

that the cohesive energy of a mole of mixture is given by the expression. . . ." In my original paper the justification of this expression was, "For non-ideal solutions also we shall neglect the change in volume, and we shall consider only the case in which the interaction between any pair of molecules is independent of the composition. We may then split the cohesive energy of a mole of the mixture in the following way. . . ."<sup>1</sup> The second statement is, therefore, not arbitrary, but depends on the first, which still appears to me to contain all the necessary assumptions. The statement of them is, however, extremely brief and a fuller statement has been published only in a journal so inaccessible to American readers that it seems worth while to quote: "(1) *The volume change on mixing is zero. (2) The mutual energy of any two molecules depends only on the distance between them and their relative orientation, but not at all upon the kind of matter between or around them. (3) The distribution of the molecules in position and in orientation is random.*"<sup>5</sup> Except for the explicit statement of the second assumption, I can therefore find no difference between my assumptions and those of Hildebrand and Wood.

(5) G. Scatchard, *Kemisk Maanedstidende* (Copenhagen), **13**, 77 (1932).

CONTRIBUTION No. 330                          GEORGE SCATCHARD  
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RECEIVED JANUARY 24, 1934

Sir:

I am glad to acknowledge the above correction by Professor Scatchard concerning the variability with temperature of the constant "A" of his equation. I might attempt to give a justification of my interpretation of his language but that would have little point. The paper by Negishi, Donnally and Hildebrand, although published later than that of Hildebrand and Wood, was written much earlier, when Professor Scatchard's intentions were less clearly discernible from his very brief presentation than they became upon fuller examination.

I would like to emphasize that the slight temperature trends in the values of "A" shown by the solubility data we presented seem to me far less important than the remarkable agreement they show with the values calculated from the data for the pure components, which should be a source

of satisfaction to Professor Scatchard. The constant "k" in my earlier equation is less significant theoretically than the "A" and is interesting now chiefly as a simple semi-empirical method practically applicable to many solutions.

The point made by Professor Scatchard concerning our Equation 8 is correct. We neglected to designate the "a" therein by type differentiating it from the "a" in Equation 7, which is his; if this is done it does not differ from 7.

In designating as an "arbitrary assumption" the particular equation referred to in the last paragraph of the above communication I did not intend to imply that it might not have a logical basis in Professor Scatchard's mind, but rather that the single sentence with which it was introduced could serve to a reader as but a slender basis for it, less convincing even than the derivation on the basis of the van der Waals equation, offered by van Laar in his prior publication of essentially the same equation. I have no quarrel with the equation itself, and I hope that this communication will remove any suspicion that Professor Scatchard and I differ in any important respects in our views regarding the validity of the methods we have both utilized.

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#### AN IRON COMPOUND OF GLUCONIC ACID

Sir:

In attempting to prepare a new iron compound, more suitable for the treatment of secondary anemia than the preparations now in use, we have been investigating the possibility of combining iron with certain polyhydroxy acids.

When 3 moles of calcium gluconate, dissolved in hot water, was treated with a solution of 1 mole of ferric sulfate, a reaction occurred with the formation of an almost quantitative amount of calcium sulfate. A normal salt, ferric gluconate, could have been expected, but, when the solution was filtered and the filtrate precipitated with four volumes of alcohol, the resultant compound was found to contain 19.6% of iron instead of the 8.7% calculated for the normal salt. Repeated experiments gave the same result. The reaction takes place quite as readily when both ingredients are suspended in water and the suspension is heated.

The purified compound was obtained in the form of light yellow amorphous powder, easily soluble in water, and stable in solution as well as in solid form. When it is exposed for a long time to the action of direct sunlight, it changes its color from yellow to greenish-gray. The solution is yellow in color when dilute, cherry-red when concentrated, and has a ferruginous taste. It is acid to litmus, and can be neutralized and even made distinctly alkaline to litmus by adding sodium carbonate or sodium hydroxide, without precipitating iron. When the solution was titrated with sodium hydroxide, using an external indicator, the amount of alkali closely corresponded to the amount necessary for the formation of a sodium salt of basic ferri-gluconic acid, which can be isolated from a neutralized solution by precipitation with alcohol. The usual quantitative tests show that the iron in our compound is in ferric condition.

Elementary analysis and other experimental evidence suggests that the compound is a basic ferri-gluconic acid rather than one in which the iron is attached to the chain with all three valences, as in the complex iron and barium compounds of certain polyhydroxy alcohols and acids prepared by Traube, Kuhbier and Harting [*Ber.*, **66**, 1545 (1933)].

*Anal.* Calcd. for  $C_6H_{13}O_9Fe$ : C, 25.28; H, 4.60; Fe, 19.61. Found: C, 25.86; H, 4.61; Fe, 19.60.

The position of the iron in the chain is as yet not definitely determined. There is evidence of intermediate compounds containing sulfur being formed in the course of the reaction, the mechanism of which we continue to study.

Clinical tests of the compound have proved it to be of definite value in the treatment of secondary anemia.

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RECEIVED FEBRUARY 19, 1934

#### THE VALIDITY OF FREUDENBERG'S DISPLACEMENT RULE

Sir:

The importance of Freudenberg's displacement rule, especially as it is founded on optical dispersion and absorption spectra, cannot be over-emphasized; for it permits the determination of the optical configuration of such substances

as  $\alpha$ -chloropropionic acid [W. Kuhn, Freudenberg and Wolf, *Ber.*, **63**, 2367 (1930)] and methyl-tertiary-butylcarbinol [Stevens, *THIS JOURNAL*, **55**, 4237 (1933)] when direct chemical methods fail due either to Walden inversion or to rearrangement.

Recently Levene and Meyer [*ibid.*, **56**, 244 (1934)] reported to have found two legitimate exceptions to the displacement rule. Obviously, any such exceptions would throw doubt on the validity of the configurations of the substances mentioned above. For this reason the pertinent part of Levene and Meyer's work has been carefully repeated with the result that their first exception has been found to be incorrect.

TABLE I  
[M]<sub>D</sub><sup>25</sup>

	Free acid	Ethyl ester	<i>p</i> -Nitrophenyl ester
1 $C_2H_5-CH[CH_3]-COOH$	-18.0	-22.9	-52.5
2 $C_4H_9-CH[CH_3]-COOH$	-24.3	-30.7	-65.7
3 $C_2H_5-CH[CH_3]-CH_2-COOH$	-10.4	-11.5	-20.0
4 $C_2H_5-CH[CH_3]-CH_2-COOH$	+ 3.6	+ 0.7	+ 5.0
5 $C_3H_{11}-CH[CH_3]-CH_2-COOH$	+ 8.1	+ 4.2	+11.2

The table contains the values found by Levene and Meyer for the rotations of five configurationally related acids and esters. The corrected value as determined by the author for the rotation of the *p*-nitrophenyl ester of methylpropylpropionic acid [No. 4 in table] is in bold-faced type. According to this corrected value, the shift in rotation, as evidenced by the change in sign on passing from the ethyl to the *p*-nitrophenyl ester is in complete accord with the displacement rule.

An investigation of Levene and Meyer's second exception, that of methylamylpropionic acid and esters [No. 5 in table] is now in progress.

**Levo  $\beta$ -Methyl- $\beta$ -propylpropionic Acid.**—The acid was prepared from 2-bromopentane and ethyl malonate and resolved with cinchonidine according to the directions of Levene and Marker [*J. Biol. Chem.*, **91**, 77 (1931)]. After resolution the acid was dissolved in aqueous sodium carbonate and washed with alcohol-free ether. The solution was then acidified, and the acid extracted with alcohol-free ether: b. p. (17 mm.) 113.5–114.5°, (bath 150°). This material was redistilled: b. p. (14 mm.) 109.0–109.5° (bath 142°),  $\alpha_D^{25}$  -1.53°, [M]<sub>D</sub><sup>25</sup> -2.19°,  $d_4^{25}$  0.9111,  $n_D^{25}$  1.4190, *Molecular Refraction*. Calcd. 36.06; found 36.06.

**Dextro *p*-Nitrophenyl Ester of Levo  $\beta$ -Methyl- $\beta$ -propylpropionic Acid.**—Ten grams of the acid [ $\alpha_D^{25}$  -1.53°] was treated with 30 cc. of redistilled thionyl chloride. The mixture was boiled for two hours on the steam-bath, and then allowed to stand overnight. The next morning the excess thionyl chloride was removed *in vacuo*. Dry