Organic Reaction Schemes and General Reaction – Matrix Types, I
Rearrangement Reactions

JAN C. J. BART and ENEA GARAGNANI
Montedison S. p. A., Istituto Ricerche "G. Donegani", Via del Lavoro, 4, Novara, Italy


A sample consisting of about 120 organic rearrangement reactions has been quantified
in terms general reaction matrices $\tilde{R}$ expressing electron-flow processes. About two thirds
of the reactions considered conform to only two distinct $\tilde{R}$-matrices, 80% to five such
schemes. The frequency distribution is qualitatively similar to that found for larger, more
randomly chosen, sets of organic reactions. Examples of the various electron-flow
processes are given. The bearings of the results on synthesis-planning are discussed.

1. Introduction

Recently, UGI and coworkers have laid the basis of a mathematical model of chemistry, with
the primary object of application to computer-assisted design of syntheses. According to this
scheme, algebraic structures represent chemical systems and chemical reactions are described as
isomerizations of ensembles of starting materials $E_A$ into a target molecule and by-products, $E_Z$.
As bond-electron (BE) matrices were chosen for the computer representation of an EM, a chemical
reaction, corresponding to the transformation of one BE-matrix into another, $E_A \rightarrow E_Z$, is effectively
expressed by addition of a reaction matrix $\tilde{R}$, i.e.
\[ E_A + \tilde{R} = E_Z. \]
On the basis of the definition of a BE matrix $\tilde{E}$ for an $n$-atomic ensemble of molecules as
an $n \times n$ matrix with $e_{ij}$ entries corresponding to the formal covalent bond order between the atoms $A_i$ and $A_j$, and $e_{ii}$ to the number of free electrons of atom $A_i$, it follows that the entries $r_{ij} = r_{ji}$ of $\tilde{R}$
express bond breaking and formation processes, with $r_{ii}$ accounting for changes in the distribution
of free electrons. In short, an $\tilde{R}$-matrix is then an algebraic expression describing the electron-flow
process of an individual chemical transformation of some concrete ensemble of starting molecules into a
resulting concrete ensemble of product molecules.

Requests for reprints should be sent to Dr. J. C. J. BART, Montedison Research Laboratories "G. Done-
gani", Via del Lavoro 4, Novara, Italy.
Table I. Organic rearrangement reaction of the type A-B + C-D -> A-C + B-D (R 1).

1. Rearrangement of substituted ethylene oxides.
2. Alkyl shifts in non-cyclic compounds.
3. WAGNER-MEERWEIN rearrangement (1,2 shift in bicyclic system).
4. Rearrangement of peroxyderivatives.
5. Rearrangement of hydroperoxide esters.
6. Wittig rearrangement.
7. TRUE-SMILES rearrangement.
8. Enol-keto tautomerism.
11. Intramolecular MICHAEL reaction.
12. Prototropic change (mobile hydrogen tautomerism).
13. Prototropic shifts in allylic systems.
14. Anionotropic change (Sx1' and Sx2').
15. Intrannular valency tautomerism.
17. Rearrangement of diazoaminobenzenes.
18. FISHER-HEPP rearrangement.
19. HOFMANN-MARTIUS rearrangement.
20. REILLY-HICKINBOTTOM rearrangement.
21. Rearrangement of N-nitroaniline.
22. Rearrangement of alkyl aryl ethers.
23. FRIES rearrangement of aryl esters to acylphenols.
24. Benzidine rearrangement.
25. CLAISEN rearrangement without allyl reversal.
26. Rearrangement of hydroxylamines.
27. Rearrangement of nitroamines.
29. Ring-chain anionotropy.
30. Ring closures of cyclohexenylethyl and cycloheptenylethyl derivatives.
31. Ring expansions of norbornylcarbinyl derivatives.
32. Thermal and acid-catalyzed rearrangements of cyclopropane and -butane derivatives.
33. DEMJANOVA rearrangement.
34. WESSELY-MOSER rearrangement.
35. AMADORI rearrangement.
36. DIMITROFF rearrangement.
37. HAYASHI rearrangement.
38. ROWE rearrangement.
39. WALLACH rearrangement.
40. THEILACKER rearrangement.
41. CHAPMAN rearrangement.
42. D-HOMO rearrangement.
43. NIERENSTEIN reaction (2° step).
44. BAKER-VENKATARAMAN transformation.
45. BARDHAN-SEN Gupta phenanthrene synthesis (1st step).
46. DARZENS synthesis of tetratin derivatives.
47. DIECKMANN reaction.
48. BARTON reaction (2° R 1).
49. BECKMANN rearrangement (2° R 1).
50. MEYER-SCHUSTER rearrangement (2° R 1).
51. RUPE rearrangement (3° R 1).

2. Procedures

Instead of setting up the R matrices corresponding to organic reactions, we rather consider here the relevant reaction schemes. In particular, these are

Table II. Organic rearrangement reactions of the type A-B + C-D + E-F -> A-C + D-E + B-F (R 2).

1. Pinacol-pinacolone rearrangement/retropinacolic change.
2. Conversion of (α-hydroxy) aldehydes and -ketones (pinacolic type transformation)*.
3. Acyloin rearrangement.
5. Halohydrin rearrangement.
7. NAMETKIN rearrangement.
8. Molecular rearrangement by neighbouring group partecipation in substitution reactions.
9. Transannular rearrangements.
10. Anionotropic change (Sx1°).
11. CLAISEN rearrangement (with allyl reversal) and analogs.
12. COPE rearrangement.
13. Rearrangements in conjugated triene systems.
15. (Rearrangement of diazo-amino-compounds)**.
16. (FISCHER-HEPP rearrangement)**.
17. Benzidine rearrangement.
18. Rearrangement of ketene acetal.
21. 1,2 Rearrangement during CLEMMESEN reduction.
22. BOGERT-COOK synthesis.
23. FAVORSKII rearrangement.
24. WESTPHALEN-LETTRE rearrangement.
25. PERKIN rearrangement (coumarin-benzofuran ring contraction).
27. LOBBY de BRUYN-VAN EKENSTEIN transformation.
28. REVERDIN migration.

* On the basis of an intramolecular reaction mechanism.
** On the basis of an intermolecular reaction mechanism.

Table III. General reaction matrix types of organic rearrangements.

R 1 A-B + C-D -> A-C + B-D
See Table I.

R 2 A-B + C-D + E-F -> A-C + D-E + B-F
See Table II.

R 3 A-B + C-D -> A + B-C + D:
1. Rearrangement of peroxyderivatives.

R 4 A-B + C=D-E-F -> A-D-B + C=E

1. NEBER rearrangement (α-amino ketones from ketoximes).

R 5 A-B + :C-D -> A-C-B + D:
1. WOLFF rearrangement (fundamental step).
2. CURTIUS rearrangement22.
3. SCHMIDT rearrangement23.
4. Azide rearrangement.
5. BAMFORD-STEVENS reaction (last step).

R 6 A-B-C-D-E -> A-C-E + B=D
1. BECKMANN rearrangement.
Table III continued

<table>
<thead>
<tr>
<th>R 7</th>
<th>A-B + C-D-E -&gt; A-D-B + C-E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>HOFMANN rearrangement(^{24}).</td>
</tr>
<tr>
<td>2.</td>
<td>LOSSEN rearrangement(^{25}).</td>
</tr>
<tr>
<td>3.</td>
<td>STIEGLITZ rearrangement of hydroxylamines.</td>
</tr>
<tr>
<td>4.</td>
<td>Haloamine rearrangement.</td>
</tr>
<tr>
<td>5.</td>
<td>FRITSCH-BUTTENBERG-WIECHELL rearrangement.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 8</th>
<th>A-B + C-D + E: -&gt; A-C + D-E + B:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>SOMMERFELT rearrangement.</td>
</tr>
<tr>
<td>2.</td>
<td>GROB’S fragmentation of (\gamma)-aminohalides and (\alpha)-aminoketoximes(^{26}).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 9</th>
<th>A-B + C-D-E -&gt; A-E + B-C + D:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Transformations in allylic alcohol derivatives. (Sni’ rearrangement of chlorosulphites and -forms).</td>
</tr>
<tr>
<td>2.</td>
<td>Acetylene-allene rearrangements.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 10</th>
<th>A-B-C + D-E -&gt; A-D-C + B-E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>MEYER-SCHUSTER rearrangement (Cfr. R 1).</td>
</tr>
<tr>
<td>2.</td>
<td>TIEMANN rearrangement, 3rd step (RNHCN -&gt; RHCONH(_2)).</td>
</tr>
<tr>
<td>3.</td>
<td>CURTIUS rearrangement.</td>
</tr>
<tr>
<td>4.</td>
<td>HOFMANN rearrangement { last step (RNCO -&gt; RH(_2)) }</td>
</tr>
<tr>
<td>5.</td>
<td>LOSSEN rearrangement.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 11</th>
<th>A-B + C -&gt; A-C + B</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Migration of alkyl groups during the FISCHER Indole Synthesis.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 12</th>
<th>A : + B-C -&gt; A-C + B:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>STEVENS rearrangement.</td>
</tr>
<tr>
<td>2.</td>
<td>GROVENSTEIN-ZIMMERMAN rearrangement.</td>
</tr>
<tr>
<td>3.</td>
<td>MEISENHEIMER rearrangement.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 13</th>
<th>A-B-C + D-E + F: -&gt; A-D + C-E + B-F</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>WEERMAN degradation.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 14</th>
<th>A-B-C-D: -&gt; A-C: + B=D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Rearrangement of nitrones.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 15</th>
<th>A-B + C-D + E-F -&gt; A-E-D + B-C + F:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>SCHMIDT reaction (azidohydrin rearrangement).</td>
</tr>
<tr>
<td>2.</td>
<td>DARAPSKY degradation (overall rearrangement step).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 16</th>
<th>A-B-C + D-E+F -&gt; A-C + B=E + D-F</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>TIEMANN rearrangement of amidoximes (overall).</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 17</th>
<th>A-B + C-D + E-F + G-H -&gt; A-D + B-H + C-E + F-G</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Rearrangement involving eight atomic centers.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 18</th>
<th>A-B + C-D + E-F-G -&gt; A-G + B-E + D-F-C</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Dienol-benzene rearrangement.</td>
</tr>
<tr>
<td>2.</td>
<td>Dienone-phenol rearrangement.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>GABRIEL-COLMAN rearrangement.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>R 20</th>
<th>A + B-C-D -&gt; A-C + B-D</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>WALLACH degradation of (a,a’)-dihaloketones.</td>
</tr>
</tbody>
</table>

derived for (a) heterolytic rearrangements in reactions of isomerization, substitution, or elimination undergone by saturated all-carbon, carbon-nitrogen, and carbon-oxygen systems, involving a shift of a group carrying an excess of electrons to an electron-deficient centre or its polar opposite (nucleophilic and electrophilic rearrangements, respectively), (b) unsaturated rearrangements, (c) aromatic electrophilic, nucleophilic and intramolecular rearrangements, and (d) molecular reactions. In general, the overall reactions considered involve only one or two molecular species. In view of the object of our study, namely the derivation of a set of \(\bar{R}\)-matrices for use in synthesis-planning and classification and codification of organic reactions (cfr. VLEUTS\(^{8}\)), we normally proceed by considering the generalized overall expression of the chemical rearrangement step, without going into finer details of mechanism, unless specifically required.

Some ambiguity in the classification of organic reactions may be unavoidable as long as reaction mechanistic aspects are obscure. In case of non-concerted mechanisms, when possible the rearrangement steps have been separated from other processes. Therefore, in this paper we do not normally take into account any preliminary steps, such as the condensation of carboxylic acid and hydrazoic acid to give acylazide in the SCHMIDT reaction or the formation of a N-haloamide in the HOFMANN reaction, and neither subsequent decomposition of the rearrangement products. We thus describe processes which account for the fundamental steps only, avoiding however those intermediates which would represent unstable products in a synthesis-tree, and other processes which may be considered to give rise to independent nodes.

A typical case of setting up reaction schemes is illustrated in the following example, referring to the HOFMANN rearrangement of N-haloamides to isocyanates in basic solutions:

\[
\begin{align*}
\text{H} & \quad \text{R-C-N' + OH}^{-} \rightarrow \text{R-N=C=O + H-OH + X^-} \\
\quad & \quad || \quad X \\
\quad & \quad \text{O} \quad (C)
\end{align*}
\]

(Reaction scheme:
A-B + C-D-E + F: -> A-D-B + E-F + C:) which might also be written as:
\[
\begin{align*}
R - C - N & \rightarrow R - N = C = O + H - X \\
\text{(Reaction scheme:)} & \\
A - B + C - D - E & \rightarrow A - D - B + C - E
\end{align*}
\]

It is the latter, simpler, scheme which has been adopted. We consider rearrangements "intramolecular" as long as such a formalism properly accounts for product formation. Effects of catalysis are not normally considered to the end of establishing the R matrix.

Another example of a change in reaction scheme, if account is taken of the reaction mechanism, is ORTON’s rearrangement of halogenoamines:

\[
\begin{align*}
\text{C}_6\text{H}_5 \cdot \text{NClAc} & \rightarrow (o- \text{ and } p-)\text{Cl} \cdot \text{C}_6\text{H}_4 \cdot \text{NHAc} \\
\text{C}_6\text{H}_5 \cdot \text{NClAc} + \text{HBr} & \rightleftharpoons \text{C}_6\text{H}_5 \cdot \text{NHAc} + \text{ClBr} \\
\text{C}_6\text{H}_5 \cdot \text{NHAc} + \text{ClBr} & \rightleftharpoons (o,p)\text{BrC}_6\text{H}_4 \cdot \text{NHAc} + \text{HCl}
\end{align*}
\]

the overall scheme is A-B + C-D + E-F \rightarrow A-C + B-E + D-F. A similar reasoning holds for rearrangements of diazoamino-compounds, of nitrosoamines (FISCHER-HEPP), etc.

In order to keep the subject matter within certain limits, such cases as non-isomeric rearrangements, common in the chemistry of allylic compounds, are considered as displacements accompanied by an anionotropic rearrangement. Thus, reactions as

\[
\begin{align*}
\text{CH}_2 = \text{CH} + \text{CHMeCl} & \rightarrow \text{CHMeCl}^- \\
\text{Me}_3\text{NCH}_2\text{CH} = \text{CHMeCl}^- & \\
\text{(Reaction scheme:)} & \\
A - B + C - D + E: & \rightarrow A - E + B - C + D:
\end{align*}
\]

are not normally included in the Tables.

Not included in the paper either are results concerning molecular rearrangements which are not known in sufficient detail, i.e. most molecular rearrangements in heterocyclic compounds.

3. Results

The classification of more than hundred of the most outstanding organic rearrangements according to their reaction electron-flow scheme and based on several reference works, is summarized in Tables I–III. It is clearly evident that R1 and R2 (Tables I and II) account for the majority of reactions investigated; this result is in accordance with findings for a more representative sample of about 1900 organic reactions. Both R-matrices describe a great variety of rearrangements, ranging from nucleophilic and electrophilic rearrangements in saturated and unsaturated systems, to aromatic electrophilic, nucleophilic and intramolecular rearrangements and "no-mechanism" reactions.

A basis for discussion of isomerizations of linear unsaturated systems has recently been provided by ARENS. From Figs. 4–7 in ref. 15 it is immediately obvious that intramolecular isomerizations (rearrangements) in linear C3 and C4 patterns are of the 1, 3 type and thus conform to R1. Similarly, a, e or 1, 5 isomerization is described by R2. In more extended systems higher order isomerization may occur which falls beyond the basis-set of R-matrices.

Most mono- and polydentate aromatic rearrangements of groups from the side-chain to the nucleus also conform to R1, such as the entries 17–24 of Table I. Typical examples of R1 type electron-flow schemes are the ring closure of cyclohexenyl-ethyl derivatives:

\[
\begin{align*}
\text{CH}_2 = \text{CH} - \text{CHMeCl} & \rightarrow \text{Me}_3\text{NCH}_2\text{CH} = \text{CHMeCl}^- \\
\text{Me}_3\text{NCH}_2\text{CH} = \text{CHMeCl}^- & \\
\text{(Reaction scheme:)} & \\
A - B + C - D + E: & \rightarrow A - E + B - C + D:
\end{align*}
\]

and such reactions as

\[
\begin{align*}
\text{Me}_3\text{NCH}_2\text{CH} = \text{CHMeCl}^- & \\
\text{(Reaction scheme:)} & \\
A - B + C - D + E: & \rightarrow A - E + B - C + D:
\end{align*}
\]

Instead, reactions in which the replacement occurs in a derivative (R9, 1) follow a different route. On the other hand, the apparently different electron flow in the acetylene-allene rearrangement according to MEYER-SCHUSTER (R10, 1):

\[
\begin{align*}
\text{PhCHC} = \text{CH} & \rightarrow \text{PhCH} = \text{CH} - \text{CHO} \\
\text{(R10, 1)} & \\
\text{OH}
\end{align*}
\]
may be reconducted to $2^*\mathbf{R}1$, namely
\[
\text{PhCH}=-\text{C}==\text{CH}\rightarrow \text{PhCH}==\text{C}==\text{CH(OH)} \rightarrow \text{OH}
\]
\[
\text{PhCH}==\text{CH}-\text{CHO} \quad (\mathbf{R}1, 50)
\]

Similarly, the \textit{Rupe} rearrangement ($\mathbf{R}1, 51$) is essentially a $3^*\mathbf{R}1$ process.

The \textit{Wagner-Meerwein} and pinacolic rearrangements in acyclic and cyclic systems\textsuperscript{16} which are in essence 1, 2 shifts of a group (alkyl, aryl or hydrogen), together with a pair of bonding electrons, may generally be classified according to $\mathbf{R}1$ (entries 1, 3) or $\mathbf{R}2$ (entries 1–7). Also anionotropic processes (tautomeric changes), and the earlier mentioned isomeric rearrangements in the chemistry of allylic compounds\textsuperscript{17}, $\text{C}==\text{C}==\text{C}-\text{X}$, which may involve migration of a nucleophilic or anionic fragment from one potentially electrophilic center to another, mainly conform to these schemes ($\mathbf{R}1, 13, 28, 29, 50, 51$; $\mathbf{R}2, 18, 19$; $\mathbf{R}9, 1, 2$). Typical $\mathbf{R}2$-type reactions are the thermal conversion of precalciferol to (iso)pyrocalciferol:

\[
\text{prec calciferol} \rightarrow \text{(iso)pyrocalciferol} \quad (\mathbf{R}2, 13)
\]
as well as
\[
\text{CH}2==\text{CHCHR} \quad \text{CH}2\text{CH}==\text{CHR} \quad \text{CH}==\text{C}-\text{O} \rightarrow \text{CHC}==\text{O} \quad (\mathbf{R}2, 19)
\]

Also, the “no-mechanism” molecular reaction processes in which two or more bonds are broken and formed simultaneously, \textit{e.g.} \textit{Claisen} and \textit{Cope} rearrangements, \textit{Diels–Alder} reaction \textit{etc.} are characterized by a very small variety of $\mathbf{R}$-matrices, mainly $\mathbf{R}1$ and $\mathbf{R}2$.

Of the rearrangement reactions, without doubt the nucleophilic 1, 2 shift, in which a group migrates from one atom to an adjacent electron-deficient atom, has received most attention\textsuperscript{18}. Typical examples of such, mainly classical carbon-to-nitrogen rearrangements are $\mathbf{R}5$, $\mathbf{R}6$, $\mathbf{R}7$, $\mathbf{R}10$, $\mathbf{R}13$ and $\mathbf{R}15$. The entries in the tables concern generally only the fundamental rearrangement steps in these processes, rather than the overall reactions. \textit{E.g.} in the C to N rearrangements in azides, hydroxylamines and halo-amines we have considered:

\[
\begin{align*}
\text{R}_3\text{C}-\text{N}2^+ & \rightarrow \text{R}_3\text{C}-\text{NH}-\text{OH} \rightarrow \text{R}_3\text{C}-\text{NH}-\text{X} \\
(\mathbf{R}5, 4) & \quad (\mathbf{R}7, 3) & \quad (\mathbf{R}7, 4)
\end{align*}
\]

Similarly, the fundamental step in the \textit{Wolff} rearrangement, the conversion of an \textit{a}-diazoketone into a ketene and nitrogen, has been taken as

\[
\text{O}=\text{C}--\text{HN}_2 \rightarrow \text{O}=\text{C}==\text{CH}+\text{N}_2 \quad (\mathbf{R}5, 1)
\]

The reaction matrix $\mathbf{R}15$ is to be considered as an extension of $\mathbf{R}5$, to which it stands in about the same relation as $\mathbf{R}1$ to $\mathbf{R}2$. In fact, the \textit{Schmidt} reaction is related to the \textit{Curtius}, \textit{Loschen} and \textit{Hofmann} rearrangements, whereas the \textit{Darapsky} degradation is an extension of the \textit{Curtius} reaction:

\[
\text{R}-\text{CHCN} \quad \text{EtOH} \quad \rightarrow \quad \text{RCHCN} \quad \text{CON}_3 \quad \text{HNCOOEt} \quad + \quad \text{N}_2 \quad (\mathbf{R}15, 2)
\]

$\mathbf{R}13$ is the reverse of $\mathbf{R}15$ and the only example so far identified is the \textit{Weereman} degradation:

\[
\text{H}_2\text{NCO}==\text{C}-\text{R} \rightarrow \text{OHC}-\text{R}+\text{NH}_3+\text{CO} \quad (\mathbf{R}13, 1)
\]

Most nucleophilic rearrangements collected under the heading $\mathbf{R}7$ refer to 1, 2 shifts in carboxyl derivatives, but also comprise the rearrangement of haloamines, \textit{e.g.}

\[
\begin{array}{c}
\text{Ar} \quad \text{C}==\text{C} \rightarrow \text{Ar}==\text{C}==\text{Ar}'+\text{HX} \\
\text{Ar} \quad \text{X}
\end{array}
\quad (\mathbf{R}7, 5)
\]

The classical C to N rearrangement of oximes, the \textit{Beckmann} reaction\textsuperscript{19}. 

---

\textsuperscript{1} J. C. J. Bart–E. Garagnan i • Organic Reaction Schemes and General Reaction – Matrix Types
R-C-R' → R-N=C-R' → R-N-C-R' (R6, 1)
\[
\begin{array}{ccc}
\text{N} & \text{OH} & \text{H O} \\
\text{(a)} & \text{(b)} & \text{(c)}
\end{array}
\]
(R1, 49)

is characterized by an overall reaction (a)→(c) of the R6 type, although the single steps in the process each conform to R1.

Typical reactions of the R10 type are steps following up the carbon-to-nitrogen rearrangements, *e.g.*
\[
\text{RNC}O + \text{H}_2\text{O} → \text{RNH}_2 + \text{CO}_2 \quad (R10, 3-5)
\]

Least studied and less well understood are the electrophilic 1, 2 shifts in which the migration is to an adjacent atom bearing an active unshared electron pair and negative charge. Electrophilic rearrangements include oxygen-to-carbon migrations (*Wittig* rearrangement, R1, 6), nitrogen-to-carbon migrations (*Stevens* (R12, 1) and *Sommelet* rearrangements (R8, 1)), carbon-to-carbon migrations (*Grovenstein-Zimmermann* (R12, 2), *Truce-Smiles* rearrangements (R1, 7) and the skeletal rearrangement in the *Bamford-Stevens* reaction (R5, 5)), and a nitrogen-to-oxygen migration (*Meisenheimer* rearrangement (112, 3)). An example of the latter is the base-catalyzed rearrangement of tertiary amine oxides to O,N,N-trisubstituted hydroxylamines:
\[
\text{R} \rightarrow (\text{CH}_3)_2\text{N}→O \rightarrow (\text{CH}_3)_2\text{N}–\text{OR} \quad (R12, 3)
\]

A good case of *Stevens'* and *Sommelet*'s electrophilic nitrogen-to-carbon migrations is that of benzyltrialkylammonium compounds:
\[
\text{R}
\] 
(R12, 1)
\[
\text{H}_2\text{Br}^+ \quad \text{H}_2\text{Br}^+ \quad \text{H}_2\text{Br}^+ \quad \text{H}_2\text{Br}^+
\]
(R12, 1)

The real rearrangement is considered from (b) onwards as the reaction (a)→(b) may be described as an elimination reaction.

Most other reaction schemes of Table III refer to isolated rearrangements between systems at a great chemical distance (high electron flow). This is not the case of the migration of alkyl-groups in the *Fischer* indole synthesis:

The *Wallach* degradation, related to the *Favorskii* rearrangement, involves the base-catalyzed formation of 1-hydroxycyclopentano-carboxylic acids from *α,α′*-dibromocyclohexanones:
The rearrangement of the \( \alpha,\alpha' \)-dihydroxyacyclohexanone intermediate follows the \( \bar{R}20 \) scheme.

Finally, \( \bar{R}4 \) has been observed in the formation of \( \alpha \)-aminoketones from ketoximes (Nebber rearrangement):

\[
\begin{align*}
\text{RCH}_2\text{CR'} & \quad \text{C}_5\text{H}_5\text{SO}_2\text{Cl} \\
\text{NOH} & \quad \text{C}_5\text{H}_5\text{OK} \\
\rightarrow & \quad \text{RCHNH}_2 \\
& \quad \text{COR'}
\end{align*}
\]

and is related to the Beckmann rearrangement (\( \bar{R}6 \)). If we admit the intermediate formation of azirines

\[
\begin{array}{c}
\text{R} - \text{CH} - \text{C} - \text{R'} \\
\text{N}
\end{array}
\]

the fundamental steps in the process may be visualized as \( \bar{R}1 \) and \( \bar{R}10 \).

4. Discussion

Examination of a representative subset of organic rearrangement schemes indicates that some twenty structural schemes (i.e., classes of \( \bar{R} \)-matrices and not specific \( \bar{R} \)-matrices) are sufficient for their description. Obviously, more significant data collections need to be examined before a complete set of reaction schemes can be formulated which is characteristic of the whole set of organic reaction types described in the literature. Similar information might prove to be valuable in computer-assisted synthesis planning as well as for the systematisation and codification of organic reactions.

With regard to the details of the set of \( \bar{R} \)-matrices derived here, we notice that several of the observed reaction schemes, precisely \( \bar{R}4, \bar{R}6, \bar{R}13, \bar{R}14, \bar{R}16, \bar{R}18 \) and \( \bar{R}20 \), were not detected in the sample of 1900 organic reactions mentioned above. As evident from Table III, these \( \bar{R} \)-matrices account for isolated reactions only. Actually, \( \bar{R}4, \bar{R}6, \bar{R}13 \) and \( \bar{R}16 \) may be considered as linear combination of other schemes.

As to the chemical constraints imposed by Ugi et al., upon \( \bar{R} \)-matrices, we notice that only 7 out of the 20 observed schemes comply with these restrictions, namely \( \bar{R}1, \bar{R}2, \bar{R}3, \bar{R}8, \bar{R}9, \bar{R}11 \) and \( \bar{R}12 \); in terms of the fraction of reactions examined it appears that the constraints properly account for over 75% of the rearrangement reactions dealt with.

As to application in synthesis planning, the present analysis thus suggests the usefulness of a very restricted set of general \( \bar{R} \)-matrices, covering a high percentage of the reactions investigated: roughly 80% of the organic rearrangements considered here appear to be described by 5 electron-flow schemes, namely \( \bar{R}1, \bar{R}2, \bar{R}5, \bar{R}7 \) and \( \bar{R}10 \).

This implies greater control on the tree proliferation in precursor generation. Definition of an optimum set of \( \bar{R} \)-matrices for this purpose must await other analyses on different and more extensive samples of organic reactions. Nevertheless, development of highly selective tree-pruning procedures for the evaluation of the nodes of the synthesis-tree is still of primary importance for the practical application of Ugi’s mathematical approach to synthesis planning.

5. Conclusions

In spite of their numerous kinds and complexities, the rearrangements of organic chemistry can be broken down into a relatively small set of electron-flow schemes or general reaction-matrix types, especially if we disregard the variety of \( \bar{R} \)-matrices with small incidence. The analysis roughly responds to the nature of other samples of organic reactions. In particular, the preponderance of two main reaction types is in common to other random reaction files. The analysis differs obviously from others based on mechanistic concepts.

It is pleasure to thank Prof. I. Ugi and Dr. J. Gasteiger at the Organische Chemie Institut, Technische Universität, München, for stimulating discussions. Helpful comments of Dr. G. Vléduts are gratefully acknowledged.

C. GILLESPIE, in preparation.
9 G. M. BADGER and J. W. CLARK-LEWIS, in “Molecu-
lar Rearrangements” (P. DE MAYO, ed.) Vol. 1,
10 P. DE MAYO (ed.), “Molecular Rearrangements”,
1963.
11 Merck Index, Merck & Co., Inc., Rahway (N.J.),
12 E. S. GOULD, “Mechanism and Structure in Organic
Chemistry”, Holt, Rinehart and Winston, New
York 1959.
13 C. K. INGOLD, “Structure and Mechanism in Or-
ganic Chemistry”, Cornell University Press, Ithaca
(1969), Chpts. X–XII.
14 E. GARAGNANI and J. C. J. BART, unpublished
results.
[1974].
16 Y. POCKER, in “Molecular Rearrangements” (P.
17 P. B. D. DE LA MARE, in “Molecular Rearrange-
ments” (P. DE MAYO, ed.) Vol. 1, p. 27–110, Inter-
18 P. A. S. SMITH, in “Molecular Rearrangements”
19 W. Z. HELDT and L. G. DONARUMA, in “Organic
Reactions” 11, Chpt. 1 [1960].
20 M. W. PARTRIDGE and H. A. TURNER, J. Pharm.
Pharmacol. 5, 103 [1953].
21 I. UGI, P. D. GILLESPIE, C. GILLESPIE, J. GASTEIGER,
and J. BLAIR, unpublished results.
22 P. A. S. SMITH, in “Organic Reactions” 3, Chpt. 9
[1946].
23 H. WOLFF, in “Organic Reactions” 3, Chpt. 8 [1946].
24 E. S. WALLIS and J. F. LANE, in “Organic Reac-
tions”, 3, Chpt. 17 [1946].