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A Novel and Versatile Separation Method for Aldehydes

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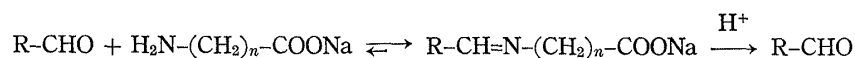
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An aqueous solution of sodium ϵ -amino-*n*-caproate can be used for efficient and simple separation of aldehydes, overcoming the difficulties associated with the NaHSO₃ method.

Keywords—separation of aldehydes; Schiff base of amino acid; ω -amino acid; sodium ϵ -amino-*n*-caproate; sodium bisulfite adduct of aldehydes

For many years, aqueous sodium bisulfite solution has generally been employed for the simple separation of aldehydic compounds from others.²⁾ However, difficulties can occur, such as incomplete extraction (see Table I), troublesome formation of precipitates, difficulty in liberating the aldehyde from the resulting sodium bisulfite adduct or extracted solution³⁾ and instability of the reagent solution.⁴⁾ In our experiments, surprisingly, citral was difficult to separate with sodium bisulfite solution and some other aldehydic compounds showed low reactivities and low recoveries (see Table I).

The authors present here a novel and useful separation method for aldehydes that overcomes the problems described above. The reaction equation may be given as follows:



According to the results of extraction experiments using several amino acids ($n=1, 2, 3, 5$ and 10), the amount of aldehyde extracted tends to increase with the value of n , as shown in Table II, and it was considered that the readily available ϵ -amino-*n*-caproic acid ($n=5$)⁵⁾ could be used for routine work.

General Procedure for Separation

Reagent A: aqueous 1.2 M solution of sodium ϵ -amino-*n*-caproate.⁵⁾

Reagent B: aqueous 0.3 M solution of sodium 11-amino-*n*-undecanoate.⁵⁾

Example of Separation—A solution consisting of vanillin, β -naphthol, cyclohexanone and isoquinoline (one gram each) in 50 ml of diethyl ether was shaken for 2.5 min in a separating funnel with 20 ml of Reagent A, then the ethereal layer was shaken again for 2.5 min with 10 ml of Reagent A. The combined aqueous layer was washed with ether and acidified with 10% hydrochloric acid to adjust the pH to 4–6. The liberated vanillin was extracted with ether, and removal of the solvent gave almost pure crystalline vanillin (976 mg, 97.6%).⁶⁾

Precipitation of the Schiff Base Salt—*p*-Anisaldehyde (1.00 g) was dissolved in 25 ml of Reagent B and the solution was cooled to 0° to precipitate colorless leaflets. These were collected by suction, and

1) Location: *Misasagi Nakauchi-cho, Yamashina-ku, Kyoto, 607, Japan.*

2) E. Knoevenagel and E. Lange, *Chem. Ber.*, **37**, 4059 (1904); C.F.H. Allen and G.W. Leubner, "Organic Syntheses," Coll. Vol. 4, John Wiley and Sons, Inc., New York 1963, p. 866; G.B. Bachman, *ibid.*, Coll. Vol. 2, 1943, p. 323; and many other papers and textbooks in the field of organic chemistry.

3) Large amounts of neutralizing agent are needed for both acidic and basic liberation of an aldehyde from saturated NaHSO₃ solution, and SO₂ gas is evolved on acidic treatment.

4) Saturated NaHSO₃ solution is slowly oxidized to afford sodium bisulfate, so a fresh solution must be used.

5) ϵ -Amino-*n*-caproic acid is cheap, but 11-amino-*n*-undecanoic acid and γ -amino-*n*-butyric acid are rather expensive for routine work.

6) When the separation was carried out with saturated NaHSO₃ solution, vanillin and cyclohexanone were both extracted.

washed with ether and with a small amount of cold water to give 2.01 g (75.9%) of the corresponding Schiff base salt.⁷⁾ The pure product was obtained as colorless needles, mp 185–200°, by recrystallization from water. IR $\nu_{\text{max}}^{\text{KBr}}$ cm⁻¹: 1650 (–CH=N–), 1610 (–COONa). ¹H-NMR (in CD₃OD–D₂O, 80 MHz) δ ppm: 8.19 (1H, s, –CH=N–), 7.63 (2H, d, aromatic protons), 6.92 (2H, d, aromatic protons), 3.81 (3H, s, –OCH₃), 3.54 (2H, t, =NCH₂–), 2.14 (2H, t, –CH₂COONa), 2.85–1.10 (16H, m, other methylene protons). *Anal.* Calcd for C₁₈H₂₈NNaO₃: C, 66.84; H, 8.27; N, 4.10. Found: C, 66.47; H, 8.56; N, 4.03. The expected structure of the Schiff base salt was confirmed by these data.

Determination by GLC of the Effectiveness of Separation of Aldehydes with Reagent A and with Saturated NaHSO₃—Two mmol of an aldehyde (or ketone) shown in Table I was dissolved in 5 ml of diisopropyl ether containing 2 mmol of internal standard (naphthalene or tetralin) (stage A), and the solution was shaken with 5 ml of Reagent A for 2.5 min (stage B), then 10% hydrochloric acid was added to adjust the pH to 4–6, and the mixture was shaken for 2.5 min (stage C). On the other hand, five ml of another lot of stage A solution was shaken for 5 min with 5 ml of freshly prepared aqueous saturated solution of NaHSO₃ (stage D). GLC of the organic layers was carried out at all stages (A through D). All experiments were carried out at room temperature and GLC was done using a column of 3% SE-30 on chromosorb-W (1 m × 3 mm), with N₂ as a carrier gas and FID detection. The results are listed in Table I.

TABLE I. Comparison of the New Method and the NaHSO₃ Method (GLC Analytical Results)

Aldehyde or ketone	New method with Reagent A		NaHSO ₃ method
	Extracted % ^{a)}	Recovered % ^{b)}	Extracted % ^{c)}
Benzaldehyde	92.6	92.4	76.8 ^{d)}
<i>p</i> -Anisaldehyde	90.2	100	60.7 ^{d)}
<i>p</i> -Dimethylaminobenzaldehyde	85.8	100	40.6 ^{d)}
<i>m</i> -Hydroxybenzaldehyde	100	100	100 ^{d)}
Piperonal	94.2	100	90.7 ^{d)}
Vanillin	100	100	92.0
<i>p</i> -Tolualdehyde	85.8	97.1	35.2 ^{d)}
<i>p</i> -Nitrobenzaldehyde ^{e)}	100	100	97.3 ^{d)}
<i>o</i> -Nitrobenzaldehyde	100	100	100 ^{d)}
<i>p</i> -Chlorobenzaldehyde	97.8	100	77.3 ^{d)}
Cinnamaldehyde	100	97.9	26.2 ^{d)}
Furfural	100	100	100
Citral (mixture of <i>cis</i> and <i>trans</i> isomers)	98.5	100	null
Citronellal ¹⁰⁾	86.6	95.0	28.0 ^{d)}
<i>n</i> -Heptanal ¹⁰⁾	85.0	100	15.0 ^{d)}
Cyclohexanone	3.8	—	99.5 ^{d)}
Cyclopentanone	41.8	100	99.0
Acetophenone	0	—	null

a) % of aldehydes or ketones: $100 \times (A - B) / A$.

b) % of aldehydes or ketones: $100 \times (C - B) / (A - B)$.

c) % of aldehydes or ketones: $100 \times (A - D) / A$. (*A*, *B*, *C*, and *D*: standardized GLC peak areas of aldehydes or ketones at stages A, B, C, and D, respectively).

d) Precipitation occurred.

e) Ethyl acetate was used as a solvent.

TABLE II. Effect of the Value of *n* in H₂N–(CH₂)_{*n*}–COONa on the Extractability of *p*-Anisaldehyde

<i>n</i>	Extracted <i>p</i> -anisaldehyde % ^{a)}
1	14.4
2	38.3
3	78.1
5	90.2
10	98.2

a) $100 \times (E - F) / E$ (*E* and *F*: standardized GLC peak areas of *p*-anisaldehyde at stages E and F, respectively).

Effect of the n Value of the Amino Acid $H_2N-(CH_2)_n-COOH$ on the Separation of p -Anisaldehyde—

Two mmol of p -anisaldehyde and two mmol of tetralin were dissolved in 5 ml of diisopropyl ether (stage E) and the solution was shaken for 2.5 min with 5 ml of aqueous 1.2 M amino acid sodium salt [sodium salt of glycine ($n=1$), β -alanine ($n=2$), γ -amino- n -butyric acid ($n=3$), ϵ -amino- n -caproic acid ($n=5$)] or with 5 ml of Reagent B ($n=10$) (stage F). GLC of the organic layers was carried out at stages E and F, and the results are listed in Table II.

Discussion

The data in Table II indicate that ability of ω -amino acids to extract aldehydes increased with n , and might be related to the length of the lipophilic moiety $[-(CH_2)_n-NH_2]$ of the ω -amino acid sodium salts. Further experiments are desirable to confirm this.

Reagent A is stable at room temperature. None of the extraction experiments with Reagent A yielded a precipitate, and the extraction percentages were very high⁸⁾ compared with those by the saturated $NaHSO_3$ method. Furthermore, the new method is more specific for aldehyde separation than the $NaHSO_3$ method (see Table I), and thus the new method seems to be superior.

Only one precaution is necessary in the new method, namely, strong acidic components such as carboxylic acids and nitrophenols should be removed by usual separation methods before the use of Reagent A.

It is very interesting that the naturally occurring γ -amino- n -butyric acid^{5,9)} has considerable reactivity towards aldehydes. The authors are now seeking to apply the reaction of aldehydes with ω -amino acid sodium salts for other purposes, such as protecting or trapping the aldehyde group in organic syntheses.

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- 7) After acidifying an aqueous suspension of the Schiff base salt, p -anisaldehyde could be recovered by usual extraction.
 - 8) When it was shaken twice with reagent A, extraction appeared to be practically complete.
 - 9) D.E. Metzler, "Biochemistry", Academic Press, Inc., New York 1977, p. 533.
 - 10) If an emulsion is formed (as in the case of citronellal and n -heptanal), some iso-PrOH should be added.