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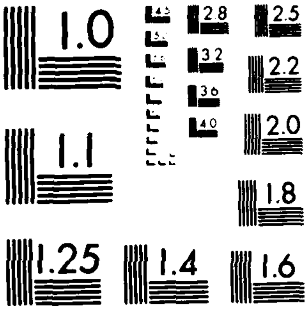

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Final Progress Report

Project Title:

THE CHEMICAL CHARACTRISTICS OF PGB$_X$

Principal Investigator:

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Cambridge, MA 02139

Contract N00014-78-C-0421

Date of Report:
August 18, 1983

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Principal Investigator: Klaus Biemann, Dept. of Chemistry
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Objectives

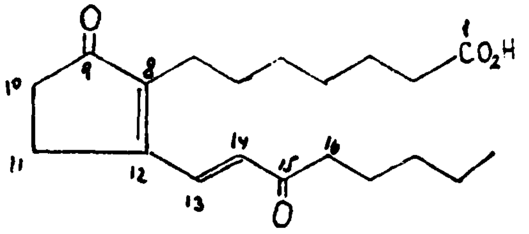
It was first attempted to separate PGB$_X$, a biologically active material obtained upon alkali treatment of 15-keto-prostaglandin-B$_1$(1), into its components, determine their molecular weight and, finally, molecular structure. When it became clear that PGB$_X$ is too complex a mixture, model studies were begun.

To investigate the mechanism by which the chemically active moiety in 15-keto-prostaglandin-B$_1$ oligomerizes to PGB$_X$ under alkaline conditions, the condensation of 3-ethyl-4-(3′-ketopenten-1-yl) cyclopent-2-enone (2) was investigated.

Summary of Results

A high pressure liquid chromatograph was used to separate various batches of PGB$_X$ and its precursors. Partial separation has been achieved. Field desorption mass spectrometry of PGB$_X$ was attempted but without success. ^{252}Cf plasma desorption mass spectrometry seems to indicate the presence of a mixture ranging from tetramers to octamers of 15-keto-PGB$_1$.

The condensation of modified models of the diene-dione moiety (2) of 15-keto-PGB$_1$(1) was then studied. It has been found that a number of dimers are involved in this reaction. Furthermore, the results indicate that the anion at C-16 is very reactive and probably the initial step. Gas chromatography (GC), high performance liquid chromatography (HPLC), field desorption (FD), fast atom bombardment (FAB) mass spectrometry, ^{1}H and ^{13}C-NMR were used for the analysis of the resulting mixtures of isomers and oligomers.



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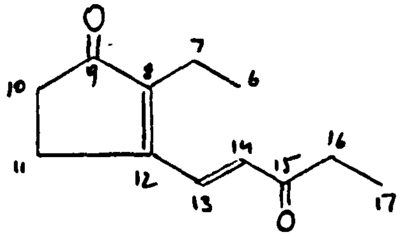
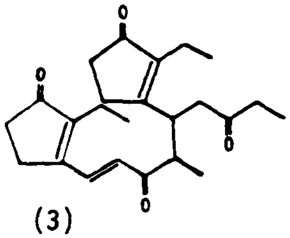


(2)

Conclusions

The base catalyzed condensation of the model ketone (2), when carried out under conditions somewhat milder than those which convert PGB_1(1) to PGB_X, produced a number of dimeric compounds. Upon separation by gas and liquid chromatography their structures (3-6) were determined by spectroscopic means and found to be most likely represented by the following:



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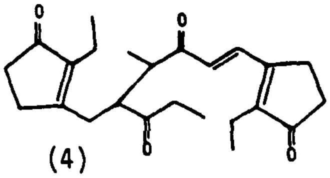

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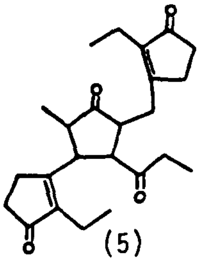

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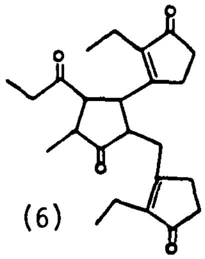
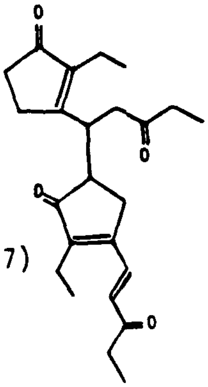


(6)

The presence of isomer (7) is not excluded.



(7)

The fact that the simpler model, under mild conditions, can undergo condensation in four or five ways indicates that the oligomer (PGB_X) obtained when treating PGB_1 with alkali must be *a* very *complex* mixture. Under those circumstances it is not surprising that the oligomer could not be separated into the individual components.

Just when this work was completed a paper appeared by G.L. Nelson and G.L. Verdine (Tetrahedron Letters, 23, v.1967-1970 (1982)) describing essentially the same results. Although the senior author of that paper (G.L.N.) had agreed to keep the Principal Investigator (K.B.) informed about his work to avoid duplication and to publish the results jointly or simultaneously, this was not done. We therefore decided not to publish our results separately later. This episode is typical of the lack of cooperation and communication that plagued the entire PGB_X project from the outset.

Technical Reports; None

Publications; Optimization of Experimental Procedures for Fast Atom Bombardment Mass Spectrometry. S.A. Martin, C.E. Costello, and K. Biemann, Anal. Chem. 54, 2362-2368 (1982).

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