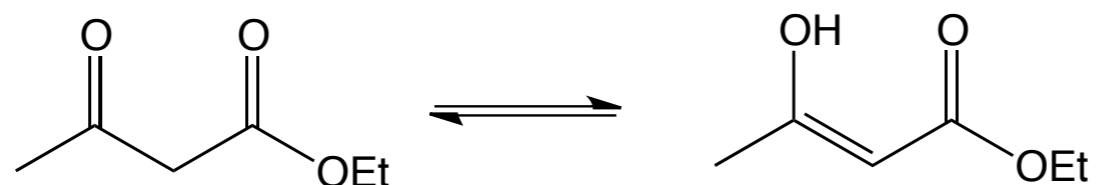


The Electronic Theory of Organic Reactions, 1922-1953

A New Set of Issues for Organic Chemists

- Can we explain chemical change?
- What causes tautomerism?

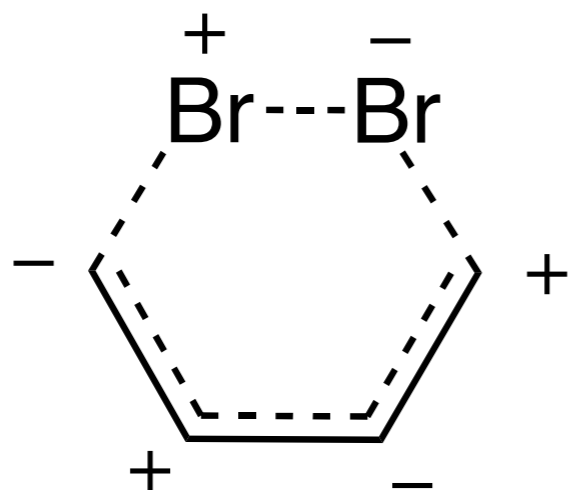


- Why do conjugated systems behave so strangely?
- Are physical methods relevant to organic chemistry?
- Reductionism: How should chemistry be affected by the new model of the atom?

Robert Robinson (1886-1975)



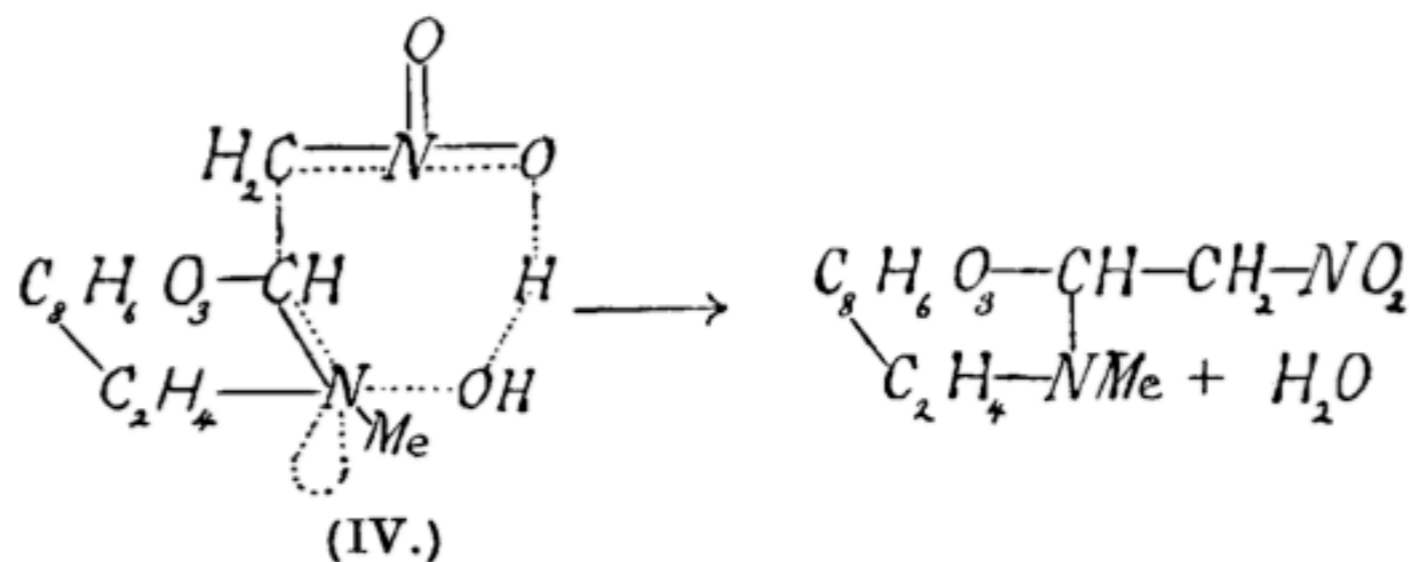
Robinson and Residual Valences



- Lapworth's polarities
- Thiele's dotted affinities
- Polarization of bonds in the intermediate complex
- No "extra" affinities, but "split" or fractional bonds.

Robinson and Residual Valences

In the case of a condensation between a pseudo-base and pseudo-acid, the theory of the reaction between ions demands two intramolecular changes, but on the hypothesis now advanced the carbon to carbon synthesis occurs in the first stage of the process and migrations are not required. This is illustrated in the case of anhydrocotarninenitromethane, and it will be seen that the *aci*-modification of nitromethane and the ammonium hydroxide form of cotarnine yield a complex (IV) in which there may be a change in affinity distribution which results in the separation of water and the production of anhydrocotarninenitromethane.

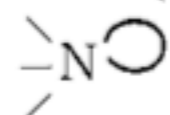


Gertrude Maud Robinson and Robert Robinson, "Researches on Pseudo-Bases. Part II. Note on Some Berberine Derivatives and Remarks on the Mechanism of the Condensation Reactions of Pseudo-Bases," *Journal of the Chemical Society*, 111 (1917): 958-69

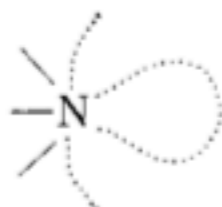
The Conjugation of Partial Valencies

DURING the past five years the author has made use of a hypothesis which has appeared to simplify the representation of the possible mechanism of reactions in certain isolated cases, and the object of the present communication is to indicate some of the lines along which the theory may receive more general application. The necessary condition precedent to chemical change is assumed to be the "activation" of one or more of the molecules taking part in the reaction; this is followed by cohesion and rearrangement of valencies, most probably synonymous with changes in position of electrons. The result is either molecular rearrangement, the formation of an additive product or of new substances by fission of the complex. The activated molecules are further assumed to be polarised and to contain partially dissociated valencies. Thus H-Cl is supposed to be chemically inert, the molecule absorbs energy and becomes H . . . Cl . . . which is the reactive form termed partially dissociated because it is a stage towards complete ionisation. In thus splitting a valency it is always understood that the two or more dotted lines, though not necessarily themselves of equal value, are quantitatively equivalent in the sum to the normal unit valency from which they have been derived and the polar character of all these fractional valencies is identical. It is possible to allocate definite signs to the partial valencies in most cases as the result of a consideration of the relative polarities of atoms evinced for example in the limiting case of true electrolytic dissociation.

A significant exception to the rule that partial valencies of similar sign emanate from the same atom at the same time exists in the case of those elements which exhibit latent valencies such as trivalent nitrogen. A neutral nitrogen

atom is represented thus:— 

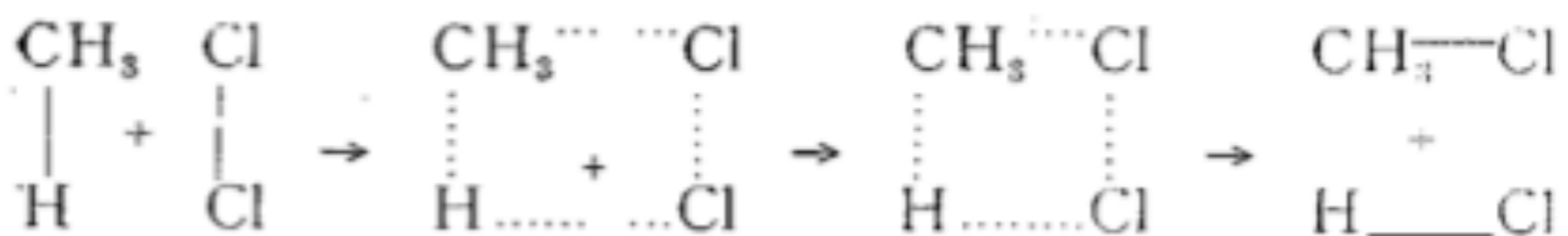
and the loop, it is supposed, can be opened up in stages with the result that two partial valencies of opposite sign are produced. This condition of affairs may be expressed by the symbol:—



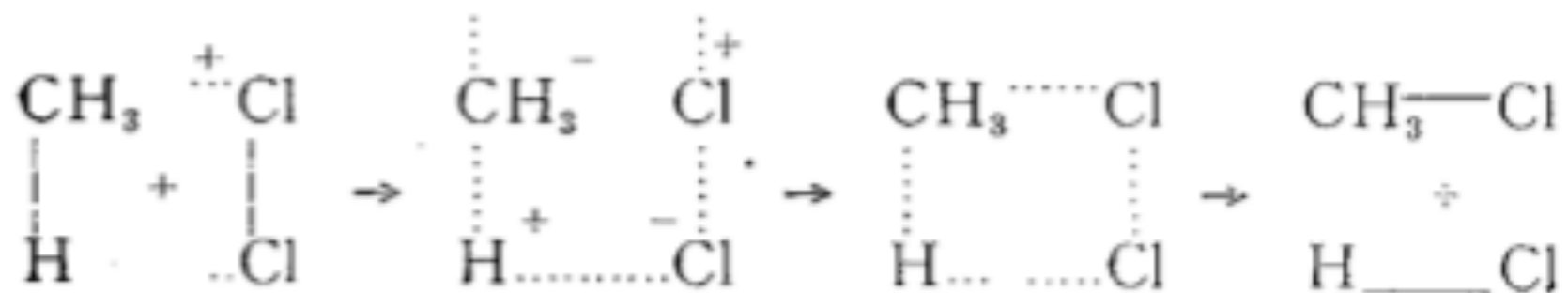
Robert Robinson, "The Conjugation of Partial Valencies," *Manchester Memoirs*, 64 (1920),

The chlorination of methane may be given as a simple illustration of the representation of a reaction in accordance with the above postulates :—

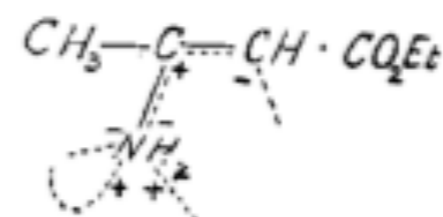
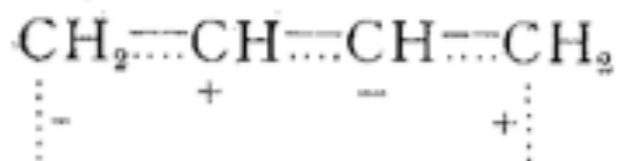
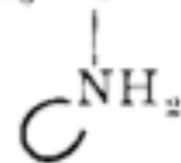
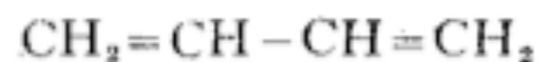
(A). *Reaction between two activated molecules.*



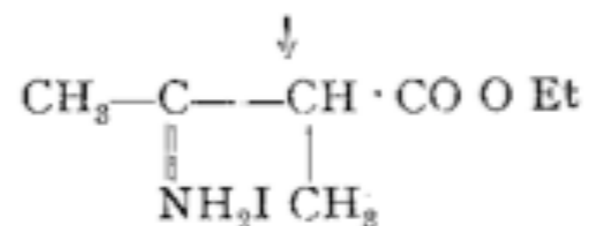
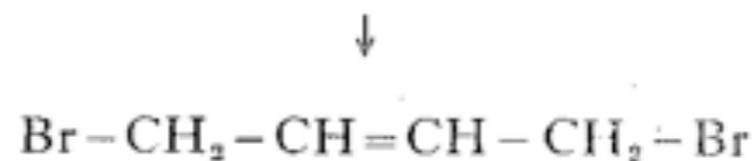
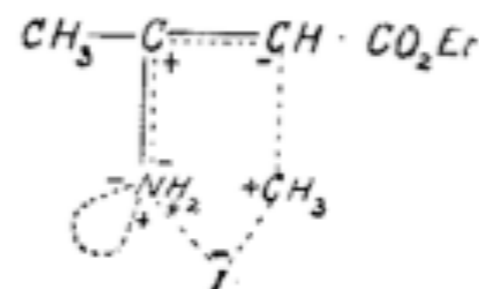
(B). *Reaction between an activated molecule and a neutral molecule.*



Robert Robinson, "The Conjugation of Partial Valencies,"
Manchester Memoirs, 64 (1920),



It is convenient to classify as "primary" those conjugated systems or partially dissociated complexes which take part in reactions characterised by addition at the ends of the chain. Thus, in reacting with bromine, butadiene undergoes a primary conjugation of its partial valencies, and the same is true of ethyl- β -aminocrotonate in reacting with methyl iodide.*



Robert Robinson, "The Conjugation of Partial Valencies,"
Manchester Memoirs, 64 (1920),

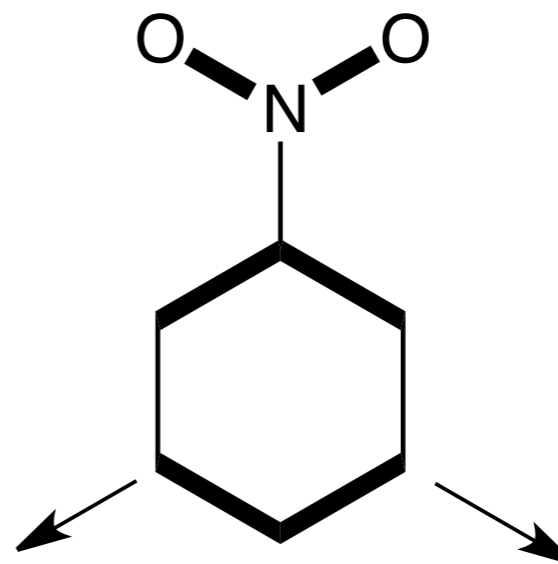
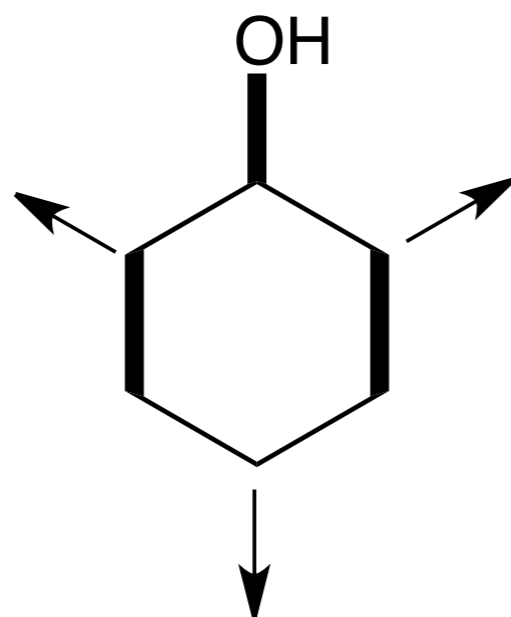
Bernard Flürscheim (1874-1955)



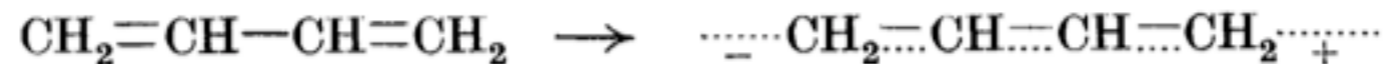
- Studied with Thiele and Werner
- Royal Institution, London (1905-1907; 1925-1928)
- Private laboratory
- In carbon chains, strong and weak links would alternate.
- Not charges, but affinities alternate.

Flürscheim's "Affinity Demand" Model

- Alternation of quantity of affinity
- Affinity is continuously divisible (partly bound, partly free)
- Atoms that can increase valency the most create the most "affinity demand"
- Works well to explain the directive ability of most groups on aromatic rings.



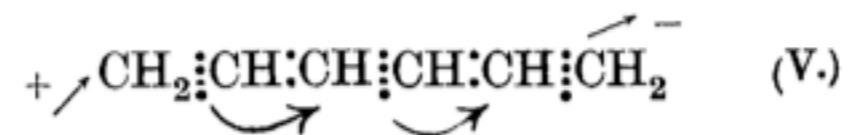
(a) *Conjugation of Ethylene Linkings.*—The representation of the active phase and conjugation of butadiene on the partial valency theory is



and on the Thomson and Lewis-Langmuir theory as now interpreted



Similarly, the conjugation of three double bonds, supposing such to occur, would be represented thus :—



William Ogilvy Kermack and Robert Robinson, "An Explanation of the Property of Induced Polarity of Atoms and an Interpretation of the Theory of Partial Valencies on an Electronic Basis," *Journal of the Chemical Society*, 121 (1922), 427-40

Christopher Kelk Ingold (1893-1971)



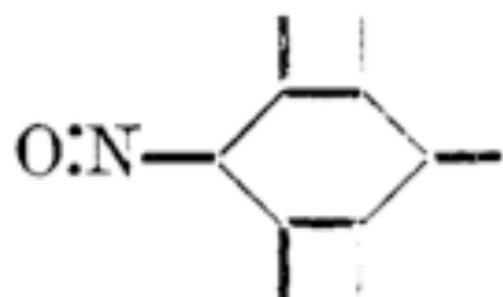
1918: PhD University College,
London (Jocelyn Thorpe)

1920: Postdoctoral work with
Thorpe

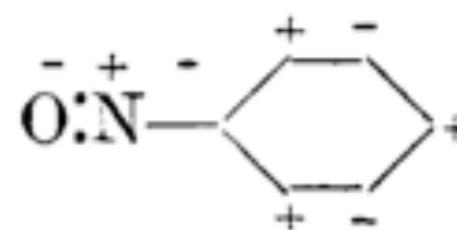
1924: University of Leeds

1930: University College, London
Influenced by Flürscheim's affinity
demand model

atoms.” The determination of the directive influence of the nitroso-group therefore possesses much greater importance than would normally attach to a similar case, because it is the simplest, indeed, perhaps, the only really simple, case which is crucial for either theory :—



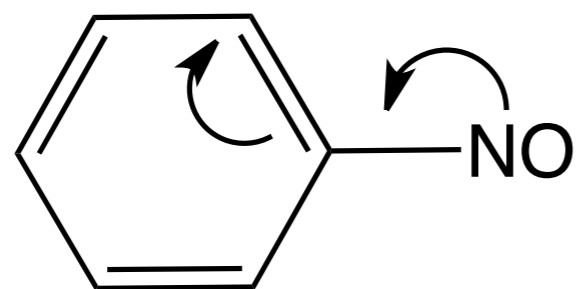
(ⁱⁱⁱN = key atom; ∴ free affinity in *op*-positions; ∴ NO-group is *op*-directive.)



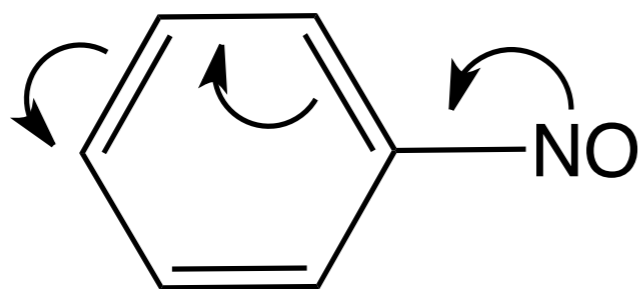
(\bar{O} = key-atom; * ∴ *m*-carbon atoms negative; ∴ NO-group is *m*-directive.)

The facts, so far as they have been ascertained, are that nitrobenzene can be directly chlorinated, brominated, and nitrated; and that in each case the group introduced enters mainly at the para-position; meta-isomerides could not be detected.†

Christopher Ingold, “The Nature of the Alternating Effect in Carbon Chains. Part I. The Directive Influence of the Nitroso-Group in Aromatic Substitution,” *Journal of the Chemical Society*, 127 (1925): 513-18

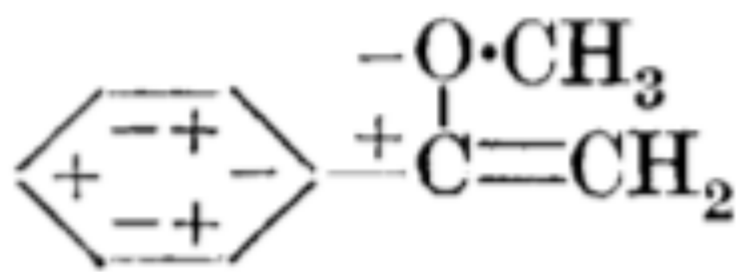


Ortho product

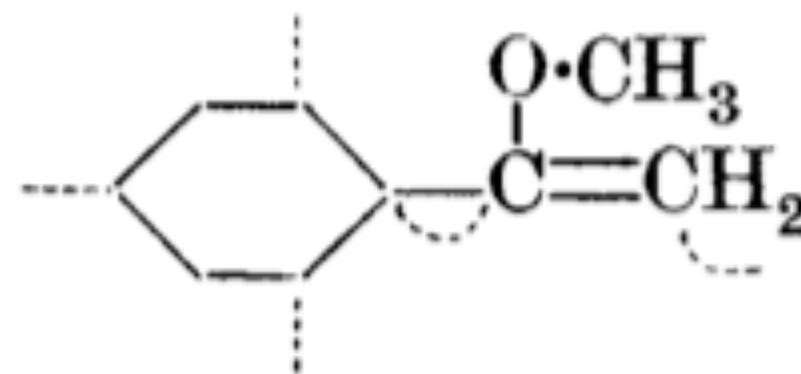


Para product

Robinson's Response to Ingold's Results



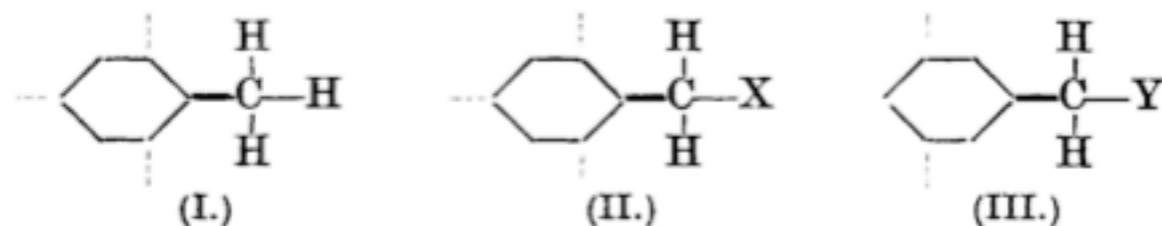
(Alternate polarities :
m-directive action.)



(Alternating affinity :
op-directive action.)

Christopher Ingold and Edith Hilda Ingold, "The Nature of the Alternating Effect in Carbon Chains. Part II. The Directing Influence of the α -Methoxyvinyl Group in Aromatic Substitution," *Journal of the Chemical Society*, 127 (1925): 870-75

(mechanism of propagation). In toluene, the phenyl group is unsaturated (possesses residual affinity), and hence the methyl carbon atom is strongly bound, a condition leading to *op*-substitution (I). If, now, one of the methyl hydrogen atoms is replaced by a feebly unsaturated atom (X), the demand made by this atom on the affinity of the carbon atom may be insufficient to counterbalance the unsaturation of the phenyl group, and again *op*-substitution will be the rule (II). On the other hand, if, in place of X, a strongly unsaturated atom (Y) be introduced, then the unsaturation of the phenyl group may be overcome, when a condition will arise leading to *m*-substitution (III):



Now bivalent oxygen is a feebly unsaturated atom, whilst trivalent nitrogen is strongly unsaturated. Hence, if we consider comparatively benzyl alcohols (IV) and benzylamines (V) (using these terms in a general sense to include alkyl and acyl derivatives, etc.), the former should be more closely represented by condition (II), and the latter by condition (III):



That is to say, the benzylamines should show a greater tendency than the benzyl alcohols towards *m*-direction, as against *op*-direction. Of course, if oxonium or ammonium salt-formation were to take place *op*-direction might result, but, whilst benzyl alcohols should exhibit *op*-direction in any event, benzylamines should show *m*-direction if and when salt formation does not occur. *It is still true, therefore, that according to the affinity theory derivatives of benzylamine should show a greater tendency towards m-substitution, and a smaller tendency towards op-substitution, than the benzyl alcohols, and that m-directive action should never prevail amongst the latter.*

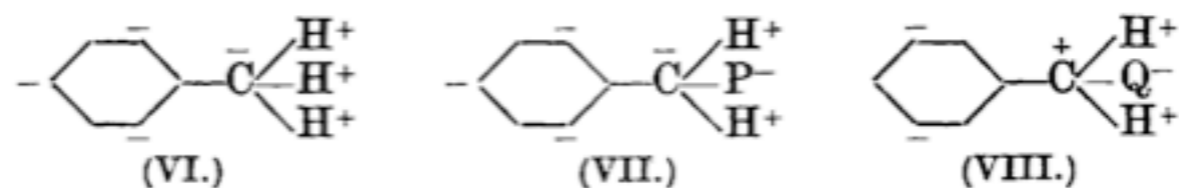
Eric Holmes and Christopher Ingold, "The Nature of the Alternating Effect in Carbon Chains. Part III. A Comparative Study of the Directive Efficiencies of Oxygen and Nitrogen Atoms in Aromatic Substitution," *Journal of the Chemical Society*, 127 (1925): 1800-21

On the other hand, according to polarity principles, hydrogen is feebly key-positive (Lapworth, *Mem. Manchester Phil. Soc.*, 1920, 64, No. 3, p. 5); thus, the *op*-substitution of toluene may be explained (VI). If, now, in place of one of the methyl hydrogen atoms a weakly negative atom (P) be introduced, this may conceivably be insufficient to counterbalance the effect of the two remaining hydrogen atoms, and, in this case, *op*-substitution will still prevail (VII). If, however, a strongly negative atom (Q) is

[View Online](#)

ALTERNATING EFFECT IN CARBON CHAINS. PART III. 1803

introduced, the influence of the hydrogen atoms should be overcome and *m*-direction should ensue (VIII).



Eric Holmes and Christopher Ingold, "The Nature of the Alternating Effect in Carbon Chains. Part III. A Comparative Study of the Directive Efficiencies of Oxygen and Nitrogen Atoms in Aromatic Substitution," *Journal of the Chemical Society*, 127 (1925): 1800-21

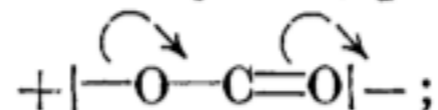
(2) $C=C-C=O$; *crotonoid*; polarisation— $+|C=C-C=O|^-$; reactivity—kationoid.

Examples are methylenemalonic ester, mesityl oxide.

(3) $C=C-O-$; *crotenoid*; polarisation— $-|C=C-O|+$; reactivity—anionoid.

Examples are ethyl β -aminocrotonate, dimethylaniline, resorcinol.

(4) $-O-C=O$; neutralised system; polarisation—

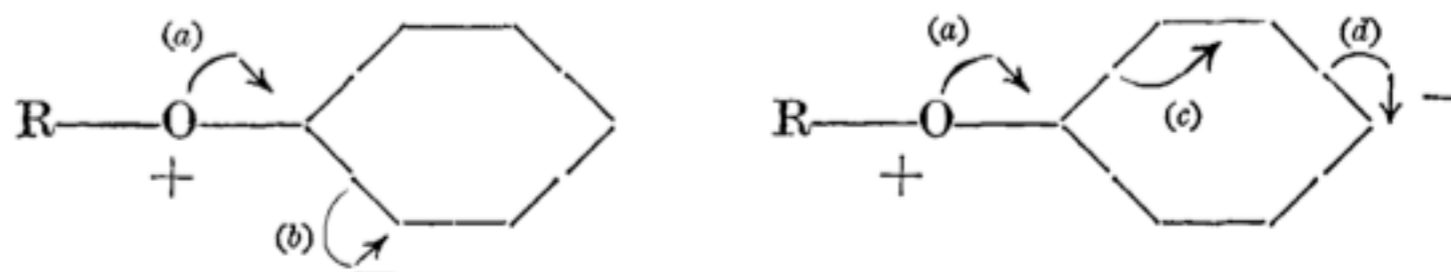


reactivity—feebly kationoid at C and special characters (see below).

Examples are esters, amides, dianisylideneacetone.

James Allan, Albert Edward Oxford, Robert Robinson and John Charles Smith, "The Relative Directive Powers of Groups of the Forms RO and RR'N in Aromatic Substitution. Part IV. A Discussion of the Observations Recorded in Parts I, II, and III," *Journal of the Chemical Society*, 129 (1926): 401-11

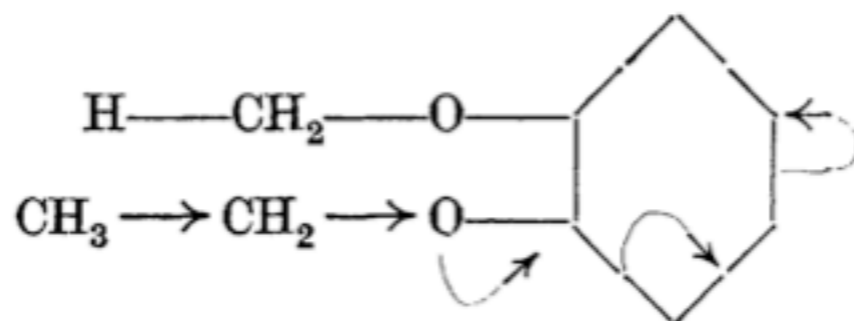
polarisation, the postulated precedent of all reactions. In the case of a phenol ether the mechanism of activation is represented by the annexed expressions.



The oxygen, by means of its free electrons, increases its covalency with the ring C_a (process a). C_a recovers its normal covalency by giving up correspondingly electrons to C_β (process b) (o -substitution) or by relinquishing $C_a C_\beta$ co-valency electrons to $C_\beta C_\gamma$ (process c). C_γ must then relinquish $C_\gamma C_\delta$ co-valency electrons

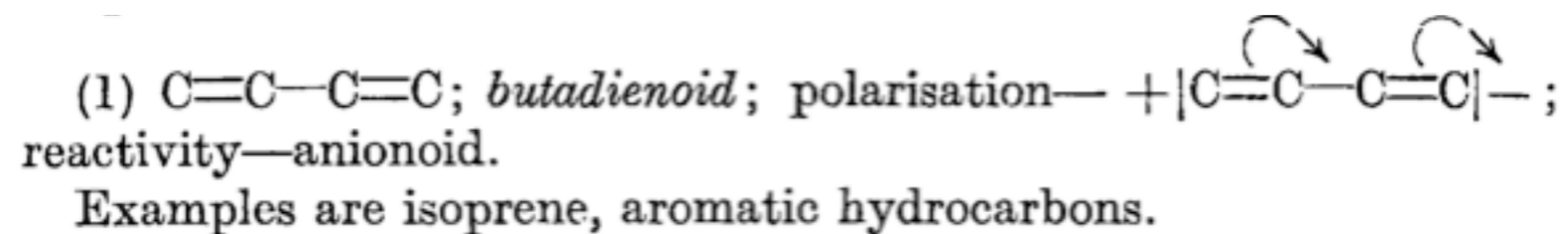
James Allan, Albert Edward Oxford, Robert Robinson and John Charles Smith, "The Relative Directive Powers of Groups of the Forms RO and RR'N in Aromatic Substitution. Part IV. A Discussion of the Observations Recorded in Parts I, II, and III," *Journal of the Chemical Society*, 129 (1926): 401-11

In the ethyl ether of guaiacol we have the condition

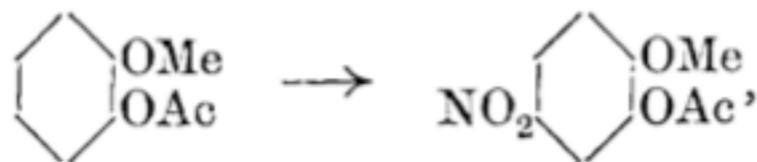
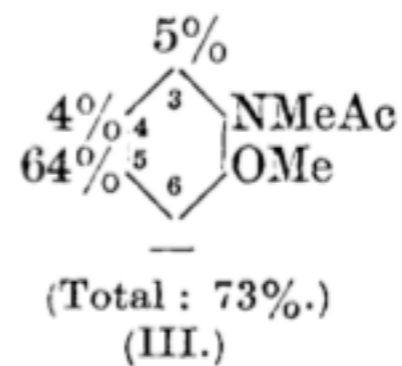
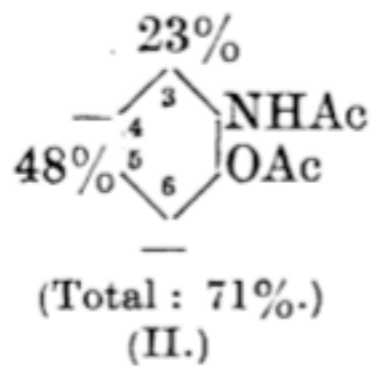
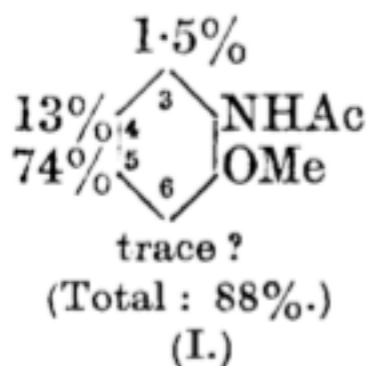


because the methyl group exercises a greater repulsion on electrons than hydrogen does. Therefore the polarisation of the crotonoid system, including the oxygen of the ethoxyl group, is facilitated as compared with the other system, not represented, which includes the oxygen of the methoxyl group. It follows that ethoxyl should have a higher directive power than methoxyl † (Found : EtO, 135; MeO, 100). The substitution of methyl for a second hydrogen atom should still further increase the directive power (Found : Pr^oO, 150). It is very interesting, however, that in the catechol series

James Allan, Albert Edward Oxford, Robert Robinson and John Charles Smith, "The Relative Directive Powers of Groups of the Forms RO and RR'N in Aromatic Substitution. Part IV. A Discussion of the Observations Recorded in Parts I, II, and III," *Journal of the Chemical Society*, 129 (1926): 401-11



James Allan, Albert Edward Oxford, Robert Robinson and John Charles Smith, "The Relative Directive Powers of Groups of the Forms RO and RR'N in Aromatic Substitution. Part IV. A Discussion of the Observations Recorded in Parts I, II, and III," *Journal of the Chemical Society*, 129 (1926): 401-11



Christopher K. Ingold and E. H. Ingold, "The Nature of the Alternating Effect in Carbon Chains. Pt. V. A Discussion of Aromatic Substitution With Special Reference to the Respective Roles of Polar and Non-Polar Dissociation; and a Further Study of the Relative Directive Efficiencies of Oxygen and Nitrogen," *Journal of the Chemical Society*, 129 (1926): 1310-28

The above results, whilst they appear inconsistent with the idea of alternating polar charges (A), agree either with Flürscheim's theory of alternating affinity content (B), or with Robinson's theory (*Chem. and Ind.*, 1925, **44**, 456) of *op*-substitution by electronic displacement in conjugated systems (C).* This theory leads to much the same key-efficiency series as Flürscheim's, if residual affinity be interpreted as an indication of the presence of loosely held, active electrons. The arrows represent the assumed electron displacements originating in a latent valency :



It will be obvious that the distribution of forces here involved is qualitatively the same as that in Flürscheim's theory, the completed change (C) corresponding with his figure for *op*-substitution :



Christopher K. Ingold and E. H. Ingold, "The Nature of the Alternating Effect in Carbon Chains. Pt. V. A Discussion of Aromatic Substitution With Special Reference to the Respective Roles of Polar and Non-Polar Dissociation; and a Further Study of the Relative Directive Efficiencies of Oxygen and Nitrogen," *Journal of the Chemical Society*, 129 (1926): 1310-28

Ingold's New System for Organic Chemistry

- Series of "Annual Reports" from 1926-1930
- Inconsistencies between older systems removed by new the new scheme
- "anionoid" \longrightarrow Nucleophilic (all bases)
- "cationoid" \longrightarrow Electrophilic (all acids)
- Inductive effect—unequal sharing of electron pairs.
- Tautomeric effect—electronic reinterpretation of the Flurscheim model of residual affinity.
- The tautomeric effect is not permanent but an "activated" form, resulting in a measurable dipole, represented by the curved arrow.
- Unification of aromatic and aliphatic organic chemistry
- "Principles of an Electronic Theory of Organic Reactions," *Chemical Reviews*, 15 (1934): 225-74
- *Structure and Mechanism in Organic Chemistry*, 1953

Edward Hughes (1906-1963)



1920s: Bangor University, North Wales

1930: Postdoctoral with Ingold

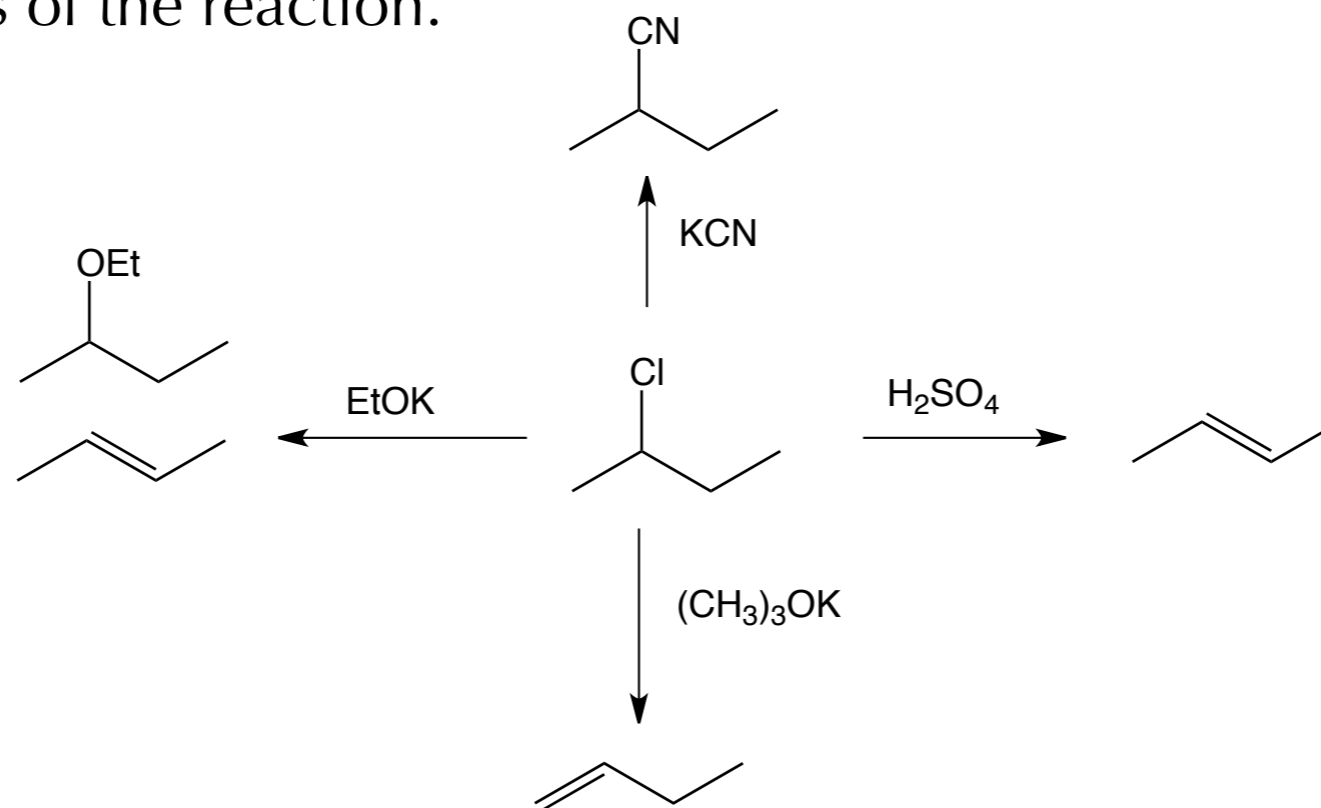
1943-1948: Bangor

1948: Second chair for chemistry at University College, London

Learned reaction kinetics techniques with Kennedy Orton at Bangor

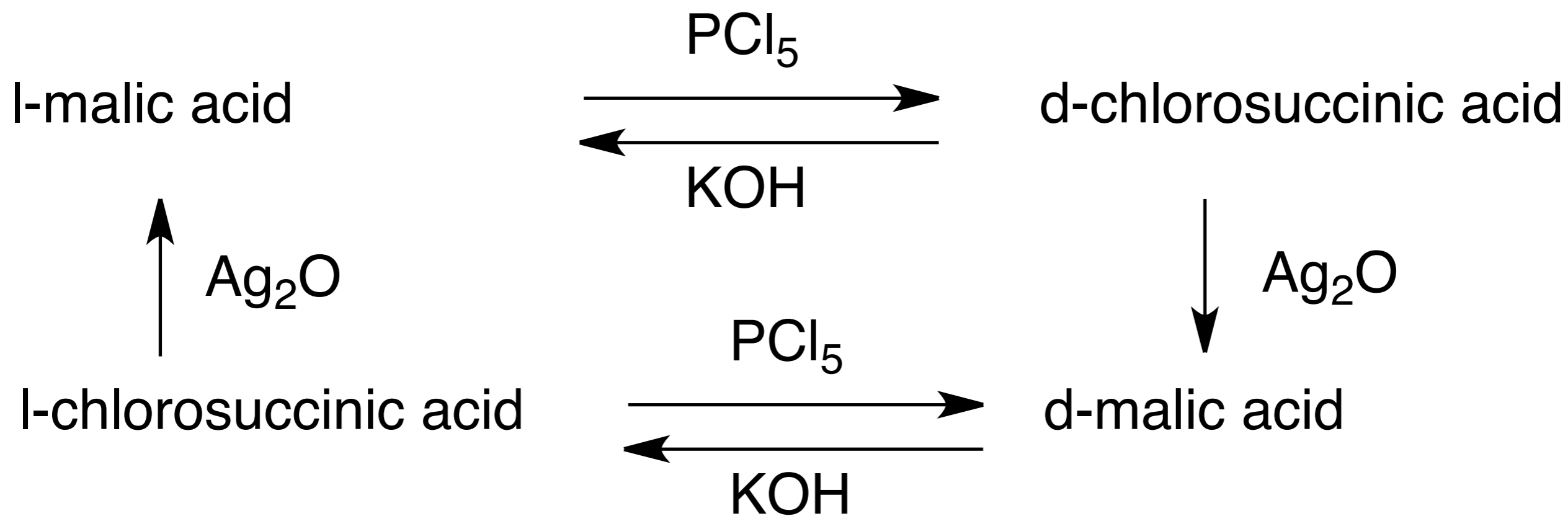
Classification of Reaction Mechanisms by Chemical Kinetics

- Reaction kinetics show bimolecular or unimolecular reactions
- The rate kinetics indicate the *molecularity* of the reaction, and its mechanism (bond formation and cleavage).
- Lewis bond formulas suggest the rearrangement of bonds
- S_N1 , S_N2 , E2 mechanisms suggested in 1933
- E1 found by Hughes in 1935
- Any given reaction can proceed in one or more ways, according to conditions of the reaction.



The Walden Inversion

(Paul Walden, 1895-1897)



Where does the inversion take place?

Explaining the Walden Inversion, 1937-48

- Mechanism revealed through kinetic studies
- Every case of S_N2 substitution leads to inversion.
- Inversion requires breaking the bond at the asymmetric center.
- Optical inversion (preserved asymmetry) always accompanies optical inversion.
- Racemization always accompanies unimolecular substitutions (production of an symmetrical, planar carbonium ion)

Characteristics of Ingold's Chemistry

- Creation of a new systematic language that reflects theory.
- Appropriation and renaming of older concepts.
- Use of physical methods
 - Chemical kinetics vs. mechanism
 - Dipoles
 - Effect of isotopic labelling on rates
 - Dissociation constants
- Anthropomorphic and economic metaphors:
nucleo**philic** and electro**philic**
“It is a commonplace of electronic theories that chemical change is an electrical **transaction** and that reagents act by *virtue* of a constitutional *affinity*, either for electrons or for atomic nuclei. When, for example, an electron-*seeking* reagent *attacks* some center in an organic molecule, ... reaction will supervene provided that the center can **supply** electrons. to the requisite extent. ... Sharing **economizes** electrons.”

Further Reading

- William H. Brock, *The Chemical Tree: A History of Chemistry*, New York: Norton, 2000, chapters 13 and 14.
- Martin D. Saltzman, "The Robinson-Ingold Controversy: Precedence in the Electronic Theory of Organic Reactions," *Journal of Chemical Education*, 50 (1980): 484-88
- J. Shorter, "Electronic Theories of Organic Chemistry: Robinson and Ingold," *Natural Product Reports*, 4 (1987): 61-66
- Mary Jo Nye, *From Chemical Philosophy to Theoretical Chemistry: Dynamics of Matter and Dynamics of Disciplines, 1800-1950*, Berkeley: University of California Press, 1993.