of large molecules and of particulate aggregates will spell the success or failure of many a research project. The book under consideration is the work-up of a 1968 symposium. It comprises 11 chapters, ranging from pore "disc" electrophoresis, gel filtration, and chromatography to separations based on size and conformation. The subject is biologically oriented, two chapters being devoted to lymphocyte separation. Anyone working on proteins, fats, polysaccharides, polynucleotides, enzymes, cells differentiated by size and morphology, and similar particles from large molecules to colloid suspensions will learn something new and useful from these surveys.

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**Induction of Ovulation.** By RODNEY P. SHEARMAN. Charles C Thomas, Publisher, Springfield, Ill. 1969. xi + 142 pp. 23.5 × 16 cm. $11.50.

This slender volume will serve as a useful survey of methods to induce ovulation in anovulatory women, whose usual problem is gonadotropin disorder. Apart from the chapter on surgical intervention, the medicinal chemist will find interest in the application of clomiphene and of cyclofenil (Sexovid®) (!) and human gonadotropins to anovulation, as well as in the spontaneous cures and placebo effects which ameliorate this condition. The pharmacology of compounds used to induce ovulation is explained nicely. For the more primitively motivated reader, there are ample photographic illustrations of virilization and hirsutism, and for the historically minded there is a retrospective section going back to ancient Egypt, when amenorrhea and irregular menstruation were treated with "douches of garlic and wine and the ingestion of wanu grease and sweet beer." The rest of the booklet offers carefully documented chapters with 343 references and an adequate index.

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