VITAMIN B12 PHOTOELECTROCATALYSED (B12/PEC) SYNTHESIS OF 2-AMINOESTERS

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Abstract: Vit. B₁₂ photoelectrocatalysed addition of alkyl bromides and carboxylic anhydrides to methyl 2-acetamidoacrylate yields 2-aminoesters.

Conjugate addition to dehydroaminoacids has attracted considerable attention as a simple route to 2-aminoacids. However, only recently synthetically useful Cu(I) catalysed addition of Grignard reagents to methyl 2-acetamidoacrylate has been reported.¹

Because of pronounced radiophilicity as a captodative olefins dehydroaminoacids are of special interest in radical reactions.²

Vit. B₁₂ mediated photoelectrochemical 1,4-hydroaddition of alkyl halides or carboxylic anhydrides to activated olefins is a mild, non chain radical C-C bond forming reaction. Catalytic cycle of this reaction consists of sequential formation and photocleavage of the Co-C bond.³

In this study methyl 2-acetamidoacrylate, readily available from alanine,⁴ was used as a acceptor. The addition of butyl bromide and acetic anhydride lead to satisfactory yield while reaction time was found longer than in corresponding additions to methyl acrylate.

Table. B₁₂/PEC synthesis of 2-aminoesters.^a

$R-X + CH_2 = C(Y)COOCH_3 \xrightarrow{Vit.B_{12},e^-,hv} R-CH_2-CH(Y)COOCH_3 + X^-$						
Entry		R	x	Y	Yield ^b (%)	Time (h)
1		$CH_3(CH_2)_3$	Br	NHCOCH3	70	5.5
2		, , ,		н	75	4.5
3		CH3CO	CH3C00	NHCOCH3	67	7.5
4		-		н	70	6
5		CH3COO(CH2)3	Br	NHCOCH ₃	72	6

- a) Elemental analyses and spectroscopic properties of new compounds are consistent with the structure.
- b) Isolated yield.

Addition of 1-acetoxy-3-bromopropane to methyl 2-acetamidoacrylate gave 2-acetamido-6-acetoxyhexanoate (entry 5) which has been used in the synthesis of 2-aminoadypinate⁵ and natural unusual aminoacids, e.g. gizzerosine.⁶

Thus, B₁₂/PEC additions of alkyl halides and carboxylic anhydrides to dehydroaminoacids afford a mild, simple route to 2-aminoacids. The investigation of the potential of this reaction in preparation of natural product precursors is continued.

In a typical experiment degassed 100 ml DMF solution of LiClO_4 (2.66 g, 25 mmol), Vit. B₁₂ (0.270 g, 0.2 mmol), 1-acetoxy-3-bromopropane (1.086 g, 6 mmol), methyl 2-acetamidoacrylate (0.705 g, 5 mmol) was electrolyzed upon irradiation⁷ at 22°C under Ar till current decreased to background. The volatile materials were evaporated in vacuo and residue was washed with ethyl acetate then evaporated. Slowly crystalizing oil was chromatographed (SiO₂, ethyl acetate/hexane, 4:1) yielding 0.880 g (72%) of 2-acetamido-6-acetoxyhexanoate.

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References and notes

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- -1.4 V vs. Ag/Ag⁺, thermostated divided cylindrical cell, Pt foil anode, carbon felt cathode (Sigratherm KFA), Hg 400 W lamp (Philips G/92/2).

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