5. The concept of "minimum loss," as formulated here, arose from discussions with Jerome Cornfield, now at the National Heart Institute, Bethesda, Md. It is also possible to maximize the "gain" function $G = q_1 - \lambda q_2$, which gives the same best dose as does the minimum loss approach.
6. Equation 4 does not always lead to a real answer. For a real answer the term inside the square root sign must be positive. This is true when $\sigma_A = \sigma_T$, or $\lambda = 1$, or when (i) $\sigma_T > \sigma_A$, then

$$\lambda \leq \frac{\sigma_T}{\sigma_A} \exp \left[- \tfrac{1}{2} \frac{(\mu_A - \mu_T)^2}{\sigma_A{}^2 - \sigma_T{}^2} \right],$$

or when (ii) $\sigma_T < \sigma_A$, then

$$\lambda \geq \frac{\sigma_T}{\sigma_A} \exp \left[- \tfrac{1}{2} \frac{(\mu_A - \mu_T)^2}{\sigma_A{}^2 - \sigma_T{}^2} \right]$$

It can be shown mathematically that the minimum loss occurs at the solution for x given by the positive value of the square root in Eq. 4. These limitations on λ imply that there are situations in which rankings are not possible (that is, when the conditions are not met). The medical and biological meaning of such a situation must then be thoroughly investigated.
7. The constant, λ, expresses the discomfiture that toxicity causes relative to the discomfiture that failing to cure would create. λ must be substantially larger than 1 when one is more willing to accept the pain and discomfort of an illness, than pain and discomfort induced by a drug. For a mild, self-limiting illness (for example, headache), in which scarcely any drug toxicity is permissible, λ should be large. In a fatal illness, such as acute leukemia, any toxicity less than lethal might be acceptable and λ could possibly be about 1. From Eq. 3 it can be shown that increasing λ will lead to a lowering of the "best" dose. This is reasonable, λ being a measure of the fear of toxicity and since the more we fear toxicity, the more we will try to avoid it. The choice of λ is largely intuitive, and in treating man, the art and sensibilities of the physician must enter. For a specific illness it may be that a range of acceptable λ's can be agreed upon among several physicians.
8. The values of the integrals of Eq. 2 are obtained from using

$$Z_A = \frac{x - \mu_A}{\sigma_A},\ Z_T = \frac{x - \mu_T}{\sigma_T}$$

as arguments in tables of the normal probability distribution.

24 January 1964 ■

Oxygen Atom Reactions with Condensed Olefins

Abstract. *Gaseous oxygen atoms, thermally generated from O_2 on a 2300°K zirconia surface, react with simple condensed olefins below 100°K. Initial results indicate that the distribution of products differs from that obtained in the gas phase at higher temperatures.*

Oxygen atoms, produced in the gas phase, can react with condensed simple olefins such as propylene and butene. Ponomarev (*1*) has reported a pressure decrease when an iridium filament was made incandescent in a vessel containing oxygen whose walls, maintained at 77°K, were coated with propylene. We have observed a pressure decrease in such a system but found little evidence of reaction. There is formation of carbon dioxide from carbon contamination of the iridium, and excessive evaporation occurs when the filament is heated above 1850°K. The pressure decrease is thus not a reliable indication of reaction.

A particularly suitable device for the thermal production of ground state oxygen atoms is the Nernst glower. This is essentially a zirconia rod that can be electrically heated to a temperature of 2300°K. With an oxygen pressure of 200 millitorr or less, sufficient dissociation occurs that the reaction of oxygen atoms at surfaces may be readily studied. The Nernst glower has the advantage of being inert in the oxygen atmosphere at operating temperatures so that a pressure decrease is a reliable measure of the extent of reaction.

Condensed olefins at 77°K reacted only very slowly with oxygen atoms, while at 90°K the reaction proceeded at a convenient rate. In a typical experiment, propylene condensed and maintained at 90°K, was exposed to oxygen atoms. The pressure was held at 40 millitorr by allowing oxygen to leak slowly into the system. After 10 minutes the glower was switched off, the excess oxygen removed, and the reaction products warmed to room temperature. The product analysis was performed by means of gas chromatography with a 3-meter column of bis [2-(2-methoxyethoxy) ethyl] ether on chromosorb at 50°C. Propionaldehyde, propylene oxide, acetone, acetaldehyde, and some minor products as yet unidentified were found. Owing to its ease of polymerization, formaldehyde is not readily eluted from a chromatographic column. Its presence among the reaction products, however, was indicated by qualitative tests. The propylene oxide : propionaldehyde : acetone ratio was 1.0 : 1.5 : 0.1. Yields of acetaldehyde were about equal to those of propylene oxide. These results are qualitatively similar to those found by Cvetanovic in gas phase studies (*2*).

As the exposure times of the condensed propylene to oxygen atoms were increased, the relative yield of propylene oxide decreased. This is ascribed to a reaction between propylene oxide and oxygen atoms. When propylene oxide alone is diluted with propane, condensed at 90°K, and exposed to oxygen atoms, propionaldehyde, acetone, acetaldehyde, and formaldehyde are produced.

It is significant that reaction between the condensed olefins and oxygen atoms differ from the gas phase results in that neither CO nor CO_2 are formed as reaction products. This indicates that the energy associated with the initial addition of the oxygen atom to the olefin is more efficiently dissipated in condensed phase reactions, and the effects attributable to "hot radical" reactions and rearrangements are at least partially supported.

Butene-1 and oxygen atoms at 90°K yielded α-butene oxide, *n*-butyraldehyde, propionaldehyde, and other minor products. It was observed that for small oxygen atom concentrations, propionaldehyde was the predominant product. High oxygen atom concentrations gave α-butene oxide and *n*-butyraldehyde as major products. In fact, the propionaldehyde yield showed little change with variation in temperature of the zirconia surface. This suggests two separate mechanisms for the three-carbon and four-carbon products. Butene-2 and oxygen atoms yield acetaldehyde and β-butene oxide. Isobutene forms isobutene oxide and acetone. These results differ from those obtained in the gas phase (*3*).

Observation of reactions in the condensed phase at low temperatures affords the advantage of simplicity largely because of the suppression of high activation energy secondary processes. This technique has been demonstrated in studies of the reactions of hydrogen atoms with condensed olefins (*4*). The method can now also be applied to a detailed study of the interaction between oxygen atoms and condensed olefins.

MILTON D. SCHEER
RALPH KLEIN

Division of Physical Chemistry,
National Bureau of Standards,
Washington 25, D.C.

References and Notes

1. A. N. Ponomarev, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk* **1952**, 1307 (1952).
2. R. J. Cvetanovic, *Can. J. Chem.* **36**, 624 (1958).
3. S. Sato and R. J. Cvetanovic, *ibid.*, p. 970.
4. R. Klein and M. D. Scheer, *J. Phys. Chem.* **67**, 1874 (1963); R. Klein, M. D. Scheer, R. Kelley, *ibid.* **68**, 598 (1964).
5. Supported by the USPHS.

29 April 1964