procedure of Smith and Shriner[20] was followed with the results given in Table I.

2-Aroylcyclanones.—To an ether solution of 12.8 g. of sodamide (0.33 mole) was added 16.2 g. (0.165 mole) of cyclohexanone. After 5 minutes an ether solution of the desired phenyl ester (0.165 mole) was added over a period of 10 minutes and refluxed for 1.5 hours. In the case of the *p*-chloro-, *p*-fluoro-, *p*-methylbenzoates and phenyl-2-naphthoate the portions were cut in half because of the decreased solubility of the phenyl ester in ether. The reaction was then cooled in an ice-bath and carefully poured onto 300 g. of crushed ice. (There was very little danger of fire when pouring the reaction mixture onto the ice; however, rinsing the flask with water does on occasion break into flames. A good hood should be used with a fire extinguisher nearby.) Methods A and B were used to isolate the diketones.

Method A.—The ice-cold solution was immediately acidified with dilute hydrochloric acid and extracted twice with ether. The ether extracts were washed with two portions of 10% sodium bicarbonate and one portion of water. An excess of aqueous copper acetate and the extracts were vigorously shaken and allowed to stand overnight. The copper chelate was filtered and dried. Decomposition of the chelate was best carried out by shaking a mixture of ether, dilute hydrochloric acid and the copper chelate in a separatory funnel. After the copper chelate had completely dissolved the ether solution was washed with water and distilled. A small amount of methanol was added to the residue and cooled to obtain the crystalline diketone.

Method B.—The cold solution was extracted with ether, from which a small amount of the diketone was obtained after evaporation of the ether. The aqueous solution was acidified with dilute hydrochloric acid and extracted with ether. The ether was thoroughly washed with sodium bicarbonate and water and distilled to leave an oil from which more of the diketone was obtained after dilution with methanol. Some of the properties of the diketones prepared are listed in Table II.

Isolation of Keto and Enol Forms of 2-(2-Naphthoyl)-cyclo-hexanone (XXII), 2-(*m*-Chlorobenzoyl)-cyclohexanone (XX) and 2-(*p*-Fluorobenzoyl)-cyclohexanone (XXI).—Some white crystals of XXII were dissolved in ether and thoroughly shaken with a saturated solution of copper acetate at various intervals for 0.5 day. As much of the aqueous solution was separated as possible. The precipitate suspended in the ether was washed with water, filtered and dried. The chelate was then suspended in ether and thoroughly shaken with dilute hydrochloric acid. After all of the chelate had gone into solution the ether was washed with water and distilled. The remaining oil was diluted with methanol. Cooling of the methanolic solution formed white needles and white diamond-shaped crystals, which melted at 99–100°, together with yellow crystals which melted at 73.5–75°.

The yellow enol form when dissolved in methanol for one day and then cooled yielded the white crystalline keto form which melts at 98–99°. The enol form shows a maximum at 324 mμ in the ultraviolet and a broad band at 1600 cm.$^{-1}$ in the infrared region. The keto form shows a maximum at 250 mμ in the ultraviolet and sharp bands at 1714 and 1680 cm.$^{-1}$ in the infrared region. Upon addition of an alcoholic solution of ferric chloride to a methanolic solution of the yellow enol form an immediate deep violet color is formed while the addition of ferric chloride to a methanolic solution of the white keto form forms a violet color only on standing.

Diketones XXI and XX were isolated from the reaction mixture as the copper chelates. The enol form was isolated on decomposition of the chelate. The enol form XXI is a white solid which melts at 56–57°. It shows an intense maximum at 315 mμ in the ultraviolet region and a broad band at 1490–1600 cm.$^{-1}$ in the infrared. The enol form of XX is a yellow solid which melts at 44.5–45.5°. It also shows an intense maximum at 312 mμ in the ultraviolet and a broad band at 1590 cm.$^{-1}$ in the infrared. Both enols give an immediate color with ferric chloride. If the enol forms were dissolved in methanol and allowed to stand for two days, the keto forms were isolated upon cooling the solution. The keto form of XX melts at 65.5–66° and shows one maximum at 245 mμ in the ultraviolet region. The keto form of XXI melts at 56–57°, shows a maximum at 248 mμ in the ultraviolet region and shows bands at 1721 and 1684 cm.$^{-1}$ in the infrared region. Both keto forms form a violet color with ferric chloride on standing in a methanolic solution.

Acknowledgment.—The infrared spectraphotometer used in this study was purchased by the assistance of a National Science Foundation Grant.

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[20] W. T. Smith, Jr., and R. L. Shriner, "The Examination of New Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 101.

COMMUNICATIONS TO THE EDITOR

CONFORMATIONAL ANALYSIS. X. THE ENERGY OF THE BOAT FORM OF THE CYCLOHEXANE RING[1,2]

Sir:

The theoretical possibility of a cyclohexane ring existing in a boat form was recognized long ago by Sachse.[3] Recently actual compounds have been shown to exist in this form preferentially,[4,5] and they do so in each case only because of their unusual environments.

Theoretical calculations have been made of the difference in energy (actually enthalpy) between the chair and boat forms of a single simple isolated cyclohexane ring.[6–8] We wish now to report an experimental measurement of this quantity.

The compounds chosen for study were the *cis* and *trans* isomers of 1,3-di-*t*-butylcyclohexane (I). The *cis* isomer can exist comfortably in the chair form with both groups equatorial, but the *trans* isomer can exist in the chair form only if one of the *t*-butyl groups occupies an axial position. Scale models indicate a tremendous distortion with such an arrangement, which would lead to molecules of very high energy.[9] The *trans* molecules might lower their energy by going into the boat

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[1] This research was supported by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of the fund.

[2] Paper IX, N. L. Allinger and V. Zalkow, *J. Org. Chem.*, **25**, in press (1960).

[3] H. Sachse, *Ber.*, **23**, 1363 (1890).

[4] Various fused systems, such as camphor, in which the cyclohexane ring is necessarily in a boat form are, of course, well known.

[5] (a) D. H. R. Barton, D. A. Lewis and J. F. McGhie, *J. Chem. Soc.*, 2907 (1957); (b) R. E. Lyle, *J. Org. Chem.*, **22**, 1280 (1957); (c) M. V. George and G. F. Wright, THIS JOURNAL, **80**, 1200 (1958); (d) C. Djerassi, N. Finch and R. Mauli, *ibid.*, **81**, 4997 (1959).

[6] P. Hazebroek and L. J. Oosterhoff, *Discussions Faraday Soc.*, **10**, 87 (1951).

[7] N. L. Allinger, THIS JOURNAL, **81** 5727 (1959).

[8] K. E. Howlett, *J. Chem. Soc.*, 4353 (1957).

[9] S. Winstein and N. J. Holness, THIS JOURNAL, **77**, 5562 (1955).

form[10] in which the *t*-butyl groups can occupy equatorial-like positions. This was shown to be the case (see below), and consequently measurement of the equilibrium between *cis*- and *trans*-I is also a measurement of an equilibrium between the chair and boat forms. From the variation of the equilibrium constant with temperature, the enthalpy and entropy changes accompanying the isomerization were found by methods similar to those employed earlier.[11] The entropy of the cyclohexane system may be presumed to be affected, perhaps seriously, by the presence of the *t*-butyl groups, but the value found for the difference in enthalpy between the boat and chair forms in this case must be quite similar to that of any simple cyclohexane system.

A mixture of the *cis* and *trans* isomers of I was prepared by reducing 2,4-di-*t*-butylphenol using Raney nickel at 180°, then chromic acid oxidation of the mixture of alcohols, and reduction[12] of the resulting ketones.[13] Distillation of the mixture of hydrocarbons through a 4-ft. packed column gave the two isomers: *cis*-I,[13] b.p. 223.3–223.5°, n^{25}_D 1.4531; and *trans*-I,[13] b.p. 229.8–230.0°, n^{25}_D 1.4563. These isomers could be separated cleanly by vapor phase chromatography using a column of glyceryl β-tricyanoethyl ether on firebrick. At 118° the retention times were about 6 and 8 minutes for the *cis* and *trans* compounds, respectively. The analysis showed the *trans* isomer obtained was contaminated with 1.6% of the *cis* while the *cis* contained less than 0.5% *trans*. The *cis* structure was assigned to the isomer of lower enthalpy and physical constants.[14]

Equilibrium between the *cis* and *trans* isomers was established by heating small samples with palladium on carbon catalyst in sealed tubes. The resulting mixtures were analyzed by vapor phase chromatography. The results of the equilibration are given in Table I.

TABLE I

EQUILIBRIUM DATA FOR THE REACTION *cis*-1 ⇄ *trans*-1.[a]

T, °K.	492.6	522.0	555.0	580.0	613.0
% *trans*	2.69	3.61	5.09	6.42	8.23

[a] The % *trans* at any given temperature was obtained from at least eleven analyses on four different samples. Two of these samples approached equilibrium from the *cis* side, and two from the *trans* side. The temperatures are considered accurate to ±1°, and the analysis to ±0.15% *trans*.

A straight line was constructed by the method of least squares which related ln *K* to 1/*T*. From the slope and intercept of the line the values of $\Delta H = +5.9 \pm 0.6$ kcal./mole and $\Delta S = +4.9 \pm 1.0$ e.u. were calculated. This value of ΔH is in reasonable agreement with the predicted values (4.0,[8] 4.75[6] and 5.1[7] kcal./mole).

The experimental value for the entropy clearly indicates that the *trans* isomer is not in the chair form. If it were, the entropy of the reaction would be no more than +1.4 e.u.[15,16]

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[10] Theoretical considerations have indicated that the regular or classical boat form is not the energetically preferred arrangement for the conformation,[6–8] the skewed or "stretched" form is of lower energy. The expression "flexible form" has been used to mean the physically real mixture of these arrangements which is thought to exist. The expression "boat form" is used in this paper to mean the physically existing arrangement other than the chair form, and usually can be taken as synonymous with the expression "flexible form."

[11] (a) N. L. Allinger and J. L. Coke, THIS JOURNAL, **81**, 4080 (1959); (b) N. L. Allinger and J. L. Coke, *ibid.*, **82**, in press (1960).

[12] Huang-Minlon, *ibid.*, **68**, 2487 (1946).

[13] Proper carbon and hydrogen analyses have been obtained for all new compounds.

[14] N. L. Allinger, THIS JOURNAL, **79**, 3443 (1957).

[15] This value is calculated by recognizing that the *trans* isomer in the chair form is a *dl* mixture, while the *cis* is *meso*. It is a *maximum* value, since the axial *t*-butyl group would have its rotational motions restricted much more than would the corresponding equatorial group.

[16] The possibility exists that the *trans* isomer is a mixture which contains an appreciable amount of the chair form with an axial *t*-butyl group. Even if this were the case, the value found for ΔH would still apply to the boat-chair equilibrium as stated.

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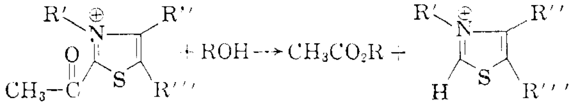
RECEIVED JANUARY 30, 1960

ON THE MECHANISM OF THIAMINE ACTION. VI.[1] 2-ACETYLTHIAZOLIUM SALTS AS "ACTIVE ACETATE"

Sir:

Implicit in the mechanism of thiamine action which we have formulated[2] is the requirement that 2-acetylthiamine be able to acetylate phosphoric acid, and thus be yet another form of "active acetate." We wish to report evidence on the kinetic lability of 2-acetylthiazolium salts (I) as support for the idea of their thermodynamic instability as well.



I

Although the weakly basic 2-acetyl-4-methylthiazole,[3,4] from oxidation of the corresponding alcohol,[1] could not be quaternized, its ketal with ethylene glycol, 2-(α-ethylenedioxyethyl)-4-methylthiazole,[3] b.p. 64° (0.15 mm.) n^{25}_D 1.5170, was reactive toward alkyl halides. The quaternary benzyl bromide salt,[3] m.p. 166–167°, was recovered in 80% yield from two days standing in 47% HBr at room temperature, but the remainder was quantitatively accounted for as 3-benzyl-4-methylthiazolium bromide. It is thus apparent that the intermediate 2-acetylthiazolium salt from this ketal hydrolysis is deacetylated by the medium, although the deacetylation of such a cation is unlikely to be acid catalyzed.

A much more striking indication of the instability of these acetyl compounds is found in the studies on 3,4-dimethyl-2-(α-hydroxyethyl)-thiazolium nitrate,[3] m.p. 133–134°, prepared from the iodide[1] by ion exchange. Oxidation of this compound with *t*-butyl hypochlorite in nitromethane, and ether precipitation of the thiazolium salts, afforded a mixture whose infrared absorption at 5.85 μ and ultraviolet absorption (in dimethoxyethane)

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[1] For part V, see R. Breslow and E. McNelis, *ibid.*, **81**, 3080 (1959).

[2] R. Breslow, *ibid.*, **80**, 3719 (1958).

[3] Satisfactory C, H and N analyses were obtained for these compounds.

[4] J. Metzger and B Koether, *Bull soc. chim. France*, 702 (1953).