Determination of rate constants for H-abstraction by 4-fluorophenyl radicals from fatty acid methyl esters by F-19 NMR

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Introduction

Phenyl radicals (Ph·) are very reactive intermediates known to rapidly abstract hydrogens and add to double bonds. 1 Rate constants for H-abstraction by Ph· from various types of substances have been determined and are generally in the range of k(Ph·,H) = 10-3 to 3 x 107 M-1 s-1. 2 Kondo et al. and coworkers used mass spectrometry to examine the rate of gas-phase reactions of Ph· with lipids, using Ph· with cationic ammonium substituents. 3 However, solution phase rate constants for H-abstraction by uncharged phenyl radicals from lipids remains, in large part, unknown. Thus, this research is attempting to measure k for H-abstraction from fatty acid methyl esters (FAME) by uncharged Ph· using 4-fluorophenyl radicals (Ar·) generated from the visible photolysis of 4-fluoro phenyl azo isobutyronitrile (FPAIN) (eq 1). The research may provide insight as to the types of effects phenyl radicals from benzoyl peroxide (BPO) may have on the human body.

BPO is an over the counter medication widely used as a treatment for acne and is on the list of World Health Organization’s list of essential medicines. 4 BPO is also known to break down to free Ph· (eq 2,3), and is accordingly frequently used as an initiator for radical polymerization. 5 Previous work has shown that BPO can act as a tumor promoter in mice skin; however, there was not enough evidence to suggest that BPO is a tumor initiator. 6 This research project is aiming to provide information relevant to the possible effects of free radicals formed from BPO on human skin. Specifically, we are measuring the rate constants of H-abstraction by Ph· from fatty acid methyl esters (methyl linoleate, methyl oleate, and methyl stearate) as respective models for diunsaturated, monounsaturated, and saturated fats.

Results

Figure 1: Preparation of 4-fluorophenylazo isobutyronitrile (FPAIN)

Figure 2: 1H NMR of purified FPAIN

Figure 3: 1H NMR of deprotonated FPAIN

Figure 4: Phosphorylation of FPAIN in the presence of a FAME and iodobenzene

Figure 5: kH calculation

Experimental

4-Fluorophenyl hydroxyl radical (1H g, 0.162 mg, Sigma Aldrich) was suspended in water with NaBH4 in a separatory funnel. It was tested with litmus paper to confirm theivity. The solution was then extracted (5X with diethyl ether) and washed with H2O, followed by filtration and collection of the organic raction in a vial. 4-Fluorophenyl hydroxyl radical (1H g, 0.162 mg, Sigma Aldrich) was suspended in water with NaBH4 in a separatory funnel. It was tested with litmus paper to confirm theivity. The solution was then extracted (5X with diethyl ether) and washed with H2O, followed by filtration and collection of the organic raction in a vial.

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