TABLE I

MONOACID ESTERS OF PENTAERYTHRITOL TRINITRATE $(O_2NOCH_2)_3—C—CH_2—O—\overset{O}{\overset{\|}{C}}—R$

R	Yield, %	M.p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
o-C_6H_4COOH	35	125.0–125.5	$C_{13}H_{13}N_3O_{13}$	37.24	37.08	3.12	3.08	10.02	9.90
$HO\overset{O}{\overset{\|}{C}}—CH_2CH_2CH_2—$	85.5	87–88	$C_{10}H_{15}N_3O_{13}$	31.17	31.33	3.92	4.09	10.90	10.83
$HO\overset{O}{\overset{\|}{C}}—CH_2\overset{CH_3}{\overset{\|}{C}}CH_2—$ CH_3	27.1	71.5–72.0[a]	$C_{12}H_{19}N_3O_{13}$	34.87	34.96	4.63	4.94	10.17	9.83

[a] Recrystallized from *n*-propyl alcohol.

acid and acetyl chloride.[3] Methylsuccinic acid[4] and β,β-dimethylglutaric acid[5] were dehydrated with acetic anhydride to form methylsuccinic anhydride[6] and β,β-dimethylglutaric anhydride.[7]

General Procedure.—Since all of the esters were prepared in the same general manner, only the preparation of pentaerythritol trinitrate hydrogen succinate is described in detail. The other compounds are described in Table I.

Pentaerythritol Trinitrate Hydrogen Succinate.—A mixture of 25 g. (0.092 mole) of pentaerythritol trinitrate, 16 g. (0.16 mole) of succinic anhydride and 150 ml. of dry acetone was heated under reflux for 8 hours. There were no signs of decomposition of the nitrate ester during this time. After removing the acetone under reduced pressure, the viscous residue was treated with an excess of aqueous sodium bicarbonate solution. The mixture was extracted with diethyl ether and the aqueous phase separated. This aqueous solution, on acidification with concentrated hydrochloric acid, deposited an oily material which quickly crystallized on cooling. The product was removed by vacuum filtration, washed well with cold water and dried to give 28.5 g. (83.5%) of a white crystalline solid, m.p. 91–92°. a sample for analysis was recrystallized from ethanol, m.p. 92–92.5°.

Anal. Calcd. for $C_9H_{13}N_3O_{13}$: C, 29.12; H, 3.53; N, 11.32. Found: C, 29.17; H, 3.62; N, 10.94.

The sodium salt was prepared by dissolving 5 g. (0.013 mole) of the acid ester in a solution of 1.05 g. (0.0125 mole) of sodium bicarbonate in 50 ml. of distilled water. Gentle warming was necessary to effect complete solution. After all of the solid had been dissolved, the water was removed under reduced pressure. The viscous residue was dissolved in 25 ml. of ethanol and diethyl ether added. The white, amorphous solid which precipitated was removed by filtering and dried in a vacuum desiccator. There was obtained 4.4 g. (84.5%) of material which did not have a definite melting point. The sample began to darken at 150° and was completely decomposed at 175°.

Anal. Calcd. for $C_9H_{12}N_3O_{13}Na\cdot{}^1/_2H_2O$: C, 26.87; H, 3.25; N, 10.44; Na, 5.72. Found: C, 26.98; H, 3.21; N, 10.15; Na, 6.01.

Esterification of Pentaerythritol Trinitrate with Methylsuccinic Anhydride.—A mixture of 5.4 g. (0.02 mole) of pentaerythritol trinitrate and 4.5 g. (0.04 mole) of methylsuccinic anhydride in 50 ml. of dry acetone was refluxed for 24 hours. After removing the acetone under reduced pressure, the residue was treated with an excess of aqueous sodium bicarbonate. The aqueous phase was extracted with diethyl ether, separated and then acidified with concentrated hydrochloric acid. An oily material separated which did not crystallize after long standing. It was extracted with diethyl ether, dried over anhydrous magnesium sulfate and the ether evaporated. This gave a viscous residue which, even after repeated attempts, failed to crystallize. It is postulated that the material was a mixture of the α- and β-methyl hydrogen succinate esters, and that this nonhomogenity accounts for its non-crystallinity. This reaction of methylsuccinic anhydride with an alcohol to give a mixture of isomeric products has been described previously.[8]

(3) W. E. Bachmann, S. Kushner and A. C. Stevenson, THIS JOURNAL, **64**, 977 (1942).

(4) G. B. Brown, *Org. Syntheses*, **26**, 54 (1946).

(5) W. T. Smith and G. L. McLeod, *ibid.*, **31**, 41 (1951).

(6) J. B. Conn, G. B. Kistiakowsky, R. M. Roberts and E. A. Smith, THIS JOURNAL, **64**, 1749 (1942).

(7) W. H. Perkin, *J. Chem. Soc.*, **69**, 1475 (1896).

(8) W. A. Bone, J. J. Sudborough and C. H. G. Sprankling, *J. Chem. Soc.*, **85**, 534 (1904); J. E. H. Hancock and R. P. Linstead, *ibid.*, 3490 (1953).

THE LILLY RESEARCH LABORATORIES
INDIANAPOLIS 6, INDIANA

A New Method for the Preparation of Diacyl Peroxides[1]

BY DELOS F. DETAR AND LOUIS A. CARPINO

RECEIVED APRIL 6, 1955

The usual methods for preparing diacyl peroxides utilize an acid chloride (or in some cases the anhydride) together with an aqueous solution of an alkali metal salt or of an alkaline earth salt of hydrogen peroxide in a variety of modifications.[2,3]

For most peroxides these methods are satisfactory. With acid chlorides that are susceptible to ready hydrolysis or which contain other functions capable of reacting with aqueous peroxidic solutions, the presence of water is detrimental.

A preliminary investigation has shown that the ether-soluble complex of hydrogen peroxide with dicyclohexylamine[4] and the complex of hydrogen peroxide with urea[5] can be used under anhydrous conditions to form benzoyl peroxide in moderate yields.

The new procedure gave a partial success with the acid chloride of *trans*-stilbene-2-carboxylic acid. A crude product containing 51–54% of peroxide was obtained whereas the usual procedures were completely unsuccessful. Up to the present time all attempts to prepare the peroxide of *o*-benzoylbenzoic acid by either the conventional or the new procedures have failed to give a peroxidic product. Some difficulty might have been anticipated since the acid chloride is reported to hydrolyze readily[6] and to react with methanol[7] to give the pseudo ester. On the other hand, ammonolysis of the acid chloride gives the normal amide. Preliminary at-

(1) This work was supported by National Science Foundation Grant NSF G439.

(2) A. V. Tobolsky and R. B. Mesrobian, "Organic Peroxides," Interscience Publishers, Inc., New York, N. Y., 1954, p. 39.

(3) R. Criegee, "Methoden der Organischem Chemie," ed. by D. Müller, Georg Thieme Verlag, Stuttgart, 1952, Vol. VIII, Part III, p. 38.

(4) T. Wagner-Jauregg, THIS JOURNAL, **74**, 1358 (1952).

(5) C. S. Lu, E. W. Hughes and P. A. Giguère, *ibid.*, **63**, 1507 (1941).

(6) J. F. Norris and V. W. Ware, *ibid.*, **61**, 1418 (1939).

(7) M. S. Newman and B. T. Lord, *ibid.*, **66**, 731 (1944).

tempts to prepare the peroxide of *cis*-stilbene-2-carboxylic acid were also unsuccessful. The above peroxides were desired as alternative routes to the *o*-benzoylphenyl radical and to the *o-cis*-β-styrylphenyl radical which are intermediates in certain reactions of the diazonium salts derived from 2-aminobenzophenone[8] and from *cis*-2-aminostilbene.[9]

Experimental

Preparation of Benzoyl Peroxide from the Urea–Hydrogen Peroxide Complex.—The urea–hydrogen peroxide complex was prepared according to the published method[6] except that the mixture of reactants, after being heated to 60°, was merely cooled in an ice-bath and the complex filtered and dried in the air. A mixture of 2.4 g. (25.5 mmoles) of the urea complex, 7.03 g. (50 mmoles) of benzoyl chloride and 50 ml. of absolute ether was stirred by means of a Hershberg stirrer and cooled in an ice-bath; then 4 g. (50.5 mmoles) of distilled pyridine was added and stirring continued in the cold for ten hours. (Later runs with other acid chlorides indicated that the reaction was complete in 3–4 hours if stirring was vigorous.) The colorless solid was filtered and then triturated first with water to remove pyridine hydrochloride, and then with methanol. This peroxide was combined with an additional amount of peroxide obtained by evaporation of the ether. The yield was 3.75 g. (62%), m.p. 104–106° dec. Analysis of the peroxide by the method of Kokatnur and Jelling[10] gave a peroxide content of 100.3%.

Benzoyl Peroxide from the Dicyclohexylamine–Hydrogen Peroxide Complex.—The complex between dicyclohexylamine and hydrogen peroxide was prepared by the method of Wagner-Jauregg.[4]

A solution of 7.05 g. (17.8 mmoles) of the complex (m.p. 92–94°) in about 175 ml. of ether was cooled to slightly below room temperature and then 5 g. (35.6 mmoles) of benzoyl chloride was added in 3–4 portions with constant swirling of the reaction flask. A white solid precipitated immediately. After standing in an ice-bath for about 0.5 hour the white solid (7 g.) was filtered and washed with a little ether. This solid was completely soluble in hot water and appeared to be the expected hydrochloride of dicyclohexylamine.

The ether filtrate on spontaneous evaporation overnight left a semi-solid mixture which smelled strongly of unreacted benzoyl chloride. The mixture was triturated with methanol and the white crystalline solid collected. The yield was 0.9 g. (21%), and a sample which was recrystallized from ethyl acetate–petroleum ether melted at 105–106° dec.

(8) D. F. DeTar and D. I. Relyea, THIS JOURNAL, **76**, 1680 (1954); D. I. Relyea and D. F. DeTar, *ibid.*, **76**, 1202 (1954).

(9) D. F. DeTar and Y. W. Chu, *ibid.*, **76**, 1686 (1954).

(10) V. R. Kokatnur and M. Jelling, *ibid.*, **63**, 1432 (1941).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF SOUTH CAROLINA
COLUMBIA, SOUTH CAROLINA

The Effect of Temperature on the Sorption of Polar Gases by Proteins[1]

BY SIDNEY W. BENSON AND R. SRINIVASAN

RECEIVED SEPTEMBER 12, 1955

In a series of recent papers from this Laboratory[2] it has been shown that the sorption of polar gases such as HCl, BF_3 and CH_3NH_2 by solid proteins is accompanied by the formation of a protein–gas complex of extremely low vapor pressure at room temperature (*i.e.* $\sim 10^{-5}$ mm.). The reproducibility of the composition of these complexes, particularly with HCl, was within ±5% in the range of ambient room temperatures (20–26°), for a very large number of proteins and was independent of sample source, presence of H_2O vapor and particle size (for sufficiently well-dispersed samples to assure fast diffusion).

On the basis of this reproducibility and the striking correlation between the composition of the complexes and the number of strongly-binding acid and basic groups in the proteins, it was proposed that the complex was a stoichiometric compound formed by acid–base interaction of the gas and protein substrate. Further evidence was adduced from the behavior of the complexes with NH_3, BF_3, etc., which indicated properties characteristic of back-titrations[3] and checked the original stoichiometry.

The assignment of a stoichiometry to a protein–HCl complex determined in the above fashion is somewhat arbitrary,[4] resting as it does on the pumping speed of the vacuum line, an arbitrarily selected sensitivity of weighing and some implicit assumptions about the vapor pressure characteristics of the "complex." In the apparatus used for the aforementioned work the arbitrary criterion employed is that the vapor pressure of HCl in equilibrium with complex is less than $\sim 10^{-5}$ mm. in the temperature range studied.[5] Important assumptions implicit in the assignment of stoichiometry are that: (1) the vapor pressures of HCl added to all other groups in the molecule are at least 1–2 orders of magnitude higher than that for the strongly binding groups considered[6]; (2) the vapor pressures of HCl on the strongly binding groups remain significantly less than 10^{-5} mm. in the temperature range used; (3) diffusion through the solid protein particles is sufficiently fast to allow vapor pressure equilibrium to be maintained.

The last assumption regarding diffusion will break down if samples are not well dispersed and we have reported spurious effects caused by slow diffusion.[2b,3] Such effects, however, are detectable and can in principle be avoided. The first and second assumptions are more serious ones. It is clear that at sufficiently low temperatures the vapor pressures of "weakly" binding sites must fall below the arbitrary 10^{-5} mm. Conversely, at sufficiently high temperatures the vapor pressures of "strongly" binding sites must rise above this value.

These observations have been confirmed in recent studies made in our laboratories on the effect of temperature on the formation of protein complexes with HCl and BF_3. For egg albumin the amount of permanently bound HCl decreases smoothly from 0.91 mmole HCl/g. protein at 22° to zero at 80°, while for β-lactoglobulin the values at the same temperatures are 1.23 and 0.15, respectively. At the higher temperature equilibrium was attained as quickly as at room temperature, but

(1) This work has been supported by a Research Grant (G-3541-C2) from the Public Health Service, National Institutes of Health, Bethesda, Md.

(2) (a) S. W. Benson and J. M. Seehof, THIS JOURNAL, **73**, 5053 (1951); (b) **75**, 3925 (1952).

(3) S. W. Benson and J. M. Seehof, *ibid.*, **77**, 2579 (1955).

(4) This has been discussed briefly in ref. 3 (see especially footnotes 13, 18).

(5) *I.e.*, this is about what the criterion of less than 0.1 mg. change in weight per day would correspond to for the pumping system used, assuming diffusion through the solid is not important in the rate process. Slow diffusion in the solid would raise the estimated vapor pressures.

(6) A difference of 2–3 kcal. in binding energy would be enough to account for such differences in vapor pressure, entropy effects being assumed the same for strongly and weakly binding groups.