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Abstract

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Technical Synthesis of Carbonyl Monomers Based on the Mannich Reaction

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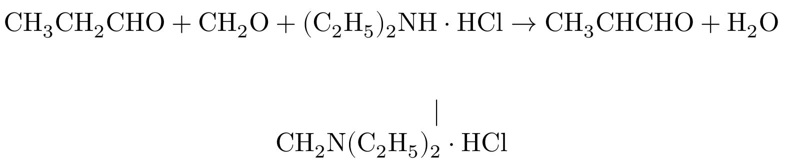
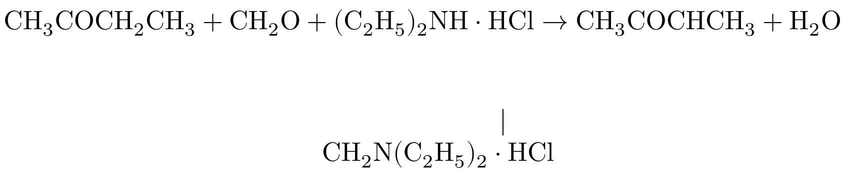
Researchers of the Mannich reaction showed relatively long ago that this reaction can be used for obtaining unsaturated compounds, including carbonyl monomers ($^{1-5}$). However, as far as we know, the reaction is not used industrially for these purposes, apparently mainly because of its irreproducibility (^{6}). We carried out a detailed study of the Mannich reaction, primarily for the synthesis of a number of technically important carbonyl monomers (α–, β-unsaturated aldehydes and ketones).

These syntheses are based on the following reactions (using the synthesis of methacrolein and methyl isopropenyl ketone as examples):

1. Aminomethylation of the corresponding carbonyl compound with formation of an intermediate product—the hydrochloride of the Mannich base:

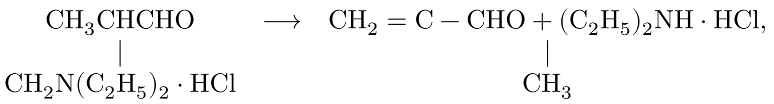


$$\mathrm{CH_3CH_2CHO + CH_2O + (C_2H_5)_2NH\cdot HCl \rightarrow \underset{\substack{|\\ CH_2N(C_2H_5)_2\cdot HCl}}{CH_3CHCHO} + H_2O} \qquad (1)$$



$$\mathrm{CH_3COCH_2CH_3 + CH_2O + (C_2H_5)_2NH\cdot HCl \rightarrow \underset{\substack{|\\ CH_2N(C_2H_5)_2\cdot HCl}}{CH_3COCHCH_3} + H_2O} \qquad (2)$$

2. Decomposition of the hydrochloride of the Mannich base with formation of an unsaturated carbonyl compound:



$$\mathrm{\underset{\substack{|\\ CH_2N(C_2H_5)_2\cdot HCl}}{CH_3CHCHO} \longrightarrow CH_2 = \underset{\substack{|\\ CH_3}}{C} - CHO + (C_2H_5)_2NH\cdot HCl,} \qquad (3)$$

Figure 1

Figure 1: Figure 1

methacrolein

$$\underset{\displaystyle CH_2N(C_2H_5)_2 \cdot HCl}{\underset{|}{CH_3COCHCH_3}} \longrightarrow \underset{\displaystyle CH_3}{\underset{|}{CH_3COC}} = CH_2 + (C_2H_5)_2NH \cdot HCl. \qquad (4)$$

methyl isopropenyl ketone

Our investigations showed that the rate of the Mannich reaction depends very strongly on the pH of the medium. Moreover, in some cases the reaction rate increases substantially with increasing pH, while in others it increases with decreasing pH. The effect of pH on the rates of reactions (1) and (2) is shown in Figs. 1 and 2. As can be seen from the graphs presented, the reaction with propionaldehyde is strongly accelerated with increasing pH, whereas the reaction with methyl ethyl ketone, on the contrary, is accelerated with decreasing pH. Thus, by regulating the pH alone, it is possible to accelerate the aminomethylation reactions significantly and to choose conditions under which these reactions proceed at relatively low temperatures, making it possible to obtain yields of reaction products close to quantitative. All these reactions are described by equations of third kinetic order in the pH region where they proceed

with the greatest rate. In Fig. 3, the dependence of C^{-2} on time at the indicated pH values is expressed by a straight line, which is characteristic of third-order reactions.

Fig. 1. Effect of the pH of the reaction mixture on the rate of interaction of formaldehyde, propionaldehyde, and diethylamine in the Mannich reaction at 35°.
1 –pH 3.05; 2 –pH 3.95; 3 –pH 7.05; 4 –pH 11.34

The effect of temperature on the rates of reactions (1) and (2) was studied. A plot of the dependence of the reaction rate constants on temperature in the coordinates $\lg K - 1/T$ showed that they are described by the Arrhenius equation. This made it possible to determine the activation energies of the reactions, which proved to be 15.73 kcal/g-mol for reaction (1), 18.3 kcal/g-mol for reaction (2), and 23.1 kcal/g-mol for the analogous reaction with acetone. The differences in the values of the activation energies are apparently connected with the different mobility of the hydrogen atom located in the α-position to the carbonyl group in carbonyl compounds; moreover, the mobility of the hydrogen atom decreases in the series: CH_2 (in aldehydes) $>$ CH_2 (in ketones) $>$ CH_3 (in ketones).

Figure 2

Figure 2: Figure 2

The decomposition of the hydrochlorides of Mannich bases proceeds under different conditions at different rates, depending on the structure of the Mannich bases obtained. Aldehyde Mannich bases decompose under the mildest conditions (reaction (3)). Decomposition proceeds upon heating to 100°, and almost quantitative yields of α, β-unsaturated aldehydes are obtained. Decomposition of keto Mannich bases (reaction (4)) proceeds under harsher conditions, but the yields of α, β-unsaturated ketones, when the reactions are carried out properly, also approach quantitative. In all cases diethylamine can be readily returned to the process.

Fig. 2. Effect of the pH of the reaction mixture on the rate of interaction of formaldehyde, methyl ethyl ketone, and diethylamine hydrochloride in the Mannich reaction at 95°.
1 –pH 0.6; 2 –pH 1.0; 3 –pH 1.75; 4 –pH 2.65; 5 –pH 3.6

On the basis of this same reaction, it is possible to obtain divinyl ketones, which until now have been practically inaccessible. These syntheses can be carried out in two ways: 1) on the basis of the interaction of saturated ketones (for example, methyl ethyl ketone) with a twofold molar amount of formaldehyde and diethylamine hydrochloride (reactions (5) and (6)); and 2) on the basis of the interaction of α, β-unsaturated ketones (for example, methyl isopropenyl ketone) with an equimolecular amount of formaldehyde and diethylamine hydrochloride (reactions (7) and (8)).

$$\mathrm{CH_3COCH_2CH_3 + 2CH_2O + 2(C_2H_5)_2NH \cdot HCl \rightarrow}$$

$$\mathrm{\rightarrow HCl \cdot (C_2H_5)_2NCH_2CH_2COCH(CH_3)CH_2N(C_2H_5)_2 \cdot HCl + 2H_2O,} \qquad (5)$$

$$\mathrm{HCl \cdot (C_2H_5)_2NCH_2CH_2COCH(CH_3)CH_2N(C_2H_5)_2 \cdot HCl \rightarrow}$$

$$\rightarrow \underset{\text{vinyl isopropenyl ketone}}{\mathrm{CH_2{=}CHCOC(CH_3){=}CH_2}} + 2\,\mathrm{(C_2H_5)_2NH \cdot HCl,} \qquad (6)$$

$$\mathrm{CH_3COC(CH_3){=}CH_2 + CH_2O + (C_2H_5)_2NH \cdot HCl \rightarrow}$$

$$\mathrm{\rightarrow CH_2{=}C(CH_3)COCH_2CH_2N(C_2H_5)_2 \cdot HCl + H_2O,} \qquad (7)$$

Fig. 3. Plot of the dependence of C^{-2} ($C = \text{g} \cdot \text{mol/l}$) on time for Mannich reactions. 1—with formaldehyde, diethylamine, and propionaldehyde at 35° pH 11.34; 2—with formaldehyde, diethylamine hydrochloride, and methyl ethyl ketone at 95° pH 0.6

Figure 3: Fig. 3. Plot of the dependence of C^{-2} ($C = \text{g} \cdot \text{mol/l}$) on time for Mannich reactions. 1—with formaldehyde, diethylamine, and propionaldehyde at 35° pH 11.34; 2—with formaldehyde, diethylamine hydrochloride, and methyl ethyl ketone at 95° pH 0.6

$$CH_2{=}C(CH_3)COCH_2CH_2N(C_2H_5)_2 \cdot HCl \rightarrow$$

$$\rightarrow \underset{\text{vinyl isopropenyl ketone}}{CH_2{=}CHCOC(CH_3){=}CH_2} + (C_2H_5)_2NH \cdot HCl. \qquad (8)$$

The conditions for carrying out these reactions are analogous to those described above for the synthesis of α-, β-unsaturated ketones. The yields of divinyl ketones are much higher when reactions (5) and (6) are used than with reactions (7) and (8). The structure of the obtained Mannich bases as β,β'-dibases leaves no doubt, since only from such dibases can divinyl ketones be obtained upon decomposition. The observed dependence of the rate of aminomethylation reactions on the pH of the medium suggests that these reactions proceed by several different mechanisms, depending on the structure of the "CH-acid component." In one case (for propionaldehyde) the Mannich reaction apparently proceeds by a nucleophilic substitution mechanism (S_N2 mechanism), first proposed by Cummings and Shelton (7). In another case (for methyl ethyl ketone and acetone), it proceeds by an electrophilic substitution mechanism (S_E2 mechanism), proposed by Hellmann (8).

Fig. 3. Plot of the dependence of C^{-2} ($C = \text{g} \cdot \text{mol/l}$) on time for Mannich reactions. **1**—with formaldehyde, diethylamine, and propionaldehyde at 35° pH 11.34; **2**—with formaldehyde, diethylamine hydrochloride, and methyl ethyl ketone at 95° pH 0.6.

Table 1 presents the monomers obtained, their constants, yields, and brief indications of the synthesis conditions.

On the basis of the Mannich reactions, we have developed and implemented a technical method for obtaining a series of carbonyl monomers (α-, β-unsaturated aldehydes and ketones) in yields close to quantitative, under very mild conditions and with very simple apparatus design.

Experimental Part

A. Synthesis of α,β-unsaturated aldehydes. Composition of the reaction mixture: 1.0 mole of diethylamine hydrochloride, 1.0 mole of formaldehyde in the form of a 35–38% aqueous solution, 1.1 moles of aldehyde, and 45–56 ml of a molar solution of sodium carbonate (to bring the pH of the reaction mixture to 7.0). After the aminomethylation reaction was complete, the unsaturated aldehyde was distilled from the reaction mixture as an azeotrope with water.

B. Synthesis of α,β-unsaturated ketones. Composition of the reac-

Table 1

Synthesis conditions and constants of the carbonyl monomers obtained

No.	Compound	Formula	Synthesis conditions*	B.p., °C	d_4^{20}	n_D^{20}
1	Methacrolein	$CH_2 = C(CH_3) - CHO$	A; 7.0; 45°; 20 min; up to 100°C; atm. pressure; 99–100%	68.4	0.845	1.4156
2	α-Ethylacrolein	$CH_2 = C(CH_2CH_3) - CHO$	A; 7.0; 120°; 1 h; up to 100°; atm. pressure; 97.8%	92.3	0.849	1.4231
3	α-Isopropylacrolein	$CH_2 = C[CH(CH_3)_2] - CHO$	A; 7.0; 120°; 1 h; up to 100°; atm. pressure; 96.5%	106.0	0.843	1.4263

No.	Compound	Formula	Synthesis conditions*	B.p., °C	d_4^{20}	n_D^{20}
4	Methyl vinyl ketone	$CH_3COCH=CH_2$	B; 1.0; 100°; 1.5 h; 150–210°; 50–80 mm; 87.0%	79 (743 mm)	0.8666	1.4115
5	Methyl isopropenyl ketone	$CH_3COC(CH_3)=CH_2$	B; 1.0; 100°; 1.5 h; 210°; 50–80 mm; 94.5	97–98	0.841	1.4220
6	Isopropyl vinyl ketone	$CH_3CH(CH_3)COCH=CH_2$	B; 0.54; 100°; 3.2 h; 150–210°; 48–50 mm; 83.4%	49 (77 mm)	0.847	1.4303
7	α-Isopropylvinyl methyl ketone	$CH_3COC[CH(CH_3)_2]=CH_2$	B; 0.6; 100°; 3.0 h; 150–210°; 60 mm; 94.5%	62.5 (56–58 mm)	0.8396	1.4270
8	Phenyl vinyl ketone	$C_6H_5COCH=CH_2$	B; 1.0; 100°; 1.2 h; 150–210°; 10 mm; 82.2%	108–112 (13–14 mm)	1.060	1.5522

No.	Compound	Formula	Synthesis conditions*	B.p., °C	d_4^{20}	n_D^{20}
9	Phenyl isopropenyl ketone	$C_6H_5COC(CH_3) = CH_2$	B; 1.9; 100°; 3.0 h; 150–210°; 6–8 mm; 83.4%	62–64 (4 mm)	1.025	1.5455
10	Divinyl ketone	$CH_2 = CHCOCH = CH_2$	B; 0.48; 100°; 10 h; 150–210°; 100–110 mm; 54.6%G; 0.75; 100°; 2.0 h; 150–210°; 100–110 mm; 47.9%	41 (62 mm)	0.8839	1.4440
11	Vinyl isopropenyl ketone	$CH_2 = CHCOC(CH_3) = CH_2$	B; 0.5; 100°; 10 h; 150–210°; 75–80 mm; 64.3%	59 (95 mm)	0.8906	1.4540

No.	Compound	Formula	Synthesis conditions*	B.p., °C	d_4^{20}	n_D^{20}
12	α-Isopropyldivinyl ketone	$CH_2 = CHCOC[CH(CH_3)_2] = CH_2$	G; 0.81; 100°; 5 h; 150–210°; 60–70 mm; 30.2%B; 0.47; 100°; 14 h; 150–210°; 20–40 mm; 82.6%	58.5–60 (28 mm)	0.851	1.4362
13	Vinyl isobutenyl ketone	$CH_2 = CHCOCH = C(CH_3)_2$	G; 0.6; 100°; 5 h; 150–210°; 39–40 mm; 79.8%G; 0.8; 100°; 2.0 h; 150–210°; 10–20 mm; 78.0%	60–71 (22 mm)	0.905	1.4750

* Indicated respectively are: procedure, pH, temperature and duration of the aminomethylation reaction; temperature and residual pressure (in mm Hg) or atmospheric pressure (atm. pressure) at which decomposition of the hydrochloride of the Mannich base was carried out; yield from theory (in wt. %).

reaction mixture: 1.0 mole of diethylamine hydrochloride, 1.0 mole of formaldehyde, 1.1 moles of ketone, and up to 2.5 ml of conc. hydrochloric acid (to create the required pH value). After completion of the aminomethylation reaction, the mixture was evaporated at 120° and under a vacuum of 40 mm Hg (to remove water), followed by decomposition of the Mannich-base hydrochloride formed, with formation of the unsaturated ketone.

B. Synthesis of divinyl ketones from saturated ketones. Composition of the reaction mixture: 1.0 mole of diethylamine hydrochloride, 1.0 mole of formaldehyde, 0.5 mole of saturated ketone, and about 3 ml of conc. hydrochloric acid (to create the required pH value). The conditions for carrying out the aminomethylation reaction and for decomposition of the dihydrochlorides of the Mannich bases are analogous to those described in procedure B.

G. Synthesis of divinyl ketones from α, β-unsaturated ketones. Composition of the reaction mixture; the conditions for carrying out the aminomethylation reaction and for decomposition of the dihydrochlorides of the Mannich bases are analogous to those described in procedure B.

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Note: Figure translations are in progress. See original paper for figures.