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Kyoto University
Joint Reaction, Transjointing and Stabilization of the Intermediate Products

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I. Joint Reaction by Formaldehyde

As well known, formaldehyde is one of the typical active components (electrophilic reagent) and acts upon numerous passive components, which have generally reactive hydrogen atoms, and exceptionlessly the methylol compounds are obtained as the primary reaction products. These methylol-compounds, though they are relatively stable in an alkaline medium, undergo generally further reaction, especially easily in acidic medium with the passive components. One can classify these reactions of formaldehyde in the following three cases, denoting the two passive components as $P_1H$ and $P_2H$ respectively:

(a) As the result of the reaction of formaldehyde upon $P_1H$ only methylol-compound and no jointed product $P_1-CH_2-P_1$ are obtained.

\[
\begin{align*}
\text{acetone} + CH_2O & \rightarrow \gamma\text{-ketobutanol} \\
\text{nitromethane} + CH_2O & \rightarrow \beta\text{-nitroethanol} \\
\alpha\text{-picoline} + CH_2O & \rightarrow 2\text{-}2(\beta\text{-oxyethyl})\text{-pyridine} \\
\text{acetaldehyde} + CH_2O & \rightarrow \text{pentaerythritol} \\
\text{acetylene} + CH_2O & \rightarrow \text{propargylalcohol and butine-diol} \\
NaHSO_3 + CH_2O & \rightarrow NaO_3SCH_2OH \\
HCN + CH_2O & \rightarrow NCCH_2OH , \ etc.
\end{align*}
\]

(b) The methylol-compound, $P_1-CH_2OH$, can be isolated as intermediate product,
but this methylol-compound can further joint the same passive component and the jointed compound, $P_1 \cdot CH_2 \cdot P_1$, is obtained as the final product.

Some examples of this case:

- phenol + $CH_2O$ -> phenol resin
- urea + $CH_2O$ -> urea resin
- melamine + $CH_2O$ -> melamine resins
- aniline + $CH_2O$ -> aniline resin
- acetoacetic ester (and other active methylene compounds) + $CH_2O$ -> methylene-bis-acetoacetic ester
- mercaptan + $CH_2O$ -> methylene-bis-mercaptan
- acid amide + $CH_2O$ -> methylene-bis-acid amide
- alcohol + $CH_2O$ -> acetal, etc.

(c) The methylol-compound, $P_1 \cdot CH_2OH$, obtained from formaldehyde and $P_1H$, can further joint another passive component, $P_2H$, and the mixed jointed product $P_1 \cdot CH_2 \cdot P_2$ is obtained as the final product.

The author is very much interested with this last case and wants to discuss this problem, giving as many examples as possible from recent publications.

Let us now select the following twenty representative passive components, which can be jointed by formaldehyde into the $P_1 \cdot CH_2 \cdot P_2$-type compounds, from a variety of compounds:

- hydrogen cyanide, sodium bisulfite, acetylene, acetone, acetaldehyde, acetoacetic acid ester, urea, phenol, acid amide, mercaptan, alcohol, ammonia, aliphatic primary and secondary amines, aniline, dimethylaniline, acetophenone, nitromethane, picoline, indole and hydrochloric acid.

Then, there should be two hundred and ten kinds of jointed compounds, when one selects arbitrary two components from these twenty compounds. It would be very interesting to examine from the literature how many among these two hundred and ten cases have already been investigated till now-a-days. The author wants to show in the following representative examples from the literatures.

1. Chloromethylation.

$$P_1H + CH_2O + HCl \rightarrow P_1 \cdot CH_2 \cdot Cl + H_2O$$

This chloromethylation reaction can be considered as one kind of the joint reaction by formaldehyde and numerous examples are already known. But this reaction is restricted by that the one component is hydrochloric acid.

2. The Mannich’s reaction

$$R-COCH_3 + CH_2O + HN<_{R'} \rightarrow R-COCH_2 \cdot CH_2 \cdot N<_{R'} + H_2O$$

$$\overset{\text{OH}}{\text{CH}_2} + CH_2O + HN<_{R} \rightarrow \overset{\text{OH}}{\text{CH}_2} \cdot N<_{R} + H_2O$$

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\[ \text{Joint Reaction} \]

\[ \text{+ CH}_2\text{O + HN}<^R \rightarrow \text{CH}_2-\text{CH}_2-N<^R + \text{H}_2\text{O} \]

\[ \text{C}=\text{CH + CH}_2\text{O + HN}<^R \rightarrow \text{C}=\text{C-CH}_2-N<^R + \text{H}_2\text{O} \]

There are also in this case many examples, but in this joint reaction the one component is restricted to amines.

3. \( R\text{-NH}_2 + \text{CH}_2\text{O} + \text{NaHSO}_3 \rightarrow R\text{-NH-CH}_2\text{-SO}_3\text{Na} + \text{H}_2\text{O} \)

This joint reaction is utilized practically for the preparation of Ionamine dyes (acetate silk dyestuffs) and one kind of ion exchange resins.

4. \( R\text{-NH} + \text{CH}_2\text{O} + \text{HCN} \rightarrow R\text{-N-CH}_2\text{-CN} + \text{H}_2\text{O} \)

\( \text{CH}_3\text{NH} + \text{CH}_2\text{O} + \text{NaCN} \rightarrow \text{CH}_3\text{N-CH}_2\text{-CN} \)

\( \text{NaOOC-CH}_2\text{-NH}_2 + \text{CH}_2\text{O} + \text{NaCN} \rightarrow \text{N(CH}_2\text{COOH)}_3 \)

\( \text{H}_2\text{N-CH}_2\text{-CH}_2\text{-NH}_2 + \text{CH}_2\text{O} + \text{NaCN} \)

\( \rightarrow (\text{HOOC-CH}_2)\text{_2N-CH}_2\text{-CH}_2\text{-N(CH}_2\text{COOH)}_2 \)

This joint reaction is very useful for the synthesis of some important technical products, for example the above mentioned N, N-dimethyl-ethylenediamine is useful for the synthesis of some cation-active surface active agents and the N-triacetic acid (Trilon A) and ethylenediamine-tetraacetic acid (Trilon B, Versene) are respectively useful as hard water softening agents.

5. \( R\text{-CONH}_2 + \text{CH}_2\text{O} + \text{NaHSO}_3 \rightarrow R\text{-CONH-CH}_2\text{-SO}_3\text{Na} + \text{H}_2\text{O} \)

There is an old example with benzamide about this reaction and the author synthesized an Igepon T-like surfactant using higher fatty acid amide.

6. Urea-formaldehyde resin and melamine resin modified by various alcohols, such as methyl-, ethyl-, butyl- and allyl-alcohol.

\( \text{CO}<^\text{NH}_2 + \text{CH}_2\text{O} + \text{C}_4\text{H}_9\text{OH} \rightarrow \text{CO}<^\text{NH-CH}_2\text{-O-C}_4\text{H}_9 \)

\( \text{H}_2\text{N-}^{-\text{C}}\text{-NH}_2 + \text{CH}_2\text{O+C}_4\text{H}_9\text{OH} \rightarrow \text{C}_4\text{H}_9\text{-O-CH}_2\text{-NH-}) \)

\( \text{N} \)

\( \text{NH-CH}_2\text{-O-C}_4\text{H}_9 \)

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This joint reaction is very important for the synthetic resin industry and it is obvious that these alkyl-ethers of the methylol-urea or methylol-melamine lose their alkyl-group partially during the hardening process, for example hardened resin from butylated methylol-urea contains 0.5~1.0 butoxyl-group per one urea molecule. 4)

The allylalcohol-modified urea resin was prepared for the first time by the author and it was shown that this resin is very water-resistant. Recently an investigation about the allylalcohol-modified melamine resin was published, 5)

7. Joint reaction among urea-derivatives, formaldehyde and amines. 6)

\[
X = C\langle\begin{array}{c}
\text{CH}_3 \\
\text{NH-CH} > \text{NH} \\
\text{NH-CH}_2 > \text{NH}
\end{array}\rangle ^{+} + \text{R}_3\text{CHO} + \text{NH}_3 \rightarrow X = C\langle\begin{array}{c}
\text{NR}_2\text{C-CH}_3 > \text{NH}
\end{array}\rangle
\]

\[
X = \text{O, S or NH; R}_1, \text{R}_2 = \text{H or org. radical}
\]

Examples;

\[
\begin{align*}
O &= C\langle\begin{array}{c}
\text{CH}_3 \\
\text{NH-CH} > \text{NH} \\
\text{NH-CH}_2 > \text{NH}
\end{array}\rangle, \\
O &= C\langle\begin{array}{c}
\text{NH-CH} > \text{NH} \\
\text{NH-CH}_2 > \text{NH}
\end{array}\rangle \text{N-C}_6\text{H}_{11},
\end{align*}
\]

8. Joint reaction among amine, formaldehyde and nitro-methane. 7)

\[
\begin{align*}
\text{R-NH}_2 + \text{CH}_2\text{O} + \text{CH}_3\text{NO}_2 & \rightarrow \text{R-NH-CH}_2-\text{CH}_2-\text{NO}_2 \\
\text{reduction} & \rightarrow \text{R-NH-CH}_2-\text{CH}_2-\text{NH}_2
\end{align*}
\]

\[
\begin{align*}
\text{O} & \text{-CH}_2-\text{CH}_2 > \text{NH} + \text{CH}_2\text{O} + \text{CH}_3\text{NO}_2 \\
& \rightarrow \text{morpholine N-CH}_2 > \text{CH-NO}_2 \\
\text{O} & \text{-CH}_2-\text{CH}_2 > \text{NH} + \text{CH}_2\text{O} + \text{CH}_3\text{CH}_2\text{NO}_2 \\
& \rightarrow \text{morpholine N-CH}_2 > \text{CH-NO}_2
\end{align*}
\]

9: Joint reaction among methylfuran, formaldehyde and amine. 8)

\[
\text{CH}_3-\bigtriangledown + \text{CH}_2\text{O} + \text{H}_2\text{N-R} \rightarrow \text{CH}_3-\bigtriangledown-\text{CH}_2-\text{NH-R}.
\]

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10. Joint reaction among carbazole, formaldehyde and piperidine.\(^9\)

\[
\begin{array}{c}
\text{NH} + \text{CH}_2\text{O} + \text{NH} \quad \xrightarrow{\text{CH}_2\text{CH}_2} \quad \text{N-CH}_2\text{N-CH}_2
\\
\text{CH}_2\text{CO} \quad \text{or} \quad \text{CO} \quad \text{NH} \quad \text{NH}
\\
\end{array}
\]

9-piperidinomethylcarbazole

11. Joint reaction among two different amines and formaldehyde. Following examples are known.

- morpholine + CH\(_2\)O + diethylamine
  \[
  \text{morpholine} + \text{CH}_2\text{O} + \text{diethylamine} \quad \rightarrow \quad \text{O}<\text{CH}_2\text{CH}_2>N-\text{CH}_2-N<\text{C}_2\text{H}_5
  \]

- morpholine + CH\(_2\)O + dibutylamine
- morpholine + CH\(_2\)O + dicyclohexylamine
- morpholine + CH\(_2\)O + piperidine
- morpholine + CH\(_2\)O + \(n\)-butylamine, aniline or o-toluidine
- morpholine + CH\(_2\)O + benzylcyanide

12. Joint reaction among amine, formaldehyde and alcohol or mercaptan.\(^{10}\)

\[
\begin{array}{c}
\text{R'NH} + \text{CH}_2\text{OH} \quad \xrightarrow{\text{R'OH or R'SH}} \quad \text{R'N-CH}_2\text{O-R'}
\\
\text{R'
\end{array}
\]

Examples:

\[(\text{C}_2\text{H}_5)_2\text{N-CH}_2 \cdot \text{O-CH}_2 \cdot \text{CH}_2 \cdot \text{CH}_3\]
\[(\text{C}_2\text{H}_5)_2\text{N-CH}_2 \cdot \text{O-CH}_2 \cdot \text{CH}_2 \cdot \text{O-CH}_2 \cdot \text{N} \quad \text{(C}_2\text{H}_5)_2\].

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13. Joint reaction among two different N-dialkylanilines and formaldehyde.

\[
R\text{N}^+\text{CH}_2\text{OH} + \text{N}^\text{CH}_2\text{N}^+\text{R} \rightarrow R\text{N}^+\text{CH}_2\text{N}^+\text{R}'
\]

Examples:

\[
\text{CH}_3\text{N}^+\text{CH}_2\text{OH} + \text{N}^\text{C}_4\text{H}_9 \rightarrow \text{CH}_3\text{N}^+\text{CH}_2\text{N}^\text{C}_4\text{H}_9
\]

14. Joint reaction among methylamine, formaldehyde and acetaldehyde.

\[
\text{CH}_3\text{NH}_2\text{HCl} + \text{CH}_2\text{O} + \text{CH}_3\text{CHO} \rightarrow \text{CH}_3\text{N}^+\text{CH}_2\text{CH}_2\text{CHO}
\]

15. Joint reaction among phthalimide, formaldehyde and alcohols.

\[
\text{HOOC} - \text{CH} = \text{N} - \text{CH}_2\text{OH} \rightarrow \text{HOOC} - \text{CH} = \text{N} - \text{CH}_2\text{Br} + \text{R} - \text{OH} \rightarrow \text{HOOC} - \text{CH} = \text{N} - \text{CH}_2\text{OR}
\]

The here obtained jointed product has a definite melting point and therefore this joint reaction can be utilized for the identification of various alcohols.

16. Joint reaction among phthalimide, formaldehyde and aromatic amine or nitrobenzene.

Examples:

\[
\text{NH}_2 - \text{CH}_3 + \text{HOOC} - \text{CH} = \text{N} - \text{CH}_2\text{OH}
\]

\[
\text{conc. H}_2\text{SO}_4 \rightarrow \text{H}_2\text{N} - \text{CH}_3
\]

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17. Joint reaction among sorbinamide, formaldehyde and cathecol.\(^{19}\)

\[
\text{CH}_3\text{-CH} = \text{CH} - \text{CH} = \text{CH} - \text{CONH}_2 + \text{CH}_2\text{O} \xrightarrow{\text{K}_2\text{CO}_3} \text{CH}_3\text{-CH} = \text{CH} - \text{CH} = \text{CH} - \text{CONH} - \text{CH}_2\text{OH}
\]

heated 2 hrs. on water bath.

18. Joint reaction among acetaldehyde, formaldehyde and methylalcohol.\(^{10}\)

It is reported that mono- and dimethylethers of pentaerythritol are obtained, when the pentaerythritol synthesis is performed in methylalcohol.

19. Joint reaction among higher fatty acid amide, formaldehyde and various components.\(^{17}\)

Following examples are recorded:

\[
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{NH}_2\text{C}_2\text{H}_5 \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH}-\text{CH}_2\text{N}_2\text{C}_2\text{H}_5
\]

\[
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{NH}_2\text{C}_2\text{H}_4\text{OH} \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH}-\text{CH}_2\text{N}_2\text{C}_2\text{H}_4\text{OH}
\]

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\[
\begin{align*}
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{alcohol}(R-\text{OH}) & \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH-CH}_2\text{-O-R} \\
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{mercaptan}(R-\text{SH}) & \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH-CH}_2\text{-S-R} \\
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{NH}_2\text{CO-CH}_2\text{Cl} & \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH-CH}_2\text{-NHCO-CH}_2\text{Cl} \\
& \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH-CH}_2\text{-NHCO-CH}_2\text{-N} \backslash \backslash \text{Cl} \\
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{NH}_2\text{CO-C}_6\text{H}_5 & \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH-CH}_2\text{-NHCO-C}_6\text{H}_5 \\
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{NH}_2\text{CONH}_2 & \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH-CH}_2\text{-NHCONH}_2 \\
\text{C}_{17}\text{H}_{35}\text{CONH}_2 + \text{CH}_2\text{O} + \text{HO-CH}_2\text{-CH}_2\text{N(CH}_2\text{-CH}_2\text{OH)}_2 & \rightarrow \text{C}_{17}\text{H}_{35}\text{CONH-CH}_2\text{-O-CH}_2\text{-CH}_2\text{N (CH}_2\text{-CH}_2\text{-OH)}_2 \end{align*}
\]


\[
\begin{align*}
\text{NH-CH}_2\text{-NH} + \text{CH}_2\text{O} + \text{NH}_3\text{CH}_3 & \rightarrow \text{C-CH}_2\text{-N} \backslash \backslash \text{CH}_3
\end{align*}
\]

21. Joint reaction among urea, formaldehyde and phenol. \(^{19}\)

\[
\begin{align*}
\text{NH}_2\text{CONH}_2 + \text{CH}_2\text{O} + \text{C}_6\text{H}_5\text{OH} & \rightarrow \text{OC} \text{NH-CH}_2\text{-} \backslash \backslash \text{OH} \\
\text{NH}_2\text{CONH}_2 + \text{CH}_2\text{O} + \text{C}_6\text{H}_5\text{NO}_2 & \rightarrow \text{OC} \text{NH-CH}_2\text{-} \backslash \backslash \text{OH} \end{align*}
\]

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22. Joint reaction between formaldehyde and one compound, which has two functional groups in its molecule and therefore results cyclic compound. Among many examples known, some of them are given below:

\[
\text{CH}_3\text{CHNHCH}_2\text{NH}_2 + \text{CH}_2\text{O} \rightarrow\]

\[
\text{CH}_3\text{CH(NH)}_2\text{NHCH}_2\text{NH}_2 + \text{CH}_2\text{O} \rightarrow\]

N-isopropyl-hexahydropyrimidine

\[
\text{CH}_3\text{COCH}_2 + \text{CH}_2\text{O} \xrightarrow{\text{K}_2\text{CO}_3} \text{CH}_3\text{COCHCH}_2\text{O} \]

\[
\text{CH}_3\text{CONHCH}_2\text{NNH}_2 + \text{CH}_2\text{O} \xrightarrow{\text{heated in alcohol}} \text{3-(p-tolyl)-6-methyl-1,2,3,4-tetrahydroquinazoline}\]

\[
\text{CONHAr} + \text{CH}_2\text{O} \xrightarrow{\text{alkali in C}_2\text{H}_5\text{OH}} \text{3-Ar-1,2,3,4-tetrahydroquinazolone-4}\]

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As above various representative examples given, many cases of the joint reaction by formaldehyde already been researched, but nevertheless, if the number of these researched cases is compared with the total number of all the considerable, i.e. two hundred and ten cases, it can be recognised that there remains yet a wide unresearched domain. From this standpoint, i.e. in order to fulfil the blank domain, the author has recently performed some experiments upon this joint reaction by formaldehyde, the results of which will be summerized in the last paragraph of this paper.

II. Transjointing Reaction

There are indeed many kinds of jointed compounds by formaldehyde, but these jointed compounds are never all in themselves stable. They suffer more or less easily transjointing by other component. When one designates this third component as $P_3H$, so the transjointing reaction can be represented as follows:

$$P_1—CH_2—P_2 + P_3H \rightarrow P_1—CH_2—P_3 + P_2H$$

The name “Transjointing” was first given by the author from the analogy in case of Transesterification, but the nomenclature “Transjointing” is more general and so Transesterification should be included in the Transjointing as only a part of the latter. The transjointing reaction of $P_1—CH_2—P_2$ by $P_3H$ occurs relatively easily in the presence of acid and there seems to exist a definite rule about the relation between $P_2H$ and $P_3H$.

But the author wants at first to show as many examples as possible and then to discuss about the above mentioned point.

1. Reaction of the chloromethyl-ether of alcohols (jointed compound from alcohol, formaldehyde and hydrochloric acid) and chloromethylamide of fatty acid (jointed compound from fatty acid amide, formaldehyde and hydrochloric acid) upon alcohols.

$$R—O—CH_2Cl + R'OH \rightarrow R—O—CH_2—O—R' + HC1$$

Acetal

$$R—CONH—CH_2Cl + R'OH \rightarrow R—CONH—CH_2—O—R' + HC1$$

Examples:

- $C_4H_9—O—CH_2Cl + C_4H_9OH \xrightarrow{\text{water bath}} C_4H_9—O—CH_2—O—C_4H_9$ (10 hrs.)

- $C_4H_9—O—CH—Br + C_2H_5OH \xrightarrow{\text{NaOH}} C_4H_9—O—CH—OC_2H_5$

- $\xrightarrow{\text{CH}_3} C_2H_5—O—CH—OC_2H_5 + C_4H_9OH$

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R-O-CH₂-Cl + pyridine $\rightarrow$ R-O-CH₂-N<sub>Cl</sub>

R-O-CH₂-N<sub>Cl</sub> + OH<sub>100°-160°</sub> + pyridine HCl $\rightarrow$ R-O-CH₂-O<sub>Cl</sub> + pyridine HCl<sup>59</sup> 70 mins.

R-CONH-CH₂OH $\rightarrow$ R-CONH-CH₂-N<sub>Cl</sub>

R-CONH-CH₂-N<sub>Cl</sub> + C₄H₉OH $\rightarrow$ R-CONH-CH₂-O-C₄H₉ + pyridine HCl<sup>59</sup>

R-CONH-CH₂-N<sub>Cl</sub> + Cellulose $\rightarrow$ R-CONH-CH₂-O-Cellulose<sup>60</sup>

\[ \text{N-CH₂-Br + R-OH (alcohol)} \rightarrow \text{N-CH₂-O-R}^{153} \]

From these examples it can be concluded that the jointed halogen is easily replaced by alcohols.

2. Transjointing between N-alkoxymethyamine (jointed compound from amine, formaldehyde and alcohol) and other various components.

Examples<sup>163</sup>:

\[ (C₂H₅)₂N-CH₂-O-CH₂-CH<sub>CH₃</sub> + CH₃CO- \rightarrow (C₂H₅)₂N-CH₂-CO-CH₃ + CH₃CH-CH₂OH \]

\[ (C₂H₅)₂N-CH₂-O-CH₂-CH<sub>CH₃</sub> + CH₃NO₂ \rightarrow (C₂H₅)₂N-CH₂-CH₂-NO₂ \]
McLeod and Robinson observed further that transjointment could occur between the above N-butoxymethyl-diethylamine and cyanoacetic ester or resorcin, but they isolated no definite product in this case.

Heou-Feo Tseow and Chang-Tsing Yang \(^{27}\) have researched the following transjointment reaction of this kind. The reaction can occur generally upon only mixing the components.

\[
\begin{align*}
\text{CH}_2\left(\text{CH}_2\text{CH}_2\right)\text{N}-\text{CH}_2\text{-O-}\text{C}_2\text{H}_5 & + \text{OH} \\
& \rightarrow \text{C}_5\text{H}_{10}\text{N}-\text{CH}_2\text{-OH} + \text{C}_2\text{H}_5\text{OH} \\
\text{CH}_2\left(\text{CH}_2\text{CH}_2\right)\text{N}-\text{CH}_2\text{-O-}\text{C}_2\text{H}_5 & + \text{OH} \\
& \rightarrow \text{C}_5\text{H}_{10}\text{N}-\text{CH}_2\text{-OH} + \text{C}_2\text{H}_5\text{OH} \\
\text{CH}_2\left(\text{CH}_2\text{CH}_2\right)\text{N}-\text{CH}_2\text{-O-}\text{C}_2\text{H}_5 & + \text{CH}_3 \\
& \rightarrow \text{C}_5\text{H}_{10}\text{N}-\text{CH}_2\text{-OH} + \text{C}_2\text{H}_5\text{OH} \\
\text{CH}_2\left(\text{CH}_2\text{CH}_2\right)\text{N}-\text{CH}_2\text{-O-}\text{C}_2\text{H}_5 & + \text{NH}_2 \\
& \rightarrow \text{C}_5\text{H}_{10}\text{N}-\text{CH}_2\text{-NH}_2 + \text{C}_2\text{H}_5\text{OH} \\
\text{CH}_2\left(\text{CH}_2\text{CH}_2\right)\text{N}-\text{CH}_2\text{-O-}\text{C}_2\text{H}_5 & + \text{NH}_2 \\
& \rightarrow \text{C}_5\text{H}_{10}\text{N}-\text{CH}_2\text{-NH} + \text{C}_2\text{H}_5\text{OH}
\end{align*}
\]
Joint Reaction, Transjointing and Stabilization of the Intermediate Products

\[
\begin{align*}
\text{CH}_2\text{CH}_2\text{N-C}_2\text{H}_5-O &+ \text{CONH}_2 \\
\quad &\rightarrow \text{C}_6\text{H}_{10}\text{N}-\text{CH}_2-\text{NHCO-} + \text{C}_2\text{H}_5\text{OH} \\
\text{CH}_2\text{CH}_2\text{N-C}_2\text{H}_5-O &+ \text{NH} \\
\quad &\rightarrow \text{C}_6\text{H}_{10}\text{N}-\text{CH}_2-\text{N} + \text{C}_2\text{H}_5\text{OH} \\
\text{CH}_2\text{CH}_2\text{N-C}_2\text{H}_5-O &+ \text{Cl} \\
\quad &\rightarrow \text{C}_6\text{H}_{10}\text{N}-\text{CH}_2-\text{OH} + \text{C}_2\text{H}_5\text{OH} \\
\text{CH}_2\text{CH}_2\text{N-C}_2\text{H}_5-O &+ \text{NO}_2 \\
\quad &\rightarrow \text{C}_6\text{H}_{10}\text{N}-\text{CH}_2-\text{OH} + \text{C}_2\text{H}_5\text{OH}
\end{align*}
\]

From these examples it can be concluded that the jointed alkoxy group is easily replaceable by amine, acid amide, phenol, naphthol and active methyl- or methylene-compounds.

3. Transjointing reaction between methylene-bis-amine (jointed compound from two amines and formaldehyde) or methylene-bis-amide (jointed compound from two acid amides and formaldehyde) and phenol, naphthol and other component.

Examples:

\[
\begin{align*}
\text{(C}_6\text{H}_{10}\text{N})_2\text{CH}_2+ \text{heated in alcohol} &\rightarrow \text{C}_6\text{H}_{10}\text{N}-\text{CH}_2-\text{NC}_5\text{H}_{10} + \text{HNC}_5\text{H}_{10} \\
\text{(C}_6\text{H}_{10}\text{N})_2\text{CH}_2+ \text{heated in alcohol+HCl} &\rightarrow \text{(CH}_8\text{)}_2\text{N}-\text{CH}_2-\text{N}(\text{CH}_3)_2 + 2\text{HNC}_5\text{H}_{10}
\end{align*}
\]

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\((\text{C}_6\text{H}_{10}\text{N})_2\text{CH}_2 + 5,5\text{-dimethyldihydroresorcin}\)

\[
\begin{array}{c}
\text{CH}_3 \quad \text{CH}_2 \\
\text{C} \quad \text{C} \\
\text{CH}_2 \quad \text{CH}_2 \\
\text{C} \quad \text{C} \\
\text{CH}_3 \quad \text{CH}_3 \\
\end{array}
\]

H_5\text{C}_2\text{OOC-NH-CH}_2\text{-NH-COOC}_2\text{H}_5 + \text{methylene-bis-urethan}

\[
\begin{array}{c}
\text{OH} \\
\text{CH}_3
\end{array}
\]

\[
\rightarrow \text{C}_2\text{H}_5\text{OOC-NH-CH}_2\text{-CH}_3
\]

N-(2-oxy-3,5-dimethylbenzyl)-urethan

\[
\begin{array}{c}
\text{OH} \\
\text{CH}_3 \quad \text{CH}_3 \\
\end{array}
\]

methylene-bis-(ethylurea) +

\[
\begin{array}{c}
\text{OH} \\
\text{CH}_3 \\
\text{CH}_3
\end{array}
\]

\[
\rightarrow \text{C}_2\text{H}_5\text{NH-CONH-CH}_2\text{-CH}_3
\]

N-ethyl-N'-(2-oxy-3,5-dimethylbenzyl)-urea

\[
\begin{array}{c}
\text{OH} \\
\text{CH}_3 \\
\text{CH}_3 \\
\end{array}
\]

C_6H_5-NHCONH-C_6H_5 +

\[
\begin{array}{c}
\text{OH} \\
\text{CH}_3 \\
\text{CH}_3
\end{array}
\]

\[
\rightarrow \text{C}_6\text{H}_5\text{-NHCONH-CH}_2\text{-CH}_3
\]

N-phenyl-N'-(2-oxy-3,5-dimethylbenzyl)-urea

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Joint Reaction, Transjointing and Stabilization of the Intermediate Products

\[
\text{NH}_2\text{CONH-CH}_2\text{-NHCONH}_2 + \text{methylene-bis-urea} \rightarrow \text{NH}_2\text{CONH-CH}_2\text{-CH}_3
\]

\[
\text{N(2-oxy-3,5-dimethylbenzyl)-urea}
\]

\[
\text{R-CH} < \text{NH-CONH} - \text{CH}_2 - \text{NHCONH}_2 < \text{CH}_3 + \text{CH}_2\text{-NO}_2 \rightarrow \text{R-CH} < \text{NHCOCH}_3 < \text{CH}_2\text{-NO}_2 + \text{NH}_2\text{COCH}_3
\]

\[
\text{bis-amide + CH}_3\text{NO}_2 \rightarrow \text{bis-amide + CH}_2\text{-COOC}_2\text{H}_5
\]

\[
\text{bis-amide + CH}_2\text{-COOC}_2\text{H}_5 \rightarrow \text{bis-amide + CH}_3\text{NO}_2
\]

From these examples it can be concluded that the jointed aminogroup or amidogroup can be easily replaced by phenol and active methyl- or methylene-compounds.

4. Transjointing reaction between the Mannich's bases (jointed compound from chiefly ketones and amines) or its analogous compounds and phenols or active methylene-compounds.

Examples:

Synthesis of tryptophan from gramine.
Synthesis of glutamic acid.

\[ \text{piperidine} + \text{CH}_2\text{O} + \text{formamino-malonate} \]

\[ \rightarrow \text{CH}_2\left(\text{CH}_2-\text{CH}_2\right)\text{N-CH}_2\text{-C(COO}_2\text{H}_5\text{)}_2\text{NHCOH} \]

(one kind of Mannich's base)

\[ \text{malonate} \rightarrow (\text{C}_2\text{H}_3\text{OOC})_2\text{CH-CH}_2\text{-C(COO}_2\text{H}_5\text{)}_2 + \text{piperidine} \]

\[ \text{NHCOH} \]

\[ \text{hydrolysis} \rightarrow \text{HOOC-CH}_2\text{-CH}_2\text{-CH-COOH} \]

\[ \text{NH}_2 \]

DL-glutamic acid

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Joint Reaction, Transjoining and Stabilization of the Intermediate Products

\[
\begin{align*}
\text{COCH}_2\text{-CH}_2\text{-N(CH}_3)_2\text{HCl} + \text{KCN} & \rightarrow \text{COCH}_2\text{-CH}_2\text{-CN} + \text{NH(CH}_3)_2 \\
\end{align*}
\]

Many other reactions which concern with the transjoining of the amino group of the Mannich's base by active methylene-compounds are given in Org. Reactions, 1. p.320.

Other examples:

5. Reduction of the Mannich base and other jointed compound into methyl-group.

Examples:

\[
\begin{align*}
\text{HO} + \text{CH}_2\text{O} + \text{piperidine} & \rightarrow \text{N} + \text{CH}_2\text{-CH}_2\text{-NC}_5\text{H}_10 \quad \text{reduction} \quad \text{N} + \text{CH}_3 \\
\end{align*}
\]

reducing agent:

\[\text{NaOCH}_2\text{+C}_2\text{H}_5\text{OH, at 220° in autoclave}\]
These examples show that the Mannich's base and other jointed compounds can be relatively easily reduced to methyl-group and that this reduction is considered as one kind of transjointing reaction of the jointed compound, the P3H-component being active hydrogen.

Now, from the above mentioned several examples about the transjointing reaction, one can abstract the following conclusion:

The transjointing reaction occurs in the following order:

a) Halogen-group is most easily replaceable.

b) Alkoxy-group is next easily replaceable.

c) Amino-group is the next and this can generally be replaced only by phenols, active methyl- or methylene compounds and not by alcohols.

d) Phenol, naphthol, active methyl- or methylene compounds are most tightly jointed by formaldehyde, i.e. when the formaldehyde joints the carbon atoms of the P1H and P2H, then the resulted bonds are most stable. But thus obtained carbon-carbon bonds are never so strong as the carbon-carbon bond in the paraffin molecule. This can be seen in the reduction example of the methylenebis-β-naphthol, or the coupling reaction of diazoniumsalt upon the same compound, resulting the α-arylazo-naphthol-(2), liberating the formaldehyde free.

e) Of course, the transjointing reaction is a kind of reversible reaction and the above order means only the magnitude of the equilibrium constant.

f) The above order coincides quite well with the order of inductive effect of the substituents.

Appendix

There are some reactions of formaldehyde, which are quite contrary to the joint reaction and in which the formaldehyde as methyleneglycol i.e. as passive component receives the action of active components. Some examples of this kind are given in the following:

\[
\text{C}_{17}\text{H}_{35}\text{CN} + \text{paraformaldehyde} + \text{HCl-gas}
\]

\[
\rightarrow \text{C}_{17}\text{H}_{35} - \text{C} - \text{O} - \text{CH}_2 - \text{Cl} \quad \rightarrow \quad \text{C}_{17}\text{H}_{35} - \text{C} - \text{O} - \text{CH}_2 - \text{N} \quad \text{Cl}
\]
cation active surfactant

\[
\text{CH}_3\text{COCl} + \text{paraformaldehyde} + \text{ZnCl}_2 \quad \rightarrow \quad \text{CH}_3\text{COOCH}_2\text{Cl} \quad \text{chloromethyl acetate}
\]

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\[
\begin{align*}
\text{CH}_3\text{—CO—O} + \text{paraformaldehyde} + \text{ZnCl}_2 & \rightarrow \text{CH}_3\text{—COOCH}_2\text{OOC—CH}_3 + \text{CH}_3\text{—COOCH}_2\text{—O—CH}_2\text{OOC—CH}_3 \\
& \text{methylene diacetate} \quad \text{dioxymethylene diacetate}
\end{align*}
\]

\[
\text{HO—CH}_2\text{—OH} + \text{CH}_2═\text{CH—CN} \rightarrow \text{NC—CH}_2\text{—CH}_2—\text{O—CH}_2\text{—O—CH}_2\text{—CH}_2—\text{CN} \\
\text{formal of ethylenecyanhydrin}
\]

\[
\text{alcohol} + \text{HO—CH}_2—\text{OH—CH}_2═\text{CH—CN} \rightarrow \text{R—O—CH}_2—\text{O—CH}_2—\text{CH}_2—\text{CN} \\
(R—OH) \quad \text{mixed formal of alcohol and ethylenecyanhydrin}
\]

III. Joint Reaction by Nitrous Acid

Nitrous acid acts as active component upon some passive components and results the nitroso-compounds, as shown below:

\[
P_1\text{H} + \text{HNO}_2 \rightarrow P_1—\text{NO} + \text{H}_2\text{O}
\]

The nitroso-compounds, thus obtained or obtained otherwise by reduction of nitro-compounds, act also as active component upon some passive components, which have generally two reactive hydrogen atoms, as shown below:

\[
P_1—\text{NO} + P_2\text{H}_2 \rightarrow P_1—\text{N}═P_2 + \text{H}_2\text{O}
\]

Thus, it can be understood, that the nitrous acid also joints two passive components at both sides of the nitrogen atom. The nitrosocompounds can, therefore, be seen as the intermediate product of the joint reaction by nitrous acid. The conditions are quite the same as in the case of joint reaction by formaldehyde. The nitrosation reaction is quite popular and the author wants to show some examples of only the second step in the following:

\[
\begin{align*}
\text{R—NO} + \text{R’—NH}_2 & \rightarrow \text{R—N}═\text{N—R’} + \text{H}_2\text{O} \\
& \text{azo compound}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3\text{N—N—NO} + [\text{CH}_2—\text{OH}] & \rightarrow \text{Meldola’s Blue} \\
\text{R—NO} + \text{CH}_2(\text{COOC}_2\text{H}_5)_2 & \rightarrow \text{R—N}═\text{C( COOC}_2\text{H}_5)_2 + \text{H}_2\text{O} \\
\text{R—NO} + \text{CH}_2&—\text{C}_6\text{H}_5 \rightarrow \text{R—N}═\text{C}<\text{C}_6\text{H}_5 \\
\text{R—NO} + \alpha—\text{Naphthol} & \rightarrow \text{R—N}═\text{O} \quad \text{(Naphthol Blue)}
\end{align*}
\]

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When \( P_1H \) is an aromatic primary amine, then the intermediate compound of the joint reaction, which corresponds to the nitrosocompound, is the diazo-compound. This diazo compounds couple with various passive components and result various azo-dyestuffs. From this point of view, the azo-dyestuffs are regarded as the jointed compounds by nitrous acid. As the methylol-compounds, which are the intermediate products of the joint reaction by formaldehyde and are more or less unstable and apt to joint the second component, the diazo-compounds are also very unstable and reactive. The conditions in both cases are quite analogous. Again, the alkylether of the methylol-compound corresponds to the diazo oxy-compound and the Mannich's base, the reaction product of methylol compound with amine, corresponds to the diazo-amino-compound. As already mentioned, the jointed compounds by formaldehyde suffer the trans-jointing reaction in various ways, so the quite analogous transcoupling reaction (Umkupplung) occurs by diazo oxy- and diazo-amino-compounds. These behaviors of the methylol- and diazo compounds will be discussed later together with the stabilization of the intermediate products.

IV. Joint Reaction by Phosgen

Phosgen acts also as active component upon various passive components and results a compound, which corresponds to the acid chloride, as shown below:

\[
P_1H + COCl_2 \rightarrow P_1-\text{COCl} + \text{HCl}
\]

The resulted acid chloride is also very reactive and reacts with the second passive component and gives ketone.

\[
P_1-\text{COCl} + P_2H \rightarrow P_1-\text{CO}P_2 + \text{HCl}
\]

Thus, the phosgen behaves quite analogously as the nitrous acid or the formaldehyde and joints two passive components at the both sides of the carbonyl group. Many popular examples of this kind are well known and therefore the author wants to omit to show these examples.

When the first passive component, \( P_1H \), is an aliphatic or aromatic primary amine, then the intermediate product is the so-called carbamylchloride, \( R-NH\text{COCl} \). This carbamyl-chloride loses often further one mole of \( \text{HCl} \), especially when the
reaction temperature is high enough and excess phosgen exists, and gives the isocyanate. This isocyanate is again very unstable and reactive, and reacts with the second passive component, producing the same product as the carbamylchloride reacted with the same component.

\[
\text{R-NH-COCl} \rightarrow \text{R-N=C=O (isocyanate)} + \text{HCl}
\]

The acid chloride of the type, R-CH₂-COCl, loses also one mole of HCl and results the ketene, R-CH=O. The thus obtained ketene is also very unstable and reactive, and reacts with various passive components, quite analogously with the isocyanate. As the acid chloride can be considered as the intermediate product of the joint reaction by phosgen, the ketene as well as the isocyanate can also be considered as the intermediate product of the joint reaction by phosgen. These three intermediate products correspond respectively to the methylol-compound or the nitroso- or diazo-compound and their transjointing behaviors and stabilization conditions are quite analogous. Of these behaviors and conditions the author wants to describe later.

V. Joint Reaction by Ortho-formic Ester

As well known, the ortho-formic ester reacts with some passive components as follows:

\[
\text{HC(OCH₃)₃} + \text{P₁H} \rightarrow \text{P₁-CH(OCH₃)₂ + C₂H₅OH}
\]

The here obtained P₁-CH(OCH₃)₂ is the diethylacetal of the aldehyde P₁-CHO. Aldehyde condenses generally with amines and active methyl- or methylene-compounds, as it is popular by the famous reaction, known as “Aldol-Condensation” or “Knoevenagel’s Cinnamic Acid Synthesis”. The acetal of aldehyde behaves in the same manner as the aldehyde itself. If the second passive component is denoted as P₂H₂, this second-step reaction can be expressed as below:

\[
P₁-\text{CH(OCH₃)₂} + \text{P₂H₂} \rightarrow \text{P₁-CH=P₂} + 2 \text{C₂H₅OH}
\]

Thus, the ortho-formic ester joints appropriate two passive components at both sides of the methin-carbon. This behavior is quite analogous to the formaldehyde or nitrous acid. The author wants in the following to show some examples of this joint reaction by ortho-formic ester, though they are somewhat old.

1. Synthesis of Astraphloxine FF, an acetate silk dyestuff.

\[
\begin{align*}
\text{C-CH} & \equiv \text{CH} - \text{CH} \equiv \text{C} \\
\text{CH}_3 & \text{CH}_3 \\
\text{CH}_3 & \text{CH}_3
\end{align*}
\]


\[
\begin{align*}
2 \text{CH}_3 + \text{C-H} & \equiv \text{CH} - \text{CH} - \text{CH} \equiv \text{N} \\
\text{CH}_3 & \text{I} \text{CH}_3 \\
\text{CH}_3 & \text{I} \text{CH}_3
\end{align*}
\]

illuminol

\[
\begin{align*}
2 \text{CH}_3 + \text{C-H} & \equiv \text{CH} - \text{CH} - \text{CH} \equiv \text{N} \\
\text{CH}_3 & \text{I} \text{CH}_3 \\
\text{CH}_3 & \text{I} \text{CH}_3
\end{align*}
\]

pyridine illuminol

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4. \( \text{CuH}_2\text{NH}_2 + \text{CH(OC}_2\text{H}_5)\text{H} \rightarrow \text{C}_6\text{H}_5\text{NH} - \text{CH} = \text{N} - \text{C}_6\text{H}_5 \)
   diphenylformamidine

5. Reaction of ortho-formic ester with some active methylene compounds.

\[
\text{HC(O}_2\text{H}_5)\text{H} + \text{CH}_2\text{<COCH}_3 \rightarrow \text{C}_6\text{H}_5\text{OCH} = \text{C}<\text{COCH}_3
\]
ethoxymethylene-acetoacetic ester

\[
\text{C}_2\text{H}_5\text{OCH} = \text{C}<\text{COCH}_3 + \text{CH}_2<\text{COCH}_3
\rightarrow \text{CH}_3\text{OOC}<\text{CH} - \text{CH} = \text{C}<\text{COCH}_3
\]
methenyl-bis-acetoacetic ester

\[
\text{CH(O}_2\text{H}_5)\text{H} + \text{CH}_2<\text{COCH}_3 \rightarrow \text{C}_6\text{H}_5\text{OCH} = \text{C}<\text{COCH}_3
\]
ethoxymethylene-acetylacetone

Thus, as seen from these examples, ortho-formic ester joints two passive components. Further these jointed compounds undergo the transjointing reaction, as shown in the following and the order of transjointing is quite similar as in the case of formaldehyde.

\[
\text{ethoxymethylene-acetylacetone} + \text{NH}_3 \rightarrow \text{H}_2\text{N} - \text{CH} = \text{C}<\text{COCH}_3 + \text{C}_2\text{H}_5\text{OH}
\]
aminomethylene-acetylacetone

\[
\text{diphenylformamidine} + \text{benzylcyanide}
\rightarrow \text{CN} + \text{H}_2\text{N}
\]
anilinomethylene-benzylcyanide

\[
\text{diphenylformamidine} + \text{malonic ester}
\rightarrow \text{COOC}_2\text{H}_5 + \text{H}_2\text{N}
\]
anilinomethylene-malonic ester

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Ryohei ODA

diphenylformamidine + 1-phenyl-3-methylpyrazolone

\[
\begin{align*}
\text{CH}_3 - \text{C} & \equiv \text{C} \equiv \text{C} \equiv \text{CH} - \text{NH} - \text{aryl} + \text{NH}_2 - \text{aryl} \\
\text{N} & \equiv \text{C} \\
\text{N} & \equiv \text{O} \\
\text{O} & \equiv \text{N}
\end{align*}
\]

1-phenyl-3methyl-4-anilinomethylene-pyrazolone

and

\[
\begin{align*}
\text{CH}_3 - \text{C} & \equiv \text{CH} \equiv \text{C} \equiv \text{CH}_3 + \text{NH}_2 - \text{aryl} \\
\text{N} & \equiv \text{C} \\
\text{N} & \equiv \text{O} \\
\text{O} & \equiv \text{N}
\end{align*}
\]

methenyl-bis-(1-phenyl-3-methylpyrazolone)

VI. Joint Reaction by Formic Ester and Carbon Monoxide

(a) Joint reaction by formic ester.

The ortho-formic ester, which was the subject in the preceding paragraph, can be considered as a jointed compound from formic ester (or its hydrated form, \( \text{H}_2\text{O} \rightarrow \text{CH} \equiv \text{OC}_2\text{H}_5 \)) and two molecules of ethylalcohol, and therefore the joint reaction by ortho-formic ester is not an essential joint reaction, but only a transjointing reaction of the jointed compounds by formic ester.

It is clear from this consideration, that there should be many examples of joint reaction by formic ester. This is indeed true and the author wants to show some examples of this kind in the following.

\[
\text{HCOOC}_2\text{H}_5 + \text{CH}_3\text{-COOC}_2\text{H}_5 \xrightarrow{\text{Na}} \text{NaOCH} \equiv \text{CH} \equiv \text{COOC}_2\text{H}_5
\]

Na-enolate of formylacetic ester

This Na-enolate of formylacetic ester is the intermediate product of the joint reaction and is unstable and reactive. This intermediate products react further with various passive components.

\[
\begin{align*}
\text{NaOCH} \equiv \text{CH} \equiv \text{COOC}_2\text{H}_5 \xrightarrow{\text{acidify}} \text{H} - \text{C} \equiv \text{CH}_2 \equiv \text{COOC}_2\text{H}_5 \\
\xrightarrow{\text{polymerise}} \text{C}_2\text{H}_5\text{OOC} - \text{CH}_2 \equiv \text{CH} = \text{C} \equiv \text{COOC}_2\text{H}_5 \\
\text{CHO}
\end{align*}
\]

one kind of joint reaction

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Joint Reaction: Transjointing and Stabilization of the Intermediate Products

\[ \text{formylacetic ester} + \text{NH}_2-\text{NH}_2 \rightarrow \text{CH}_2-\text{CH} \]
\[ \text{pyrazolone} \]

\[ \text{formylacetic ester} + \text{NH}_2-\text{OH} \rightarrow \text{C}_2\text{H}_5\text{OOC}-\text{CH}_2-\text{CH}=\text{N}-\text{OH} \]

\[ \text{oxime} \]

\[ \text{formylacetic ester} + \text{NH}_2-\text{NH}-\text{CONH}_2 \rightarrow \text{C}_2\text{H}_5\text{OOC}-\text{CH}_2-\text{CH} = \text{N}-\text{NH}-\text{CONH}_2 \]

\[ \text{semicarbazone} \]

\[ \text{formylacetic ester} + \text{NH}_2-\text{CH}=\text{N} \rightarrow \text{C}_2\text{H}_5\text{OOC}-\text{CH}_2-\text{CH} = \text{N}-\text{NH}-\text{CONH}_2 \]

\[ \text{or} \quad \text{C}_2\text{H}_5\text{OOC}-\text{CH}=\text{CH}-\text{NH} \]

\[ \beta\text{-anilino-acrylic ester} \]

\[ \text{formylacetic ester} + \text{CH}_3-\text{C} \rightarrow \text{CH}_3-\text{C} \]
\[ \text{acetamidine} \]
\[ \text{4-oxy-2-methyl-pyrimidine} \]

\[ \text{formylacetic ester} + \text{thiourea} \rightarrow \text{S}=\text{C} \]
\[ \text{thiouracil} \]

\[ \text{formylacetic ester} + \text{cyanoacetic ester} \]
\[ \rightarrow \text{C}_2\text{H}_5\text{OOC} \]
\[ \text{C}_2\text{H}_5\text{OOC}-\text{CH}_2-\text{CH}-\text{C} \]
\[ \text{1. 3-dicyan-cyclobutane-1, 3-dicarboxylic acid} \]
\[ \text{2. 4-diacetic acid tetraethylster} \]

\[ \text{formylacetic ester} + (\text{CH}_3)_2\text{NH} \rightarrow (\text{CH}_3)_2\text{N}-\text{CH}=\text{CH}-\text{COOC}_2\text{H}_5 \]

\[ \text{formylacetic ester} + \text{NH}_2-\text{N}<\text{HN}_2 \rightarrow \text{NH}_2-\text{C} \]
\[ \text{2-amino-4-oxy-pyrimidine} \]

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Recently the following joint reaction has been published

\[
\text{CH}_3\text{COOC}_2\text{H}_5 + \text{HCOOC}_2\text{H}_5 \xrightarrow{\text{C}_2\text{H}_5\text{Na}} \text{Na}[\text{OCH=CH—COOC}_2\text{H}_5]\n\]

\[
+ \text{CH}_3\text{NO}_2 \quad \text{in benzene} \quad \xrightarrow{\text{O}_2\text{N—CH}_2—CH—CH}_2\text{COOC}_2\text{H}_5 \quad \text{ethyl } \gamma\text{-nitro-} \beta\text{-hydroxybutyrate}
\]

\[
\text{CH}_3\text{CH}_2\text{COOC}_2\text{H}_5 + \text{H—COOC}_2\text{H}_5 + \text{CH}_3\text{NO}_2 \rightarrow \text{O}_2\text{N—CH}_2—\text{CH—CH}_2\text{COOC}_2\text{H}_5 \quad \text{ethyl } \alpha\text{-methyl } \beta\text{-hydroxy-} \gamma\text{-nitrobutyrate}
\]

\[
\text{CH}_3\text{COCH}_3 + \text{HCOOC}_2\text{H}_5 + \text{CH}_3\text{NO}_2 \rightarrow \text{O}_2\text{N—CH}_2—\text{CH—CH}_2—\text{COCH}_3 \quad \text{4-hydroxy-5-nitro-2-pentanone}
\]

\[
\text{C}_2\text{H}_5\text{COC}_2\text{H}_5 + \text{HCOOC}_2\text{H}_5 + \text{CH}_3\text{NO}_2 \rightarrow \text{O}_2\text{N—CH}_2—\text{CH—CHCOC}_2\text{H}_5 \quad \text{4-methyl-5-hydroxy-6-nitro-3-hexanone}
\]

\[
\text{COCH}_3+\text{HCOOC}_2\text{H}_5+\text{CH}_3\text{NO}_2 \quad \rightarrow \quad \text{O}_2\text{N—CH}_2—\text{CH—OH—CH}_2—\text{CO—} \quad \text{\beta\text{-hydroxy-} \gamma\text{-nitro-butyrophenone etc.}
\]

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The above examples concern only with the formylacetic ester, but there are further many examples about formylacetone and other α-formylcarboxylic acids. The author wants to describe his own research upon this joint reaction in the last paragraph of this paper.

(b) Joint reaction by carbonmonoxide.

The Reppe's synthesis of acrylic acid and its derivatives from acetylene, carbonmonoxide and water (or alcohol) can be considered as one kind of joint reaction by carbonmonoxide.

\[
\text{CH} = \text{CH} + \text{CO} + \text{H}_2\text{O} \rightarrow [\text{CH}_2 = \text{CH}] \rightarrow \text{CH}_2 = \text{CH} - \text{COOH}
\]

\[
\text{CH} = \text{CH} + \text{CO} + \text{ROH} \rightarrow \text{CH}_2 = \text{CH} - \text{COOR}
\]

Analogously the oxo-synthesis (hydroformylation) and its related reactions can also be considered as another kind of joint reaction by carbonmonoxide, though the mechanism is recently recognized as radical reaction.

\[
\text{CH}_2 = \text{CH}_2 + \text{CO} \rightarrow [\text{CH}_2 - \text{CH}_2] \rightarrow \text{CH}_3 - \text{CH}_2 - \text{CHO} \rightarrow \text{CH}_3 - \text{CH}_2 - \text{CH}_2\text{OH} \quad (\text{CH}_3 - \text{CH}_2 - \text{CONHR}, \text{CH}_3 - \text{CH}_2 - \text{COSR})
\]

VII. Joint Reaction by Benzaldehyde

Considering the foregoing statement and demonstration of many examples, it can be expected that there would be further many compounds, which joint two passive components at their both sides. But the author wants to restrict for the joint reaction so that it only implies the reaction, in which two passive components are jointed at one atom of the active component, as the carbon-atom of formaldehyde or the nitrogen-atom of nitrous acid. The reaction, such as the diester formation of dibasic acid, can be considered also as a joint reaction, when the joint reaction is taken in wide sense, but if so considered, almost all of the condensation reactions must be taken into account. Then the joint reaction loses its meaning completely. There should be also a kind of joint reaction, in which two active components are jointed at one atom of a passive component, such as the formation of di- or tri-alkylamines from ammonia and alkylchlorides. This kind of joint reaction is also very interesting, though the cases of this joint reaction seem pretty scarce. The author wants to put this type of reaction outside of the present category and to discuss elsewhere.
Now, as the formaldehyde all other aldehydes should behave likely, i.e. they joint two passive components at the both sides of the carbonyl carbon atom. The author wants to give some examples only with the benzaldehyde in the following.

1. benzaldehyde + dimethylaniline

\[
\text{leuco-base of Malachite green.}
\]

2. benzaldehyde + NH\textsubscript{2}-Ar

\[
\text{(Schiff's Base)}
\]

3. benzaldehyde + CH\textsubscript{3}CO-R

\[
R'-\text{NH}_2 \quad R'-\text{NH}_2
\]

4. benzaldehyde + CH\textsubscript{3}CO-R

\[
\text{R'-MgX}
\]

5. benzaldehyde + aniline

\[
\text{1-phenylethane}
\]
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6. benzaldehyde + NH$_2$ - R $\rightarrow$ CH=$\equiv$ N - R $\rightarrow$ CH- NH - R

7. benzaldehyde + NH$_2$ - R $\rightarrow$ CH=$\equiv$ N - R

Pyridine and quinoline are regarded as the intra-molecular Schiff's base and so there are many examples which resemble to the above reactions.

VIII. Stabilization of the Intermediate Products of the Joint Reaction

As already explained in paragraph II the intermediate products of the joint reaction are generally unstable, i.e. very reactive. The methylol-compounds, diazo-compounds, isocyanates and ketenes are the typical examples of these unstable intermediate products. The final jointed compounds are of course the objects of the organic synthesis, but there are many cases, in which the unstable intermediate products must be kept in the stable state before practical use. Some typical examples of this kind are seen in the case of naphthol-dyeing and urea or melamine-formaldehyde resin treatment of cellulosic material. In the former case the diazoniumsalts must be kept stable, especially in the case of printing with naphthol dyes. In the latter case the methylol-urea or methylol-melamine must be kept stable, so as to remain water soluble and to penetrate deep into the fiber and then there to harden.

In order to stabilize the unstable intermediate product the principle of transjointing is widely used.

In the transjointing reaction:

\[ P_1-CH_2-P_2 + P_3H \rightarrow P_1-CH_2-P_3 + P_2H \]
\[ P_1-N=P_2 + P_3H \rightarrow P_1-N=P_3 + P_2H \]

$P_1-CH_2-P_3$ or $P_1-N=P_3$ is the aimed final product and $P_1-CH_2-P_2$ or $P_1-N=P_2$ is the stabilized intermediate product. But it is required for the stabilization, that the first jointed compound $P_1-CH_2-P_2$ or $P_1-N=P_2$ should neither be too unstable nor too stable, but in just a proper degree stabilized. If the primary
jointed compound is too unstable, such as the diazo-oxy-compound, then it has no meaning for stabilization, on the other hand, if it is too stable, then severe conditions such as heating at higher temperature or for a longer time are required to bring the transjointing reaction in completeness, and again here is no meaning. For diazo-compound, it has long been known that the sarcosine, methyl-taurin or appropriate N-methyl-aniline-sulfonic acid are the most suitable stabilizing agents. The stabilized diazo-compounds, for example diazo-imino-sarcosine, are known as the component of the Rapidogen dyestuffs. The transjointing reaction can be expressed as follows:

\[
\text{Ar} - \text{N}=\text{N} - \text{N}(\text{CH}_3) - \text{CH}_2\text{COONa} + \text{Naphthol AS-AS} \]

\[
\text{H}^+ \rightarrow \quad \text{N}=\text{N} - \text{Ar} + \text{NH}-\text{CH}_2-\text{COOH} \]

\[
\text{NHOC} \quad \text{OH} \quad \text{CH}_3
\]

For the stabilization of methylol-urea or -melamine alcohols, such as methyl-, ethyl- or butyl-alcohol are generally used, i.e. the jointed compound, as given below, is used.

\[
\text{OC} \quad \begin{array}{c} \text{NH} - \text{CH}_2 - \text{OCH}_3 \\ \text{NH} - \text{CH}_2 - \text{OCH}_3 \end{array}
\]

But these alkylethers of the methylol-urea or -melamine are not yet enough stable, and it seems that in this case also some appropriate secondary amines as those for the stabilization of diazo-compound are more suitable.

For the stabilization of ketene the acetone is the most suitable component as Hagemeyer determined.\(^{44}\)

\[
\text{CH}_2=\text{C}=\text{O} + \text{CH}_3\text{COCH}_3 \xrightarrow{\text{H}_2\text{SO}_4} \text{CH}_3\text{COO} - \begin{array}{c} \text{CH}_2 \\ \text{CH}_3 \end{array}
\]

This isopropenyl acetate reacts acetylicating upon other passive components in the presence of a little amount of sulfuric acid, liberating acetone free.

For the stabilization of isocyanate it seems that suitable stabilizing agent is not yet known. Fujio Masuo (Prof. of Kyoto Technical and Textile College, Japan) has recently performed a systematic research upon this problem and found that the 1-phenyl-3-methyl-pyrazolone is relatively a suitable stabilizing agent. The stabilized form in this case is follows:

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When this intermediate jointed compound is mixed with other passive component, whose jointed compound with the isocyanate is the aimed product, and heated at about 103°—130°, so occurs the transjointing reaction and the aimed product is obtained. For example, when cellulose fiber is impregnated with the above mentioned 1-phenyl-3-methyl-pyrazolone-4-carboxylic acid amide and the fiber thus treated is baked, at appropriate temperature so water-repellant finishing is attained.

At all events, it is very remarkable that the stabilization of methylol-, diazo-compounds, ketene and iso-cyanates is in principle all the same, being an application of the transjointing reaction.

IX. Some Experiments upon the Joint reaction with Formaldehyde and Formic Ester

The following joint reactions were undertaken and in each case the expected product was obtained.

1. Laurylamide, formaldehyde and sulfamic acid
   \[ \text{C}_{11}\text{H}_{23}\text{CONH—CH}_2—\text{NH—SO}_3\text{H} \] (a new anion-active surfactant)

2. Laurylamide, formaldehyde and polyethylene glycol-phenylether
   \[ \text{C}_{11}\text{H}_{23}\text{CONH—CH}_2—\bigg(\text{CH}_2—\text{CH}_2—\text{O}\bigg)_n—\text{CH}_2—\text{CH}_2\text{OH} \]
   a new non-ionic surfactant

3. Acetone, formaldehyde and thioglycolic acid
   \[ \text{CH}_3\text{COCH}_2—\text{CH}_2—\text{CH}_2—\text{S—CH}_2—\text{COOH} \]

4. Acetone, formaldehyde and malonic acid
   \[ \text{CH}_3\text{COCH}_2—\text{CH}_2—\text{CH}_2—\text{COOH} \]

5. Acetone, formaldehyde and dimethylaniline
   \[ \text{CH}_3\text{COCH}_2—\text{CH}_2—\text{CH}_2—\text{N(CH}_3)_2 \]

6. Acetone, formaldehyde and NaCN
   \[ \text{CH}_3\text{COCH}_2—\text{CH}_2—\text{CN} \] (levulinic acid nitrile)

7. Acetone, formaldehyde and nitromethane
   \[ \text{CH}_3\text{COCH}_2—\text{CH}_2—\text{CH}_2—\text{NO}_2 \]
8. Acetone, formaldehyde and benzamide
   → CH₃COCH₂ – CH₂ – NHCO – C₆H₅
9. Acetone, formaldehyde and acetoacetic ester
   → CH₃COCH₂ – CH₂ – COCH₃
   \[ \text{COOC₂H₅} \]
10. Acetone, formaldehyde and aniline
    → CH₃COCH₂ – CH₂ – NH – C₆H₅
11. Methyl-undecyl-ketone, formaldehyde and dialkylamine
    → C₁₁H₂₃COCH₂ – CH₂ – N\( \text{C₂H₅} \)
    \( \text{C₂H₅} \)
    (a new cation-active surfactant)
12. Synthesis of a-formylstearic acid ester and condensation of this product
    with thiourea.
    \[ \text{C}_{16}\text{H}_{33} – \text{CH} – \text{COOC}_{2}\text{H}_{5} \rightarrow \text{C}_{16}\text{H}_{33} – \text{CH} – \text{COOC}_{2}\text{H}_{5} \]
    \[ \text{CHO} \]
    \[ \text{C}_{16}\text{H}_{33} – \text{CH} – \text{CO} – \text{NH} \]
    \[ \text{CH} – \text{N} – \text{C} = \text{S} \]
    etc.

The precise experimental data will be given later.

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