<0.5 g. of oil, which was dissolved in 20 ml. of ethanol and treated with a solution of 1.0 g. of *p*-toluenesulfonic acid in 10 ml. of ethanol. The resulting salt (<70 mg.) was either 4,5,6,1- or 1,2,5,6-tetrahydro-3-benzoylpiperidinium *p*-toluenesulfonate (XI), m.p. 105–106°; IR (mineral oil) 1685 cm.$^{-1}$ (C=O, $\alpha,\beta,\alpha',\beta'$-unsaturated ketone) and no band in the 3500-cm.$^{-1}$ region.

Anal.—Calc. for $C_{19}H_{21}NO_4S$: C, 63.49; H, 5.89; N, 3.90; S, 8.92. Found: C, 63.9; H, 6.62; N, 3.72; S, 8.82.

While acid may conceivably have been present in trace amounts in the benzene fraction of the reaction mixture, formation of XI from VI by acid catalysis is contrary to all chemical precedent and to all experience with Compounds V, VI, and XII (2, 3, 11–15). This, as well as the fact that the neutral, benzene-soluble oil contains bromine which must be organically bound, clearly requires functionalization of the C_8—OH group of V. Thus, in the presence of CNBr, formation of alkyl cyanate (XIII) must occur. Subsequent considerations clearly implicate this as the first step. Formation of the α-bromo ketone (XIV) from the α-cyanato ketone (XIII) is consistent with both the chemistry of alkyl cyanates (8–10) and the well-known conversion of I to V under *quasi*-Favorskii conditions. The latter reaction is now known to proceed (with retention of configuration) through internally assisted ion pairs (3, 11–15). There is no precedent to support participation of the corresponding cyanamide moiety of XV in cyanate–bromide exchange. In fact, quite the reverse is true (13, 15). This tends to rule out XV as a precursor to XVI and suggests that cyanate formation is the first step.

Predilection of CNBr for the hydroxyl group rather than the amine group in V is explicable on the basis of the following facts. The carbonyl (benzoyl) group has an acid-strengthening effect on the hydroxyl group (3, 4). The hydroxyl group, undoubtedly as a function of its (axial) stereochemistry, is totally hydrogen bonded; as a result, the nitrogen bears significant positive character (3, 4, *cf.*, 5). This rationale augurs well for the absence of measurable quantities of VI in the benzene-soluble fraction and requires that XIV is the precursor of XVI, the principal component of the benzene-soluble fraction. While olefin might have been generated at the levels of XIII–XVI, it may also have been formed from XVII during the workup.

In view of the fact that only one characterizable compound could be isolated from the reaction mixture, and in view of the interesting chemical and stereochemical aspects of this reaction, further investigations are now in progress using optically pure V.

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Efficient Deoxygenation of Water by Gas Permeation

Keyphrases □ Oxygen levels in water—technique for reduction, gas permeation □ Deoxygenation of water—by gas permeation □ Gas permeation—utilized for reducing oxygen levels in water □ Water—deoxygenation by gas permeation

Sir:

The oxidative processes which drug moieties undergo involve dissolved molecular oxygen, which is assumed to be a free radical propagated route (1, 2). Schou (3) noted that dissolved oxygen levels must reach a critical concentration before the chain reactions are initiated. In a consideration of the kinetic implications of oxidative degradation, it would appear worthwhile to investigate the possibility of developing a simple, rapid, and economical procedure to deoxygenate water used in the preparation of liquid pharmaceutical systems. Therefore, we recently made preliminary studies in the deoxygenation of solvent water utilizing a gas permeator[1] equipped with dacron fibers.

The operation of gas permeators is based on the principle of selective separation using the membrane walls of hollow fibers. The selectivity of the membrane permits removal of a particular component in the system, depending upon the type of fiber employed; the separation follows Fick's law of diffusion. The selection of the proper membrane fiber is based on solubility considerations, because the component to be removed should be more soluble than the water in the membrane.

Cole and Genetelli (4) recently demonstrated that laboratory models of gas permeators are efficient and prac-

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[1] Permasep, DuPont.

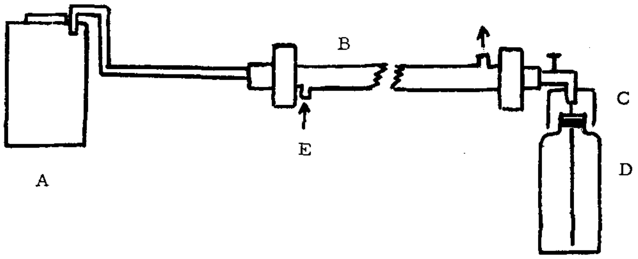

Figure 1—*Gas permeator system. Key: A, pressure tank; B, permeator; C, nitrogen hood; D, collection tank; and E, nitrogen flush.*

tical alternatives to air blowing as a method for reducing dissolved gas levels in waste water. This technique is especially applicable to removal of pollutants in waste water, since the concentrations of gases is relatively low and the pollutant is transferred across the membrane at a higher molar concentration.

The system is simple in both design and construction. It consists of a large number of hollow fibers of suitable composition (dacron, nylon, polypropylene, *etc.*) enclosed in a hollow, noncontaminating metal tube. The water to be treated is forced through the fibers; the dissolved gases permeate the fiber walls and are carried off by a vacuum or nitrogen flush. The overall flux required is small since the concentration of permeant is low. The only pressures involved are those required to compensate for hydraulic losses in the separator.

Our apparatus was slightly modified from that of Cole and Genetelli (4), since we were working with a standard-size permeator whose technical data are shown here:

permeator number	015-70-0264
serial number	DP-168
shell inner diameter	3.81 cm. (1.50 in.)
shell pressure rating	1500 psig.
fibers	Dacron
number of tubes	741,600
tube outside diameter	32.8 μ
tube inner diameter	16.5 μ
tube percent hollow	25.46%
number of leaking tubes	38
number of leaking tubes, %	0.005%

Table I—Effect of Gas Permeation upon Dissolved Oxygen Levels and Resulting pH

Pass Number	Dissolved Oxygen, p.p.m. at 25°	pH
0 (oxygenated, normal conditions)	8.37	6.12
1	0.70	6.80
2	0.12	7.30

Deionized water in a pressure tank was forced through the permeator under 100 lb. of pressure using nitrogen gas. A nitrogen flush was employed to remove the permeant from around the fiber bundle. The deaerated solvent water was collected at a rate of 30 ml./min. under a nitrogen hood to prevent air contamination. After consideration of solubility characteristics of available fibers, a dacron fiber was utilized in the system; it was felt that this membrane would be most efficient in removal of dissolved oxygen. A basic diagram of the system is shown in Fig. 1.

The efficiency of the gas permeator in reducing dissolved oxygen levels and the effect of multiple passes through the system were investigated by measuring dissolved oxygen levels at 25° with a dissolved oxygen analyzer[2] having a sensitivity of 0.01 p.p.m. O_2.

As seen in Table I, dissolved oxygen levels were reduced greater than 90% with a single pass through the permeator and were reduced more than 98% with a double pass. Decarbonation of the deionized water occurred simultaneously with deoxygenation, as evidenced by a change in the pH with each pass through the permeator. There may be some leaching of alkali from the column or impurities in the nitrogen gas, since the pH 7.30 is higher than expected.

This technique appears to be an efficient method of reducing dissolved oxygen levels in water. Its applicability for the protection of oxygen-sensitive pharmaceuticals will be reported in a future communication.

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[2] Delta Scientific model 106.