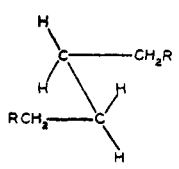
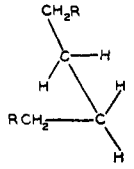
ally accepted value of approximately 2.8 kcal., for which there is considerable support.[3,4]

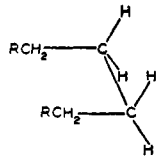
In calculating statistical entropies (gas phase, 25°) for *n*-butane and for a number of other hydrocarbons including cyclohexane and the alkylcyclohexanes, Pitzer[4,5] achieved a remarkable degree of correspondence with observed entropies by employing 0.8 kcal. for the steric energy of the skew form (V) of the *n*-butane structure as compared with the stable staggered constellation IV, and



IV



V



VI

3.6 kcal. for the barrier to rotation through the eclipsed form VI. Application of these values to the "boat" and "chair" constellations of cyclohexane (VII and VIII, respectively) led to an estimated energy difference (gas phase, 25°) of 5.6 kcal. in favor of the "chair" form (VIII), since this structure possesses 6 skew interactions of the *n*-butane

VII

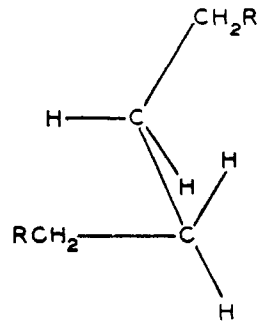
VIII

type, whereas the "boat" form involves 4 skew and 2 eclipsed interactions.

Extension of these ideas to the *cis*- and *trans*-decalins gives a stability order, I > II > III, with an energy difference of 2.4 kcal. between I (6 staggered, 12 skew) and II (3 staggered, 15 skew). The heat of isomerization, I → II, determined by careful measurement of the heats of combustion (liquid phase, 25°) of pure samples of *cis*- and of *trans*-decalin is 2.12 kcal.[6]

For the purpose of direct comparison the calculated value (2.4 kcal.) must be corrected by a small factor for the difference in heats of vaporization of the two isomers at 25°. Such a correction could be derived from a knowledge of vapor pressure–temperature relationships by use of the Clausius–Clapeyron equation. Unfortunately, although the requisite data have been reported,[7] their validity, particularly at temperatures below 50° is doubtful.[8] The correction factor has therefore been approximated from an empirical equation, $\lambda_{25} = 5.4 + 0.036t_{\text{normal b.p.}}$, employed for a similar purpose by Klages.[9] Using the boiling points of *cis*- and of *trans*-decalin, 194.6 and 185.5°, respectively, the energy difference between I and II, corrected to the liquid phase at 25°, is estimated to be 2.07 kcal. Correspondence between the calculated and observed values is considerably better than could reasonably be expected of such a method of approximation.

The energy difference between II and III is more difficult to estimate. The "2-boat" form III possesses, in addition to 4 staggered, 8 skew, and 4 eclipsed *n*-butane interactions, 2 interactions of type IX, produced by a rotation of 60° from the stable staggered configuration (IV). The magnitude of this interaction cannot be evaluated in a simple way, owing to discontinuities in the rotational potential barrier curve of the Pitzer treatment. Neglecting these interactions, however, it is possible to arrive at a minimum value for the energy difference between II and III of 8.8 kcal.



Introduction of an angular methyl group (*cf.* the steroids) into *cis*- and *trans*-decalin (II and I, respectively) has the interesting consequence of lowering the energy difference between these structures from 2.4 to 0.8 kcal. In *trans*-decalin (I) the angular methyl group, being polar with respect to both rings, gives rise to 4 additional skew interactions, whereas in *cis*-decalin (II), in which the angular methyl group is polar with respect to one ring and equatorial with respect to the other, only 2 additional skew interactions result.

(3) G. B. Kistiakowsky, J. R. Lacher and F. Stitt, *J. Chem. Phys.*, **7**, 289 (1939).

(4) K. S. Pitzer, *Chem. Revs.*, **27**, 39 (1940).

(5) C. W. Beckett, K. S. Pitzer and R. Spitzer, THIS JOURNAL, **69**, 2488 (1947).

(6) G. F. Davies and E. C. Gilbert, *ibid.*, **63**, 1585 (1941).

(7) W. F. Seyer and C. W. Mann, *ibid.*, **67**, 328 (1945).

(8) W. F. Seyer, *ibid.*, **67**, 2281 (1945) (correction). In this connection it should be noted that in reference 7 the constants A, B and C (Table II) of the equation $\ln P = AT^{-1} + B \ln T + C$ do not correspond to the data of Table I, nor to the heats of vaporization, *cis*, 10210 cal.; *trans*, 9960 cal., calculated for these substances at their respective boiling points.

(9) F. Klages, *Ber.*, **82**, 358 (1949). Application of the above expression to the analogous case of the *cis*- and *trans*-1,2-dimethylcyclohexanes gives an estimated difference between the heats of vaporization of these substances at 25° of 227 cal. The experimentally determined value (A.P.I. Reports) is 325 cal.

DEPARTMENT OF CHEMISTRY
THE RICE INSTITUTE
HOUSTON 1, TEXAS

RECEIVED NOVEMBER 17, 1951

NEW COMPOUNDS

N-Methyl-di-β-propionyloxyethylamine[1]

To 59.6 g. (0.5 mole) of N-methyldiethanolamine was added dropwise with rapid stirring 65.1 g. (0.5 mole) of propionic anhydride. After 2 hours, when the mixture had cooled, 65.1 g. of additional propionic anhydride was added. Saturated K_2CO_3 solution was then added to the cooled reaction mixture until evolution of CO_2 had ceased. The mixture was extracted twice with ether and the ethereal solution was dried over sodium sulfate. After removal of the ether, the yellowish fluid was distilled twice under reduced pressure; distilling range, 114.8 to 115.2° (1 mm.); yield 91.5 g. (79%). The product was water-clear; $d^{29.8}_4$ 1.0072; $n^{29.1}_D$ 1.4367; R_D calcd. 60.25 cc., R_D exptl. 60.12; pK'_a 6.62 (37°).

(1) This compound was prepared in the course of work under a contract, recommended by the National Defense Research Committee between the Office of Scientific Research and Development and the Johns Hopkins University.

Anal. Calcd. for $C_{11}H_{21}NO_4$: N, 6.06. Found: (kjeldahl) N, 6.08.

This diester hydrolyzes in water in two successive steps to the monoester and to N-methyldiethanolamine, respectively, $k_1 = 0.0079$ min.$^{-1}$ and $k_2 = 0.0037$ min.$^{-1}$ at *p*H 7.4, 37°.

DEPARTMENT OF PHYSIOLOGICAL CHEMISTRY
JOHNS HOPKINS SCHOOL OF MEDICINE BARNETT COHEN
BALTIMORE 5, MD. ERVIN R. VAN ARTSDALEN

RECEIVED SEPTEMBER 21, 1951

S-(2-Methyl-1,4-naphthoquinonyl-3)-β-mercaptopropionic Acid

To a solution of 35.2 g. (0.2 mole) of 2-methyl-1,4-naphthoquinone in 800 ml. of 95% ethanol was added 21 g. (0.2 mole) of β-mercaptopropionic acid. The mixture was allowed to stand at 20° for two days at which time all of the starting material went into solution. The red brown solid remaining after removal of the solvent *in vacuo* was dissolved in 500 ml. of hot 50% alcohol. On cooling for one week an orange precipitate formed which was collected, washed with cold ether, and recrystallized from benzene to give 10 g. of bright orange needles, m.p. 161° (cor.).

The filtrate was concentrated, diluted with ether, and extracted with 10% sodium carbonate until color was no longer extracted. The alkaline extracts were extracted with 100 ml. of ether, which removed 2 g. of the starting quinone. The cooled alkaline solution was neutralized with 20% acetic acid and extracted with ether until the extract was colorless (*ca.* 500 ml.). The dark residue from this extract solidified on standing, and was dissolved in hot benzene, treated with charcoal, and twice crystallized to yield 7 g., m.p. 161° (cor.). A mixed melting point with the needles from the original reaction mixture showed no depression. The total yield of S-(2-methyl-1,4-naphthoquinonyl-3)-β-mercaptopropionic acid was 17 g. (30%). *Anal.* Calcd. for $C_{14}H_{12}O_4S$; C, 60.85; H, 4.37. Found: C, 61.23; H, 4.38.

The compound is soluble in chloroform and ether but less soluble in ethanol (5 g./liter in 95% ethanol), ligroin and benzene and insoluble in water. It has no odor when pure.

DEPARTMENT OF PHARMACOLOGY
STATE UNIVERSITY OF IOWA
IOWA CITY, IOWA CALVIN HANNA

RECEIVED DECEMBER 26, 1951

Di-(diazoacetyl) and 3,5-Dinitro-ω-diazoacetophenone

Di-(diazoacetyl).—A solution of 3 g. of oxalyl chloride in 30 ml. of absolute ether was added dropwise with ice-cooling and stirring to a solution of diazomethane (from 21.5 g. of N-nitrosomethylurea) in 250 ml. of absolute ether. After the vigorous reaction had subsided the ether was removed *in vacuo*. A red, highly lachrymatory oil with suspended yellow crystals remained. After filtration and washing with a little ether the crystals were crystallized from benzene; yield 1.2 g. (37%), m.p. 122–123° (dec.).

Anal. Calcd. for $C_4H_2N_4O_2$: C, 34.8; H, 1.5; N, 40.6. Found: C, 35.1; H, 1.8; N, 40.7.

The substance is soluble in methanol and ethanol, insoluble in water.

The nature of the remaining red oil is being investigated.

3,5-Dinitro-ω-diazoacetophenone.—A solution of 5 g. of 3,5-dinitrobenzoyl chloride in 140 ml. absolute ether was added slowly with stirring and cooling to a solution of diazomethane (from 10 g. N-nitrosomethylurea) in 100 ml. of absolute ether. After three hours standing at room temp. the reaction mixture was cooled to −10°. The yellowish crystals obtained were recrystallized from methanol; yield 2.0 g. (39%), m.p. 106° (dec.).

Anal. Calcd. for $C_8H_4N_4O_5$: C, 40.7; H, 1.7. Found: C, 41.2; H, 1.7.

DEPARTMENT OF ORGANIC CHEMISTRY
THE HEBREW UNIVERSITY MAX FRANKEL
JERUSALEM, ISRAEL M. HARNIK

RECEIVED NOVEMBER 8, 1951

COMMUNICATIONS TO THE EDITOR

PITUITARY HORMONES. III.[1] THE ISOLATION OF CORTICOTROPIN-B

Sir:

Fractionation of pepsin digests of corticotropin with oxycellulose and by countercurrent distribution has yielded a product which is approximately 300 times as active as Armour Standard La-1-A ACTH. This material, which has the highest adrenocorticotropic activity yet reported, behaves as a pure substance. It is designated corticotropin-B, since its properties are different from those of corticotropin.

Swine pituitary gland extracts of activities of about 2 to 5 u./mg.[2] were purified with oxycellulose (10% carboxyl)[3] to give corticotropin fractions active at approximately 60 to 100 u./mg. These were then digested with pepsin (3.7 mg./g.) at *p*H 2.5 for twenty-four hours at 37°. Material insoluble in 5% trichloroacetic acid solution was discarded, and after removal of excess trichloroacetic acid by ether extraction, corticotropin-B concentrates were isolated by lyophilization.

When corticotropin-B concentrates of potencies about 100 u./mg. or higher were subjected to countercurrent distributions of 200 transfers, using the system *s*-butyl alcohol/0.5% aqueous trichloroacetic acid, corticotropin-B was obtained as a major component and reproducibly characterized by a distribution coefficient of about 0.6. The acetate salt of corticotropin-B was isolated from this fraction as an amorphous white solid by the use of Amberlite IRA-400 on the acetate cycle and lyophilization. A sample was redistributed through twenty transfers in the same solvent system and the fractions analyzed by their ultraviolet absorption

(1) The first two papers of this series are, I, N. G. Brink, M. A. P. Meisinger and K. Folkers, THIS JOURNAL, **72**, 1040 (1950); and II, N. G. Brink, F. A. Kuehl, Jr., M. A. P. Meisinger, M. N. Bishop and K. Folkers, *ibid.*, **74**, 480 (1952).

(2) Preparations were assayed by a modification of the adrenal ascorbic acid depletion method of M. A. Sayers, G. Sayers and L. A. Woodbury, *Endocrinol.*, **42**, 379 (1948). Results are expressed in U. S. P. units per milligram. Because of the variations in the assay, all values must be regarded as approximate. However, key samples of highest potency were assayed repeatedly at different dose levels to eliminate large errors in the estimation of activity.

(3) E. B. Astwood, M. S. Raben, R. W. Payne and A. B. Grady, THIS JOURNAL, **73**, 2969 (1951).