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# The Solid-Phase Synthesis of Amino Acid-Derived Diacetylene Lipids

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**Abstract:** We prepared amino acid-derived diacetylene monomers using solid-phase organic synthesis. The solid-phase synthetic method allowed for the rapid and efficient preparation of functional diacetylenes. Amino acids having hydrophobic sidechains such as alanine, leucine, and phenylalanine, as well as hydrophilic sidechains such as aspartic acid and lysine, were successfully coupled to the diacetylene lipid. The diacetylene monomers prepared in this way were subjected to routine procedures for the generation of polydiacetylene vesicles. Depending on the nature of the side-chains, pink to blue colored polydiacetylenes were generated.

*Keywords*: solid-phase synthesis, diacetylene, amino acids.

## Introduction

Since the pioneering discovery of blue-to-red color transitions induced by specific ligand-receptor interactions in polymerized diacetylenes,[1] the development of efficient sensory systems based on polydiacetylenes (PDAs) has gained much attention in the context of fundamental and applied research.[2] Most of the functional diacetylene monomers, reported thus far, have been prepared by using solution-phase synthetic methods, which require multi-step purification procedures.[3] A potentially more useful approach for the preparation of functional diacetylenes, which can overcome the limitations involving the solution-phase synthesis, relies on the employment of solid-phase synthetic methods. Recently, solid-phase synthesis has evolved into a key technology for the preparation of a large number of diverse, biologically important ligands.[4] Thus, we felt that combining the emerging fields of solid-phase synthesis and diacetylene chemistry would lead to new and efficient routes for the preparation of PDA-based chemosensors. As part of our continuing efforts for the development of polydiacetylene-based chemosensors,[5] we now report the solid-phase synthesis of functional diacetylene lipid monomers. Our initial effort aimed at testing this proposal focused on the solid-phase synthesis of amino acid-derived, diacetylene lipids. Amino acid and peptide-modified diacetylenes were selected for this effort owing to the fact that peptides are attractive targets for drug discovery. This is a consequence of their high affinities and specificities toward biological receptors and the fact that large peptide libraries can be synthesized by using a combinatorial format.[6]

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## Experimental

10,12-Pentacosadiynoic acid (PCDA) was purchased from GFS Chemicals. The Rink resin, Fmoc-protected amino acids, and reagents for solid-phase synthesis were purchased from Advanced Chemtech. The solid-phase synthesis of amino acid-modified diacetylene monomers were performed according to the general procedures described in 'Advanced Chemtech Handbook of Combinatorial & Solid Phase Organic Chemistry' (1998 edition). Spectroscopic data for the amino acid-derived diacetylene monomers synthesized on solid support are as follows:

**$NH_2$-Gly-PCDA**: M. p. 128-129 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.88 (t, 3H), 1.20-1.80 (m, 32H), 2.24 (m, 6H), 3.96 (d, 2H), 5.40 (s, 1H), 6.00 (s, 1H), 6.20 (s, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$=14.6, 18.8, 19.6, 23.1, 25.9, 28.7, 28.8, 29.0, 29.1, 29.3, 29.5, 29.6, 29.7, 29.9, 30.0, 32.3, 36.3, 36.7, 43.2, 65.5, 65.6, 68.4, 77.5, 77.7, 77.9, 173.8, 175.6.

**$NH_2$-Ala-PCDA**: M. p. 124-125 °C; $^1$H NMR (300 MHz, $CDCl_3$): $\delta$=0.88 (t, 3H), 1.2-1.8 (m, 35H), 2.19 (t, 2H), 2.25 (t, 4H), 4.54 (q, 1H), 5.52 (s, 1H), 6.2 (d, 1H), 6.44 (s, 1H); $^{13}$C NMR (100 MHz, $CDC_3$): $\delta$=15.0, 19.0, 20.0, 23.5, 26.3, 29.1, 29.5, 29.7, 29.9, 30.1, 30.3, 30.4, 32.7, 37.3, 48.9, 65.9, 66.0, 78.1, 78.3, 173.7, 175.0.