protein mixtures. The proteins were fractionated, crystallized, dried and relyophilized from water solutions of different concentrations.

Specific areas ranged from about 0.20 to 4.00 sq. m./g. for proteins lyophilized from concentrated solutions, and 6.00 to 14.00 sq. m./g. for dilute solutions. Denatured egg albumin had a smaller area than the undenatured material. Salt–protein mixtures showed much smaller areas. Spray-freezing the dilute protein solutions into liquid nitrogen baths and then drying the resultant powder raised the areas four-fold. Electron microscope studies were made of all the proteins used.

The low specific surface areas are in qualitative accord with the large particles observed under the electron microscope. The areas obtained from water adsorption data of other workers are from 40–200-fold larger than the nitrogen areas. These comparisons lead to the conclusion that water and nitrogen adsorption are quite different phenomena. The former is more closely related to hydration of specific groups within the protein molecule with probable physical change in the protein dimensions.

Measurements on egg albumin were made with both nitrogen and oxygen at two different temperatures. From these isotherms, a calculation of the partial molal heats of adsorption as a function of volume adsorbed may be made. The net heats calculated in this way are in good agreement with the net heats obtained from the BET plots for the first layer.

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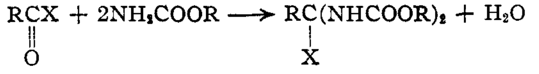
[CONTRIBUTION FROM THE LABORATORY OF THE U. S. CHEMICAL CORPORATION]

# The Preparation of Indanone Derivatives by a Carbamate–Aldehyde[1] Reaction

BY WILLIAM M. KRAFT

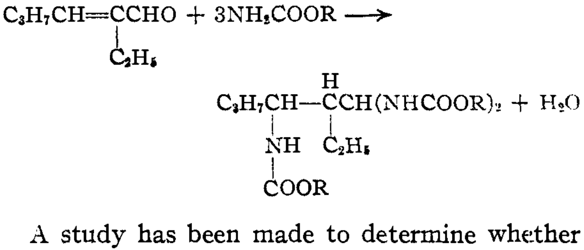
The recent publication of Kraft and Herbst[1a] of the research investigating the condensation of carbonyl compounds with carbamates described the reaction of one mole of saturated aliphatic aldehydes and pyruvic acid with two moles of aliphatic carbamate. In the case of the unsaturated



$$\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{RCX}} + 2\mathrm{NH_2COOR} \longrightarrow \underset{\underset{\displaystyle \mathrm{X}}{|}}{\mathrm{RC}}(\mathrm{NHCOOR})_2 + \mathrm{H_2O}$$

where X = H or COOH.

aldehyde, 2-ethylhexen-2-al-1, reaction was in a one to three ratio, two carbamate molecules adding at the carbonyl group, while the third added at the double bond, presumably at the $\beta$-position.

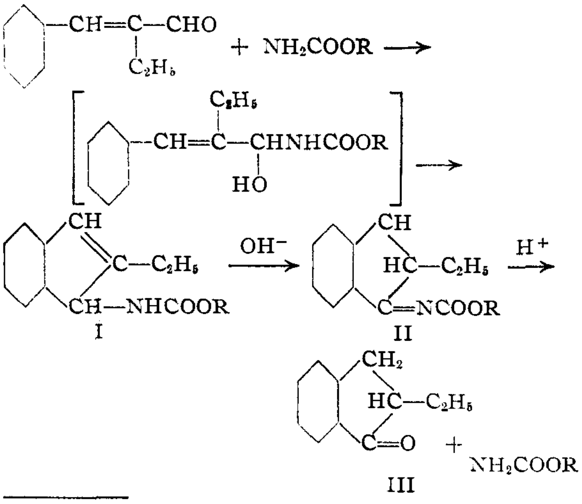


$$\mathrm{C_3H_7CH{=}\underset{\underset{\displaystyle C_2H_5}{|}}{C}CHO} + 3\mathrm{NH_2COOR} \longrightarrow$$

$$\mathrm{C_3H_7\underset{\underset{\underset{\displaystyle COOR}{|}}{\underset{\displaystyle NH}{|}}}{CH}{-}\overset{H}{\underset{\underset{\displaystyle C_2H_5}{|}}{C}}CH(NHCOOR)_2} + \mathrm{H_2O}$$

A study has been made to determine whether the latter type of reaction is a general one for $\alpha,\beta$ unsaturated aldehydes such as crotonaldehyde, cinnamaldehyde and $\alpha$-ethylcinnamaldehyde in reactions with ethyl, isopropyl and benzyl carbamate. It was found that reactions with crotonaldehyde and cinnamaldehyde required two moles of carbamate to one of the aldehyde. Yields with cinnamaldehyde were low and were attended by resin formation (also noted by Martell[2]).

The $\alpha$-ethylcinnamaldehyde-carbamate reaction was peculiar in that the reaction products all indicated a 1:1 addition. These products were unaffected by refluxing for several hours in dilute or concentrated mineral acids; consequently, it was considered unlikely that the usual addition reaction, at the carbonyl group, had occurred. However, when the product of the reaction was treated with dilute aqueous alkali, another crystalline material (II) was obtained, which on further treatment with dilute mineral acids regenerated the original carbamate and another compound, a ketone (III). Speculation as to the nature of this latter compound indicated the follow-



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(1) This paper was presented before the Organic Division of the American Chemical Society, in Atlantic City, N. J., April, 1947.

(1a) W. M. Kraft and R. M. Herbst, *J. Org. Chem.*, **10**, 478 (1945).

(2) T. R. Lewis, Jr., F. R. Butler and A. E. Martell, *J. Org. Chem.*, **10**, 145 (1945).

TABLE I

CONDENSATION PRODUCTS

No products were obtained in 2-methylpenten-2-al-1 reactions.

| Aldehyde | Carbamate | Moles A/C | Yield, % | M. p., °C. | Formula | Nitrogen, % Calcd. | Nitrogen, % Found |
|---|---|---|---|---|---|---|---|
| Crotonaldehyde | Isopropyl | 1/2 | 61 | 163.5–165 | $C_{12}H_{22}O_4N_2$ | 10.85 | 10.96 |
| | Benzyl | 1/2 | 65 | 160–161 | $C_{20}H_{22}O_4N_2$ | 7.91 | 7.90 |
| Cinnamaldehyde | Isopropyl | 1/2 | 49 | 196–197 | $C_{17}H_{24}O_4N_2$ | 8.75 | 8.88 |
| | Benzyl | 1/2 | 48 | 185–188 | $C_{25}H_{24}O_4N_2$ | 6.73 | 6.89[a] |
| α-Ethylcinnamaldehyde | Ethyl | 1/1 | 55 | 104–105 | $C_{14}H_{17}O_2N$ | 6.06 | 6.24[b] |
| | Isopropyl | 1/1 | 60 | 130 | $C_{15}H_{19}O_2N$ | | |
| | Benzyl | 1/1 | 48 | 119–119.5 | $C_{19}H_{19}O_2N$ | 4.77 | 4.97 |

[a] Lewis, Butler and Martell, *J. Org. Chem.*, **10**, 145 (1945), report 187°. [b] *Anal.* Calcd. for $C_{14}H_{17}O_2N$: C, 72.70; H, 7.41; mol. wt., 231.3. Found: C, 72.56; H, 7.18; mol. wt., 230.

ing to be a possible scheme. This was borne out by subsequent chemical evidence.

The presence of a group in the alpha position of the aldehyde may facilitate the ring closure reaction. Similar observations have been made in the preparation of substituted cyclic ketones.[3]

Isolation of III as the 2,4-dinitrophenylhydrazone and the semicarbazone was accomplished. These derivatives were compared and shown to be identical with those prepared from an authentic sample of 2-ethyl indanone synthesized from sodiodiethyl ethyl malonate and benzyl chloride, followed by hydrolysis, decarboxylation and ring closure in sulfuric acid.

Preliminary experiments with α-methylcinnamaldehyde have indicated similar results to those with the ethyl compound.

This type of synthesis affords a new route to substituted indanone derivatives from readily available aromatic, unsaturated, aldehydes.

## Experimental[4]

**Carbamates.**—Ethyl carbamate was purchased from Eastman Organic Chemicals. The isopropyl carbamate was prepared by the method previously described.[1a]

Benzyl carbamate was prepared from ethyl carbamate by an ester exchange reaction with benzyl alcohol in the presence of aluminum isopropoxide as follows:

To 44.5 g. (0.5 mole) of ethyl carbamate, in a 250-ml. three-neck flask with a thermometer and a 20-cm. asbestos-lagged column attached, were added 54.1 g. (0.5 mole) of benzyl alcohol and 60 ml. of toluene. The column was packed with glass beads because better fractionation of the ethanol–toluene azeotrope was obtained. The system was heated at 110–125° kettle temperature, to remove any water in the reagents and then was cooled to 100°. Aluminum isopropoxide (2.0 g.) was added in one portion and the system heated at 130–140° kettle temperature, removing the ethanol–toluene azeotropic mixture at 77° vapor temperature. Of the 46 ml. of distillate, 28 ml. was water miscible as compared to a theoretical amount of 29 ml. of ethanol.

The residue, after one recrystallization from toluene, yielded 64.5 g. (85.5%) of benzyl carbamate melting at 86–87°. The same reaction using sodium methylate as catalyst gave poor yields.

Crotonaldehyde and cinnamaldehyde of commercial grade (Eastman Kodak Co.) were used after distillation.

α-Ethylcinnamaldehyde was prepared by the reaction of butyraldehyde with benzaldehyde. To a mixture of 7.5 g. of potassium hydroxide in 7.5 g. of water and 175 g. of ethanol was added 118 g. of benzaldehyde. The system was cooled to 5° and 50 g. of butanal was added over a period of three hours and allowed to stand at room temperature overnight. After acidification and distillation, 65 g. (58%) of pure α-ethylcinnamaldehyde was obtained, boiling at 111–112° (7 mm.), $n^{25}D$ 1.5822.

TABLE II

PRODUCTS OF ALKALINE TREATMENT OF α-ETHYLCINNAMALDEHYDE

| Carbamate | Yield, % | M. p., °C. | Formula | Nitrogen, % Calcd. | Nitrogen, % Found |
|---|---|---|---|---|---|
| Ethyl | 81 | 113.5–114.5 | $C_{14}H_{17}O_2N$ | 6.06 | 6.13[a] |
| Benzyl | 85 | 128–130 | $C_{19}H_{19}O_2N$ | 4.77 | 5.01 |

[a] *Anal.* Calcd. for $C_{14}H_{17}O_2N$: C, 72.70; H, 7.41; mol. wt., 231.3. Found: C, 72.45; H, 7.68; mol. wt., 232 and 229.

### Condensation Products

The general procedure is similar to that previously described, in which the aldehyde and carbamate were mixed with a few drops of mineral acid. However, it has been found that acetyl chloride, sulfonyl chloride and phosphorus oxychloride are more active condensing agents than the mineral acids, especially in the preparation of 1:1 condensation products as indicated below.

The 2:1 condensation products were prepared by the method already described.[1a]

**1:1 Condensation Products (I, R = $C_2H_5$). 2-Ethyl-3-carbethoxyaminoindene.**—To a mixture of 8.0 g. (0.05 mole) of α-ethylcinnamaldehyde and 4.5 g. (0.05 mole) of ethyl carbamate in 20 ml. of xylene, heated to reflux, 0.78 ml. of phosphorus oxychloride was added. The vigorous reaction was allowed to subside and the system cooled to room temperature. (Additional phosphorus oxychloride or the use of benzene lead to no greater yields.) The crude product (11.3 g.) obtained after evaporation of the solvent at room temperature, was recrystallized from 50 ml. of ethanol and gave 6.4 g. (55%) of a product (I) melting at 104–105°. The product decolorized permanganate slowly in neutral acetone solution but decolorized it quickly in an acidic acetone solution.

**Alkaline Treatment (II, R = $C_2H_5$). 2-Ethyl-3-carbethoxyiminoindane.**—When 0.7 g. of I was refluxed with 30 ml. of 0.1 *N* sodium hydroxide in 60 ml. of ethanol for two hours, followed by neutralization with 0.1 *N* hydrochloric acid, there was precipitated 0.56 g. of a white crystalline material (II) melting at 113.5–114.5°. A mixed melting point of I and II was 88–92°.

**Acid Treatment (III). 2-Ethylindanone.**—Product II (0.5 g.), when refluxed for ten minutes in dilute hydrochloric acid, yielded the original carbamate and a ketone product isolated as a 2,4-dinitrophenylhydrazone and a semicarbazone, later shown to be identical with the corresponding derivatives of 2-ethylindanone. Because of the high water solubility of ethyl carbamate, the benzyl derivative (prepared in a similar way to the ethyl com-

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[3] W. S. Johnson, "Organic Reactions," Vol. II, John Wiley and Sons, New York, N. Y., 1944, p. 163.

[4] Melting and boiling points are uncorrected.

pound) was employed in the identification of the carbamate residue. Benzyl carbamate crystallized from the reaction mixture and was identified by Kjehldahl analysis for nitrogen and a mixed melting point with an authentic sample.

The semicarbazone of III melted at 197–201°, dec., while that of an authentic sample of 2-ethylindanone melted at 202°, dec. The 2,4-dinitrophenylhydrazones, respectively, melted at 173–175° and 172–174°, while a mixed melting point of the two was 172–174°.

**2-Ethylindanone.**—A sample of 2-ethylindanone was prepared from α-ethyl-β-phenylpropionic acid by cyclization in 85% sulfuric acid according to the method of Speight, *et al.*[5] The acid was made as follows: one-tenth mole of sodium was added to 75 ml. of absolute ethanol in a 250-ml. reflux flask. Eastman Kodak Co. grade diethyl ethylmalonate (18.8 g.) was added in several portions, with stirring, and the mixture heated on the steam-bath. Benzyl chloride (12.7 g.) was then added dropwise, the system refluxed for five hours, whereupon it was no longer alkaline to litmus. Excess alcohol was removed under vacuum. The solution was treated with 20 ml. of dilute acetic acid. The oil which separated was refluxed with an excess of 3 *N* potassium hydroxide for six hours and then neutralized with dilute sulfuric acid. The α-ethyl-β-phenylpropionic acid was obtained by distillation at 270–273° (765 mm.) and weighed 11.6 g. (58%).

## Summary

1. Crotonaldehyde and cinnamaldehyde have been shown to form products with isopropyl and benzyl carbamate in which the molar ratio is one aldehyde to two carbamate molecules.

2. The reaction of α-ethylcinnamaldehyde and carbamates is in a one to one molar ratio and is attended by ring closure to form substituted indanone derivatives. The identity of the products has been established by comparison with authentic samples.

NEWARK, NEW JERSEY RECEIVED APRIL 20, 1948

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[5] E. A. Speight, A. Stevenson and J. F. Thorpe, *J. Chem. Soc.*, **125**, 2185 (1924).

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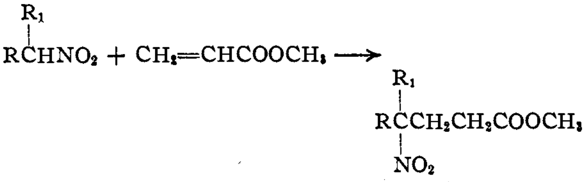
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DEPAUW UNIVERSITY AND THE RESEARCH DIVISION OF COMMERCIAL SOLVENTS CORPORATION]

# Reactions of Nitroparaffins. II. Addition of Nitroparaffins to Unsaturated Esters

BY MILTON C. KLOETZEL[1]

Addition of nitromethane, as the sodio derivative, to esters of benzalmalonic, cinnamalmalonic and benzoylacrylic acids has been described by Kohler, *et al.*[2,3] When piperidine and other feebly basic condensing agents were employed, uncrystallizable colored oils were obtained, which could not be purified.

Triethylamine has now been found to be an effective catalyst for the Michael type condensation of methyl acrylate with nitroparaffins (Table I).[4]



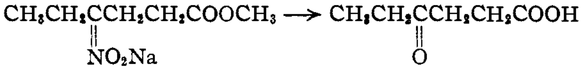
$$R\overset{\overset{\displaystyle R_1}{|}}{C}HNO_2 + CH_2{=}CHCOOCH_3 \longrightarrow R\overset{\overset{\displaystyle R_1}{|}}{\underset{\underset{\displaystyle NO_2}{|}}{C}}CH_2CH_2COOCH_3$$

I, R = $CH_3$; $R_1$ = H
II, R = $C_2H_5$; $R_1$ = H
III, R = $R_1$ = $CH_3$

Treatment of methyl acrylate with three moles of 1-nitropropane and one-half mole of triethylamine at 30° afforded 57% and 80% yields of methyl 4-nitrohexanoate (II) after two and seven days, respectively. Extension of the reaction period to fourteen days did not increase the yield.

Methyl crotonate and methyl methacrylate gave no evidence of reaction with 1-nitropropane under similar conditions, even after standing for seven days. Likewise, methyl cinnamate was recovered quantitatively after standing at 30° for fourteen days with three moles of 2-nitropropane and one mole of triethylamine. A comparable hindering effect resulting from substitution on either the α- or the β-carbon of the acceptor has been observed[5] in other Michael condensations.

Properties of the 4-ketohexanoic acid (V) obtained by acidification of the aci-nitro ester sodium salt (IV) from II[6] corresponded to those previously described for this keto acid.[7] This transformation therefore established the structure of II.



$$CH_3CH_2\underset{\underset{\displaystyle NO_2Na}{\|}}{C}CH_2CH_2COOCH_3 \longrightarrow CH_3CH_2\underset{\underset{\displaystyle O}{\|}}{C}CH_2CH_2COOH$$

IV V

Methyl acrylate reacted with nitroethane and with 2-nitropropane within four days, under conditions similar to those described for preparation of II, to yield 66% and 81% of methyl 4-nitropentanoate (I) and methyl 4-methyl-4-nitropentanoate (III), respectively.

When attempts were made to effect condensation of nitroparaffins with methyl acrylate, methyl methacrylate or methyl crotonate by means of the more active catalyst diethylamine,[8] the prod-

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[1] Present address: University of Southern California, Los Angeles 7, California.

[2] Kohler and Engelbrecht, THIS JOURNAL, **41**, 764 (1919).

[3] Kohler and Darling, *ibid.*, **52**, 424 (1930).

[4] While this investigation was in progress, Bruson, U. S. Patents 2,342,119 and 2,390,918 [*C. A.*, **38**, 4619 (1944); *ibid.*, **40**, 2456 (1946)] reported the condensation of simple nitroparaffins with methyl and ethyl acrylate, under the catalytic influence of benzyltrimethylammonium hydroxide.

[5] Connor and McClellan, *J. Org. Chem.*, **3**, 570 (1939).

[6] Compare Nef, *Ann.*, **280**, 263 (1894); Hass and Riley, *Chem. Revs.*, **32**, 398 (1943).

[7] Maire, *Bull. soc. chim.*, [4] **3**, 285 (1908).

[8] Compare Kloetzel, THIS JOURNAL, **69**, 2271 (1947).