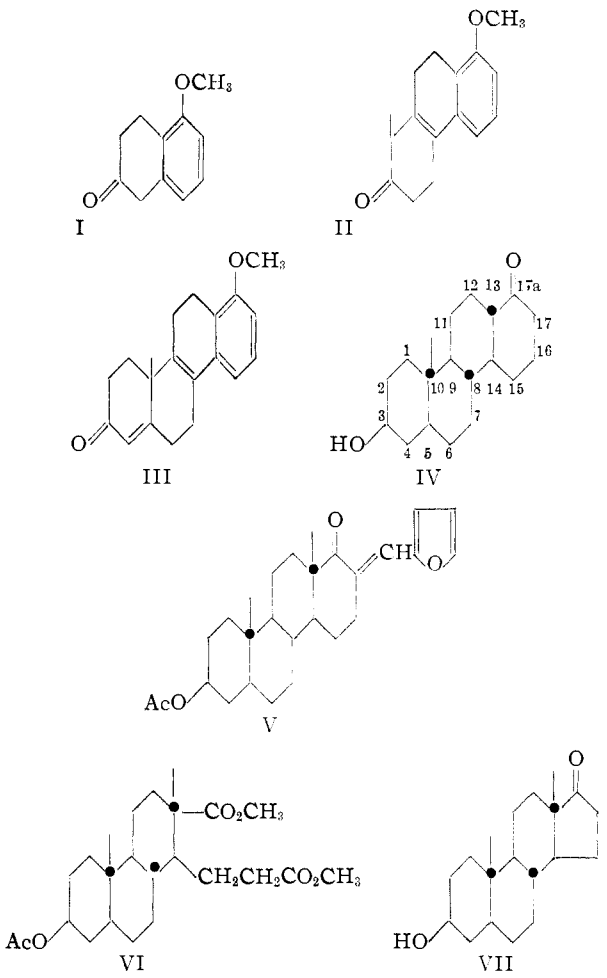

naphthalene,[2] was treated in the presence of sodium methoxide with 1-diethylamino-3-pentanone methiodide[3] followed—without isolation of the intermediary tricyclic compound II (m.p. 96.5–97°; C, 78.94; H, 7.55)—by methyl vinyl ketone[4] to produce the methoxyketomethyloctahydrochrysene III (m.p. 174.2–175°; C, 81.48; H, 7.61), which is thus very readily available in quantity. Reduction of 20 g. of III with lithium and alcohol in ammonia[5] followed by acid hydrolysis gave upon chromatography 5 g. of unsaturated ketonic material consisting of *dl*-D-homo-18-nor-13,14-dehydroepiandrosterone (IV with C=C at 13, 14) (m.p. 163.5–164°; λ_{max}^{EtOH} 248.5 mμ, log ε 4.12; C, 78.75; H, 9.78), and the 16,17-dehydroisomer (IV with C=C at 16,17) (m.p. 138–139°; λ_{max}^{EtOH} 226 mμ, log ε 3.89; C, 79.33; H, 10.27). Hydrogenation of the former, the preponderant isomer, over palladium catalyst gave, after isomerization with alkali, exclusively *dl*-D-homo-18-nor-epiandrosterone, IV (m.p. 159–161°; C, 78.50; H, 10.43). This same substance was produced directly on hydrogenation of the 16,17-dehydro ketone; hence the mixture of unsaturated ketones could be employed for production of pure IV. Only traces of other ketonic materials were formed in the lithium treatment; thus the two combined reduction steps, during which no less than six new asymmetric centers are introduced, nevertheless constitute stereospecific production of IV from III.

Condensation of IV with furfural, methylation,[6] and acetylation yielded an easily separable mixture of *dl*-17-furfurylidene-D-homoepiandrosterone acetate V (m.p. 192–192.5°; C, 76.19; H, 8.53), and the preponderant oily 13-iso ("lumi") compound (3-hydroxy compound, m.p. 88–90°; C, 78.26; H, 9.16). The infrared spectrum of the former was identical with that of V prepared from authentic D-homoepiandrosterone.[7]

Ozonolysis of *dl*-V followed by esterification with diazomethane afforded *dl*-dimethyl 3-β-acetoxyetioallohomobilianate VI (m.p. 136–137°; C, 68.12; H, 9.29) having an infrared spectrum identical with that of VI prepared by degradation of authentic epiandrosterone. Dieckmann cyclization of *dl*-VI with potassium *t*-butoxide, followed by acid hydrolysis, gave *dl*-epiandrosterone (m.p., 161–162°; C, 78.42; H, 10.49) having an infrared spectrum indistinguishable from that of authentic *d*-epiandrosterone. Resolution studies are in progress.

Similarly *dl*-13-iso-V yielded *dl*-13-iso-VI (m.p. 116.5–117.5°; C, 68.36; H, 9.29), which was converted to *dl*-lumiepiandrosterone (m.p. 157–158°; C, 78.32; H, 10.09), having an infrared spectrum identical with that of authentic lumiepiandrosterone.[8]

Studies to be reported in detail later have shown that intermediates can be obtained readily with the 11-oxygen function, and we are currently studying the application of our general scheme to the synthesis of the 11-oxygenated adrenal hormones as well as to other 11-desoxy hormones.

(2) J. W. Cornforth and R. Robinson, *J. Chem. Soc.*, 1855 (1949).

(3) *Cf.* J. W. Cornforth and R. Robinson, ref. 2.

(4) *Cf.* The Wilds method—A. L. Wilds, J. W. Ralls, W. C. Wildman and K. E. McCaleb, THIS JOURNAL, **72**, 5794 (1950)—for directing the orientation of ring addition in the Robinson-Mannich base type of reaction through the agency of a vinylogously active methyne hydrogen.

(5) These conditions differ from those generally preferred by A. J. Birch, *Quart. Rev.*, **4**, 69 (1950), in that lithium was employed according to A. L. Wilds and N. A. Nelson (in press) and a large excess of alcohol was used.

(6) The procedure of W. S. Johnson, THIS JOURNAL, **65**, 1317 (1943), was used, the 3-hydroxyl being protected from methylation as the tetrahydropyranyl ether; see C. W. Greenhalgh, H. B. Henbest and E. R. H. Jones, *J. Chem. Soc.*, 1190 (1951).

(7) Obtained from epiandrosterone by the procedure of D. A. Prins and C. W. Shoppee, *J. Chem. Soc.*, 494 (1946).

(8) J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, **34**, 2053 (1951).

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RECEIVED APRIL 6, 1953

"THERMODYNAMIC PROPERTIES OF GASEOUS DIFLUORODICHLOROMETHANE (FREON-12)": A CORRECTION

Sir:

It has been called to my attention that Fig. 3 in the paper of this title[1] gives a misleading impression of the accuracy of the data of Buffington and

(1) J. F. Masi, THIS JOURNAL, **74**, 4738 (1952).

Fleischer[2] on the gaseous heat capacity of CF_2Cl_2. While the graph in question was not intended as a direct comparison of experimental data, it seems to imply a consistent disagreement of about +1% between the Buffington and Fleischer experiments and the more recent precise values being reported. The actual comparison of experimental C_p at one atmosphere gives the deviation of the older work from that of this paper as −0.16, −0.05 and +0.78%, respectively, at 0, 25.8 and 49.9°, the temperatures of Buffington and Fleischer's measurements.

(2) R. M. Buffington and J. Fleischer, *Ind. Eng. Chem.*, **23**, 254 (1931).

NATIONAL BUREAU OF STANDARDS
WASHINGTON, D. C. JOSEPH F. MASI

RECEIVED APRIL 1, 1953

ON A PROBABLE ENZYMATIC CONVERSION OF HYDROXYCHALCONE GLYCOSIDE INTO HYDROXYBENZALCOUMARANONE GLYCOSIDE

Sir:

The co-existence of glycosides[1] of hydroxychalcones and hydroxybenzalcoumaranones in species of *Cosmos* and *Coreopsis* suggested that there may be enzymatic interconversion. Some preliminary evidence for a "Chalconase" was obtained by macerating fresh rays of *Cosmos sulphureus* or *Coreopsis lanceolata* in a glass mortar with an equal quantity of water, $^2/_5$ of McIlvaine's buffer solutions of various *p*H, and $^1/_{10}$ to $^1/_{25}$ of *M*/20 potassium cyanide. The latter was used in order to inhibit the activity of polyphenoloxidase. A hydroxybenzalcoumaranone gives a purple coloration and a hydroxychalcone gives a red one with 1 *N* sodium hydroxide solution, but the former color is apt to be obscured by the red color produced by the chalcones present. When left at *p*H 3–4 the color of the solution hardly changed; it only changed to red on the addition of sodium hydroxide solution. At *p*H 7–8 the color changed eventually to brown, owing to autoxidation in alkaline medium. The conversion of chalcone into benzalcoumaranone did not take place to any extent in these cases. However, after the mixtures were allowed to stand at *p*H 5–6, the color given by the addition of sodium hydroxide solution was strongly purple accompanied by no reddish tint, showing the complete disappearance of chalcone compound. In good accord with these observations, the brown spot of the chalcone, which was clearly visible on paper chromatograms under ultraviolet light, completely disappeared after standing at *p*H 5–6, and the golden yellow spot of the corresponding benzalcoumaranone made its appearance quite strongly. The chromatograms usually were run with *n*-butanol–acetic acid–water (4:1:1) as solvents. The time required for complete reaction was 10–15 minutes under the optimum *p*H of 5–6. This comparatively rapid conversion was effectively prevented by heating at 100° for about ten minutes.

These observations may be effected by an enzyme in the tissue of the rays. This enzyme unfortunately has not yet been extracted from the rays, owing to its insolubility in water. It is, however, at least evident that this enzyme has little to do with the usual metal-bearing oxidases which suffer severe inhibition by cyanide, although the enzyme concerned effects dehydration in the presence of oxygen.

The powder, prepared from rays after extracting several times with cold alcohol at room temperature until the anthochlor pigments were completely removed, proved to be effective in bringing about this reaction. It is very interesting to note that, when the powder thus prepared from the rays of one species was added to any chalcone glycoside isolated from other plant species, the enzymatic conversion occurred readily and apparently at the same rate and to the same degree. For example, the ray powder of *Cosmos sulphureus* proved to be active in forming benzalcoumaranone when added to the extract of the rays of *Coreopsis lanceolata*, *C. tinctoria*, *Bidens laevis* and *Dahlia variabilis*.

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RECEIVED FEBRUARY 2, 1953

ENZYMATIC REACTION OF CROTONYL COENZYME A[1]

Sir:

Evidence from various sources indicates that reactions (1),[2,3] (2)[2,4,5,6] and (3)[7] are catalyzed by soluble enzyme preparations from liver and heart.

(1) β-Hydroxybutyral-S-CoA + $DPN^+ \rightleftharpoons$ acetoacetyl-S-CoA + DPNH + H^+

(2) Acetoacetyl-S-CoA + CoA-SH $\rightleftharpoons$ 2 acetyl-S-CoA

(3) 2 Acetyl-S-CoA + 2 oxalacetate $\rightleftharpoons$ 2 citrate + 2 CoA-SH

Recent results strongly suggest the occurrence in liver and heart of an enzyme catalyzing reaction (4). The name crotonase is suggested for this enzyme.

(4) Crotonyl-S-CoA + $H_2O \rightleftharpoons$ β-hydroxybutyryl-S-CoA

(1) Supported by grants from the U. S. Public Health Service, the American Cancer Society (recommended by the Committee on Growth, National Research Council), the Williams–Waterman Fund of Research Corporation, and by a contract (N6onr279, T.O.6) between the Office of Naval Research and New York University College of Medicine. The following abbreviations are used: Coenzyme A (reduced), CoA-SH; acyl coenzyme A derivatives, acyl-S-CoA; oxidized and reduced diphosphopyridine nucleotide, DPN^+ and DPNH; adenosine triphosphate, ATP; μM, micromoles; TRIS, *tris*-(hydroxymethyl)-aminomethane.

(2) F. Lynen, L. Wessely, O. Wieland and L. Rueff, *Angew. Chem.*, **64**, 687 (1952).

(3) J. R. Stern, M. J. Coon and A. del Campillo, THIS JOURNAL, **75**, 1517 (1953).

(4) E. R. Stadtman, M. Doudoroff, and F. Lipmann, *J. Biol. Chem.*, **191**, 377 (1951).

(5) J. R. Stern, M. J. Coon and A. del Campillo, *Nature*, **171**, 28 (1953).

(6) D. Goldman, *Federation Proc.*, **12**, 209 (1953).

(7) S. Ochoa, J. R. Stern and M. C. Schneider, *J. Biol. Chem.*, **193**, 691 (1951).

(1) M. Shimokoriyama, and S. Hattori, THIS JOURNAL, **75**, 1900 (1953).