A Brief History of the Chemistry of Ether

The Benedictine Monk Basil Valentine (Johann Thölde) (FL. 1604)

Who prepared muriatic acid (hydrochloric acid) by the action of oil of vitriol (sulfuric acid) on marine salt, prepared muriatic ether (ethyl chloride).

"This I also say that, when the spirit of common salt (HCl) unites with the spirit of wine (ethanol), and is distilled three times, it becomes sweet, and it loses its sharpness."

Roscoe and Schorlemmer, Treatise on Chemistry, Vol. III, Pt. I, 1884, pg. 342.

Valerius Cordus
(1515-1544)

b. Siemershausen, Hesse, 1515

Baccalaureate, Marburg, 1531

Doctorate, Wittemberg ?

lectures on Pedanius Dioscorides (c. 40-c. 90)

Joachim Ralla, Leipzig,
apothecary
Botanical Specimens of Germany
1535-1540

Distillation ?

Dispensatorium published, 1546

Botanical Studies in Italy
1542-1544
Dies of malaria

De artificiosis extractionibus
Gesner edits Cordus's works,
1561

Leake, C. D., Valerius Cordus and the Discovery of Ether, *Isis*. **1925**, *7*, 14-24.

"...Equal parts of thrice rectified spirit of wine (ethanol) and oil of vitriol are allowed to remain in contact for two months, and then the mixture is distilled from a water or sand bath. The distillate consists of two layers of liquid, of which the upper one is oleum vitrioli dulce verum."

Roscoe and Schorlemmer, Treatise on Chemistry, Vol. III, Pt. I, 1884, pg. 342.

oleum vitrioli dulce verum

floats on water
volatile
} ether

oily "pinque"
spoiled "perdit" by water
} diethyl sulfate

Robinson, T. On the nature of sweet oil of vitriol. *J. Hist. Med.* **1959**, *14*, 231-233.

A rose by any other name ...

Oleum vitrioli dulce (verum)

Valerius Cordus (1515-1544)

Aqua Lulliana

Raimondus Lullius (~1232-1315)

Oleum dulce Paracelsi

Philippus Aureolus Paracelsus
Theophrastus Bombastus (1493-1541)

"…it [that sulfur] is the most notable of all of the extracts of vitriol… Moreover, it possesses an agreeable taste; even chickens will eat it, whereupon they sleep for a moderately long time and reawaken without having been injured.…" Leake, C.D., loc cit.

Liquor anodyni mineralis Hoffmannii

F. Hoffmann (1660-1742)

Mémoire sur les Ethers composés

Par MM. J. Dumas et P. Boullay fils.

Ann. Chim. Phys. **1828**, *37*, 15.

1 vol. vapeur d'éther, { 2 vol. hydrog. bi-carboné.
1 vol, vapeur d'eau.

1 vol. vapeur d'alcool, { $\frac{1}{2}$ vol. vapeur d'éther.
$\frac{1}{2}$ vol. vapeur d'eau.

1) EtOH = CH_2=CH_2 + H_2O

2) Et_2O = 2 CH_2=CH_2 + H_2O

$$d = g/V = mP/RT$$

3) EtOH = 1/2 Et_2O + 1/2 H_2O

The Etherin Theory

Mémoire sur les Ethers composés

Par MM. J. Dumas et P. Boullay fils.
Ann. Chim. Phys. **1828**, *37*, 15.

Acétate d'ammoniaque hydraté.	$2\ Az\ H^3$	$H^6\ C^4\ O^3$	$\dot{H}\ H$
Acétate d'hydr. bi-carb. hydraté (*éther acétique*).	$4\ H^2\ C^2$	$H^6\ C^4\ O^3$	$\dot{H}\ H$

$C^4H^{14}N^2O^4 = C^2H^7NO^2$ $C_2H_7NO_2$

$C^{12}H^{16}O^4 = C^6H^8O^2$ $C_4H_8O_2$

$C(6)^8C(12)^4H^{16}O^4 = C(6)^4C(12)^2H^8O^2$ $C(12)_4H_8O_2$

"Acidic" carbons, C = 12; "Basic" carbons, C = 6.

On Sixes and Twelves

"One Christmas was so much like another, in those years around the sea-town corner now and out of all sound except the distant speaking of the voices I sometimes hear a moment before sleep,

that I can never remember whether it snowed for six days and six nights when I was twelve or whether it snowed for twelve days and twelve nights when I was six."

"A Child's Christmas in Wales" --- Dylan Thomas

The Etherin Theory

Applied to Ether and Ethanol

Hydrate d'hydr. bi–carb. bi-basique (*éther sulfu-rique*).	$4\,H^2\,C^2$	....	$\dot{H}\,H$
Hydrate d'hydr. bi-carb. (*alcool*)...............	$4\,H^2\,C^2$	....	$2\,\dot{H}\,H$

$$C^8H^{10}O = C(6)^8H^{10}O = C(12)^4H^{10}O = C_4H_{10}O$$

$$C^8H^{12}O^2 = C(6)^4H^6O = C(12)^2H^6O = C_2H_6O$$

"Basic" carbons have C = 6

The Etherin Theory

Applied to Glucose and Sucrose

Bi-carbonate d'hyd. bi-carb. hydraté (*sucre de cannes*)...............	$4\,H^2\,C^2$	$4\,\dot{C}$	$\dot{H}\,H$
Bi-carbonate d'hydr. bi-carb. bi-hydraté (*sucre de raisins*)...............	$4\,H^2\,C^2$	$4\,\dot{C}$	$2\,\dot{H}\,H$

Glucose $C(6)^{12}H^{12}O^{6}$ = $C(12)^{6}H^{12}O^{6}$ = $C_6H_{12}O_6$

Sucrose $C(6)^{12}H^{10}O^{5}$ = $C(12)^{6}H^{10}O^{5}$ = $C_{12}H_{22}O_{11}$

$8\,C^2H^2 + 8\,CO + 3H_2O = C(6)^{24}H^{22}O^{11}$ or $C(12)_{12}H_{22}O_{11}$

All carbons have C = 6!

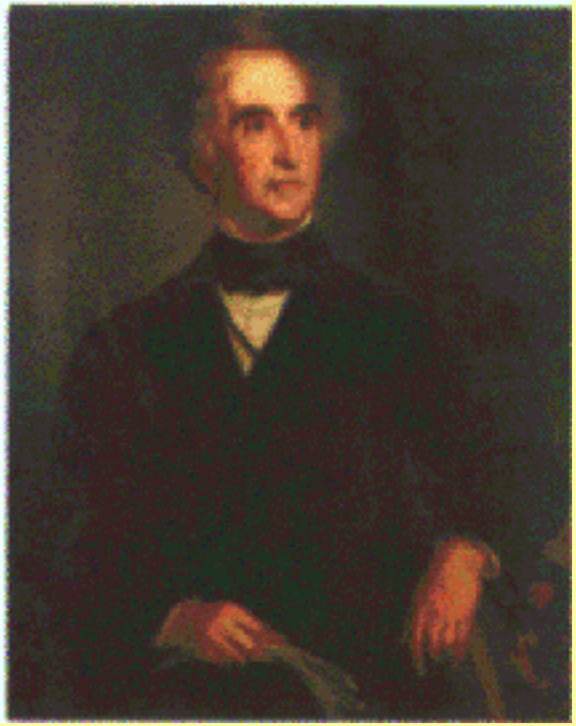
Sucrose is Formed from Glucose and Fructose

This discussion brings to mind a wonderful story told to me by Professor Harry Wasserman (Yale), who during the late 1940's was a graduate student of Professor R. B. Woodward at Harvard. Apparently Woodward had received a notice of a $1,000 prize for the first person to accomplish a chemical synthesis of sucrose. He went into the laboratory and said to his students that all they had to do was connect two molecules of glucose together [...and lose a molecule of water] and they would have themselves $1,000. One student, obviously not overwhelmed by Woodward's stature in the field even at such a young age, replied that if you did it that way,

the prize would be $2,000!

Ueber die Constitution des Aethers und seiner Verbindungen

J. Liebig, *Ann. Pharm.*, **1834**, *9*, 1.



Justus Liebig
1803-1873

*) $C_4H_8 + H_2O$ = Aether.

$C_4H_8 + 2\,H_2O$ = Alcohol.

$(C_4H_8 + H_2O) + \overline{A}$ = Essigäther.

$C_4H_8 + 2\,ClH$ = leichter Salzäther.

$C_4H_8 + 2\,SO_3$ = Weinschwefelsäure.

$2\,C_2H_4 + 2\,CO_2 + H_2O$ = Rohrzucker.

$2\,C_2H_4 + 2\,CO_2 + 2\,H_2O$ = Traubenzucker.

Liebig on Dumas

subscripts

double formulas

H =1, C =12, O =16

Liebig's Ethyl Radical Theory (1834)

C_4H_{10}	E = Radikal des Aethers = C_4H_{10}
$C_4H_{10}O$	E + O = Aether
	E + 2O = Holzgeist
$C_4H_{12}O_2 = C_2H_6O$	EO + H_2O = Hydrat (Alcohol)
$C_4H_{10}Cl_2 = C_2H_5Cl$	E + Cl_2 = Chlorur (Chlorwasserstoffäther)
	E + I_2 = Iodur (Iodwasserstoffäther)
	E + B_2 = Bromur
	E + S = Sulfur?
$C_4H_{10}O + C_2O_3 = C_6H_{10}O_4$	EO + Ox = Oxalat (Oxaläther)
	EO + BO_3 = Benzoat (Benzoeäther)
	EO + N_2O_3 = Nitrit (Salpeteräther)
$C_4H_{10}O + C_4H_6O_3 = C_8H_{16}O_4 = C_4H_8O_2$	EO + $\bar{A}$ = Acetat (Essigäther)
	3EO + $\bar{A}$ = Acetal
	(EO + H_2O) + 2SO_3 = Weinschwefelsäure

Ethyl Radical Theory

Sucrose and Glucose

Rohrzucker . . .	$= 4CO_2 + 2EO + H_2O$
Kryst. Milchzucker	
Schleimsäure . . .	$= C_6H_{10}O_8$ . . . . .
Traubenzucker . .	$= 4CO_2 + 2EO + 4H_2O$

Sucrose $4CO_2 + 2C_4H_{10}O + H_2O = C_{12}H_{22}O_{11}$!

Glucose $4CO_2 + 2C_4H_{10}O + 4H_2O = C_{12}H_{28}O_{14} = C_6H_{14}O_7$

$4CO_2 + 2C_4H_{10}O + 2H_2O = C_{12}H_{24}O_{12} = C_6H_{12}O_6$!

Liebig and Wöhler

Friedrich Wöhler
1800-1882

Justus Liebig and Friedrich Wöhler, the latter of urea synthesis fame (1828), published a landmark paper in 1832 on the chemistry of the benzoyl radical. Liebig had invited Wöhler to collaborate with him in his laboratory in Giessen upon the death of Wöhler's wife.

Although the two were close friends, their personalities were quite opposite, a 19th century odd couple so to speak. Wöhler's wise counsel to Liebig follows:

" To make war upon Marchand (or any one else for that matter) is of no use. You merely consume yourself, get angry, and ruin your liver and your nerves --- finally with Morrison's Pills. Imagine yourself in the year 1900, when we shall both be decomposed again into carbonic acid, water, and ammonia, and the lime of our bones belongs to the dog who then dishonors our grave. Who then will care whether we lived in peace or in strife? Who then will care anything about your scientific controversies --- of your sacrifices of health and peace for science? No one: but your good ideas, the new facts you have discovered, these, purified from all that is unessential, will be know and recognized in the remotest times. But how do I come to counsel the lion to eat the sugar!"

F. J. Moore, A History of Chemistry, ***1918****, pg. 124.*

The Theory of Types to 1849

Dumas (1840) — Substitution and the "Older Type Theory"

$$C_2H_4O_2 \xrightarrow{3Cl_2} C_2HCl_3O_2$$

Gerhardt (1839) — Double Decomposition and Residues

$$C_6H_5H + HNO_3 \longrightarrow C_6H_5NO_2 + H_2O$$

Gerhardt (1848) — Unitary Theory

Wurtz (1849) — Primary amines, the Ammonia Type

Type Theory

1850 - The ammonia type

$$N\left\{\begin{matrix} H \\ H \\ H \end{matrix}\right. \qquad N\left\{\begin{matrix} C_2H_5 \\ H \\ H \end{matrix}\right.$$

$$N\left\{\begin{matrix} C_2H_5 \\ C_2H_5 \\ H \end{matrix}\right. \qquad N\left\{\begin{matrix} C_2H_5 \\ C_2H_5 \\ C_2H_5 \end{matrix}\right.$$

Gerhardt's Four Types - 1853

$N\left\{\begin{array}{l}H\\H\\H\end{array}\right.$	$O\left\{\begin{array}{l}H\\H\end{array}\right.$	$\left\{\begin{array}{l}H\\Cl\end{array}\right.$	$\left\{\begin{array}{l}H\\H\end{array}\right.$
ammonia	**water**	**hydrochloric acid**	**hydrogen**
$N\left\{\begin{array}{l}C_2H_5\\H\\H\end{array}\right.$	$O\left\{\begin{array}{l}C_2H_5\\H\end{array}\right.$	$\left\{\begin{array}{l}C_2H_5\\Cl\end{array}\right.$	$\left\{\begin{array}{l}C_2H_5\\H\end{array}\right.$
ethylamine	**ethanol**	**ethyl chloride**	**'ethyl hydride'**

The Water Type
(1850-1852)

"The following experiments were made with the view of obtaining new alcohols, by substituting carburetted hydrogen for hydrogen in a known alcohol."

Alexander Williamson
(1824-1904)

"Iodide of potassium was readily formed on the application of a gentle heat, and the desired substitution was effected; but, contrary to expectation, the compound thus formed had none of the properties of an alcohol -- it was nothing else than common ether, $C_4H_{10}O$."

Theory of Etherification, *J. Chem. Soc.*, **1852**, *4*, 106.

The Water Type

1850 - 1852

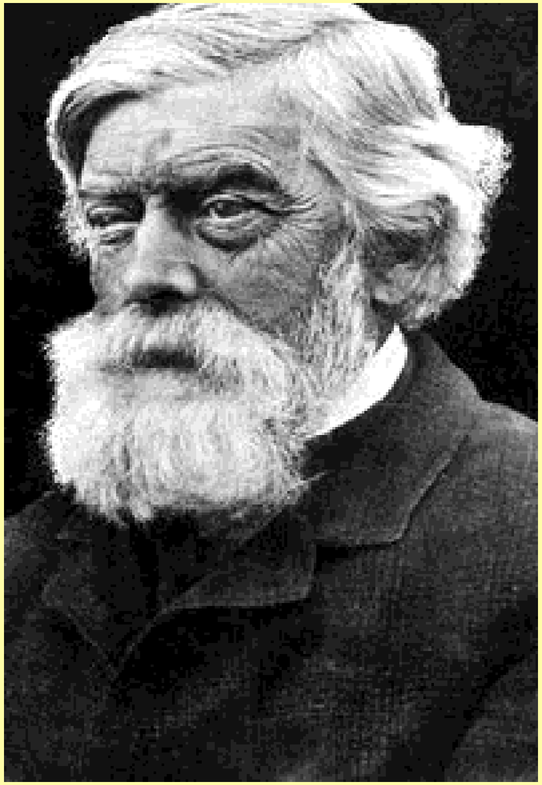
$$O\left\{\begin{matrix} C_2H_5 \\ K \end{matrix}\right. + \left\{\begin{matrix} C_2H_5 \\ I \end{matrix}\right. \not\longrightarrow O\left\{\begin{matrix} C_4H_9 \\ H \end{matrix}\right. + KI$$

butyl alcohol

butyl alcohol

$$O\left\{\begin{matrix} C_2H_5 \\ K \end{matrix}\right. + \left\{\begin{matrix} C_2H_5 \\ I \end{matrix}\right. \longrightarrow O\left\{\begin{matrix} C_2H_5 \\ C_2H_5 \end{matrix}\right. + KI$$

ether



Alexander Williamson (1824-1904)

The Williamson Ether Synthesis

$$\begin{matrix} C^2\,H^5 \\ K \end{matrix}\ O + C^2\,H^5\,I = IK + \begin{matrix} C^2\,H^5 \\ C^2\,H^5 \end{matrix}\ O.$$

$$C_2H_5OK \quad + \quad C_2H_5I \quad = \quad KI \quad + \quad C_4H_{10}O$$

$$C_2H_5OH \quad + \quad C_2H_5OH \quad = \quad H_2O \quad + \quad C_4H_{10}O$$

Dumas

$EtOH = 1/2\ Et_2O + 1/2\ H_2O$

Liebig

"EO_2H_2" $= H_2O + EO$
($E = C_4H_{10}$)

Williamson's Experiment
Interpreted by the Older Theory

Older Theory:

Half of the ether is preformed; half not.

$$\begin{matrix} C^4 H^{10} O \\ K^2 O \end{matrix} + C^4 H^{10} I^2 = 2\, IK + 2\,(C^4 H^{10} O).$$

Williamson Theory:

Each reactant contributes half of the carbons in ether.

$$\left.\begin{matrix} C^2 H^5 \\ K \end{matrix}\right\} O + C^2 H^5 I = IK + \left.\begin{matrix} C^2 H^5 \\ C^2 H^5 \end{matrix}\right\} O.$$

Williamson's Reasoning

"But although the insufficiency of this explanation [i.e., the older theory] becomes evident on a little reflection, I devised a further and more tangible method of arriving at a conclusion. It consisted in acting upon the potassium compound (i.e., $C^4H^{10}O.K^2O$) by iodide of methyl, in which case I should, if that compound ($C^4H^{10}O.K^2O$) were ether and potash, the resulting mixture should consist of ether ($C^4H^{10}O$) and oxide of methyl (C^2H^6O); whereas, in the contrary case, [i.e., Williamson's formulation] a body of the composition C^3H^8O should be formed. Now this substance was actually obtained, and neither ether nor oxide of methyl."

<u>Theory of Aetherification</u>, *Philosophical Magazine 37, 350 (1850).*

How to Distinguish Between the Two Theories?

$$\begin{matrix}C^4H^{10}O\\ K^2O\end{matrix} + C^4H^{10}I^2 = 2\,IK + 2\,(C^4H^{10}O).$$

$$\begin{matrix}C^4H^{10}O\\ K^2O\end{matrix} \quad + \quad C^4H^{10}I^2 \quad = \quad 2IK \quad + \quad \begin{matrix}C^4H^{10}O\\ C^4H^{10}O\end{matrix}$$

$$\left.\begin{matrix}C^2H^5\\ K\end{matrix}\right\} O + C^2H^5I = IK + \left.\begin{matrix}C^2H^5\\ C^2H^5\end{matrix}\right\} O.$$

$$\begin{matrix}C^2H^5 & \\ & O\\ K & \end{matrix} \quad + \quad C^2H^5I \quad = \quad IK \quad + \quad \begin{matrix}C^2H^5 & \\ & O.\\ C^2H^5 & \end{matrix}$$

The Williamson Experiment

$C^4H^{10}O$ + $C^2H^6I^2$ = 2IK + $C^4H^{10}O$ ethyl ether
K^2O C^2H^6O methyl ether

Ethylate of methyl:

C^2H^5 C^2H^5
O + CH^3I = IK + O.
K CH^3

Methylate of ethyl: } identical

CH^3 C^2H^5
O + C^2H^5I = IK + O.
K CH^3

Conclusions:

1) Ethyl is not C_4H_{10} but rather C_2H_5

2) Methyl is not C_2H_6 but rather CH_3

3) The two residues "R" in ethers are equivalent.

4) Water is HOH; alcohol is ROH; ether is ROR'

5) The water type is defined:

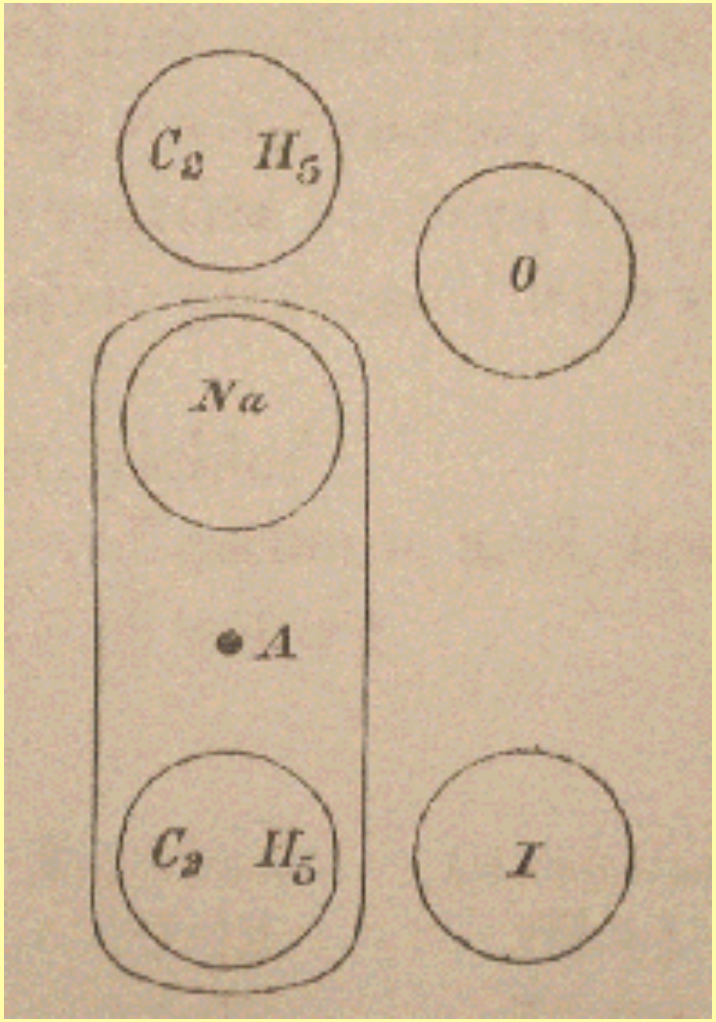
$$\left.\begin{matrix}H\\H\end{matrix}\right\}O \qquad \left.\begin{matrix}R\\H\end{matrix}\right\}O \qquad \left.\begin{matrix}R\\R'\end{matrix}\right\}O$$

6) In the formation of an ether each reactant contributes one carbon group.

The First Mechanism of a Chemical Reaction?

"The reaction is easily understood by the following diagram, in which the atoms C^2H^5 and Na are supposed to change places by turning round upon the central point A."

<u>On Etherification</u>, A. W. Williamson, *J. Chem. Soc.*, **1852**, *4*, 229.



What of Valerius Cordus?

$$\frac{\begin{matrix}H\\H\end{matrix}\ SO^4}{\begin{matrix}C^2H^5\\H\end{matrix}\ O} = \frac{\begin{matrix}H\\C^2H^5\end{matrix}\ SO^4}{\begin{matrix}H\\H\end{matrix}\ O}.$$

"...it consists in stating the fact, that sulphuric acid and alcohol are transformed into sulphovinic acid and water, by half the hydrogen of the former changing places with the carburetted hydrogen of the latter; …"

and ...

$$\frac{\begin{matrix}H\\C^2H^5\end{matrix}\;SO^4}{\begin{matrix}H\\C^2H^5\end{matrix}\;O} = \frac{\begin{matrix}H\\H\end{matrix}\;SO^4}{\begin{matrix}C^2H^5\\C^2H^5\end{matrix}\;O}.$$

"The sulphuric acid thus reproduced comes again in contact with alcohol, forming sulfovinic acid, which reacts as before; and so the process goes on continuously, as found in practice."

Theory of Etherification, *J. Chem. Soc.*, **1852**, *4*, 106.

Williamson's, the Proper Victorian, Rebuttal to Kolbe's Williamson's Theory of of Water, Ethers, and Acids.

"It thus becomes incumbent on me to offer a few further remarks on the subject; and in analysing his [Kolbe's] arguments, I shall unavoidably be led to explain, more particularly than I wish to do, the characteristic defects and errors of Dr. Kolbe's theoretical notions, to which his original misconception was owing. As the discussion is of Dr. Kolbe's own seeking, he will of course not be offended at my freedom in criticising his views."

On Dr. Kolbe's Additive Formulas, A. Williamson, *J. Chem. Soc.*, **1852**, *4*, 122.

The End