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SYNTHESIS OF DIENIC ACIDS. APPLICATION OF ARNDT - EISTERT REACTION TO UNSATURATED DIAZOKETONES

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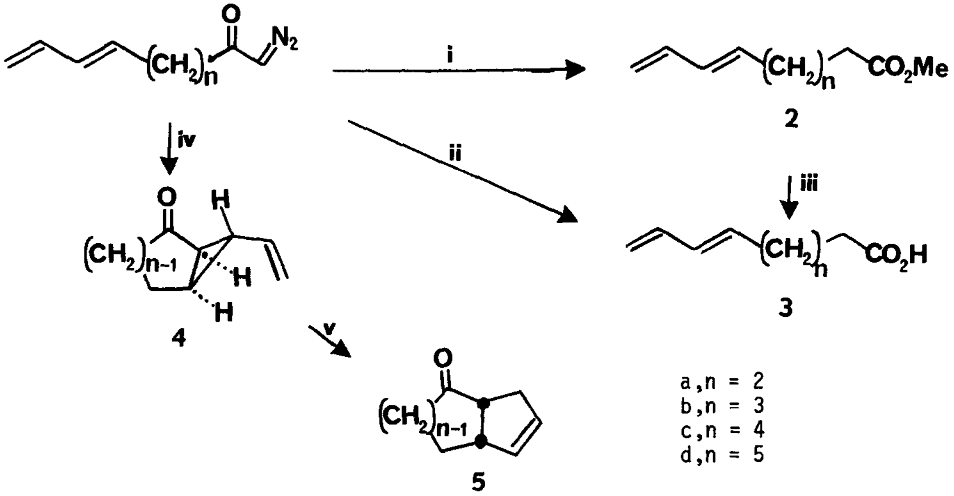
Abstract: Different modes of decomposition of dienic diazoketones have been studied, leading to either formation of vinyl-cyclopropanes or Wolff-rearranged acids or esters. Preparation of four homologous dienic acids is described.

Recently we required a series of homologous diazoketones 1 in connection with our investigation of the intramolecular carbenoid addition to 1,3-dienes[1] to produce cyclopentene annulated polycyclic systems such as 5.



Reagents: i Sodium benzoate/Et_3N,MeOH; ii $Ag_2O/Na_2CO_3/Na_2S_2O_3/H_2O$
iii KOH/H_2O; iv $Cu(acac)_2$/benzene 25°C: v 500°C/$Pb(CO_3)$ - coated glass.

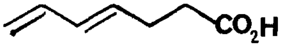
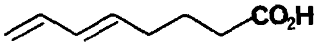
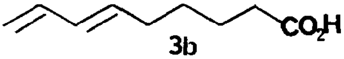
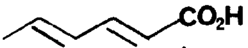
Fig. 1.

The obvious homologation procedure, namely the Wolff-rearrangement of diazoketones, has been reported to give low yields[2] (< 10%) of the corresponding acids or esters and numerous byproducts in cases where the unsaturation site was present in a non-rigid system and less than six carbon atoms removed from the diazo group; in the case of α,β-unsaturation, formation of pyrazolines was observed[3]. The review of the literature[4,5] suggested that Arndt-Eistert synthesis was successful in high yields only with 7-octenoyl chlorides and higher homologues. No evidence was found for successful Wolff rearrangement of linear α,β-unsaturated diazoketones without protection of the double bond[11].

We now wish to report a procedure for homologation of dienic acids (in which the olefinic moiety is available to the carbenoid) in high yields through a controlled decomposition of diazoketones <u>1</u>.

In a typical experiment, a solution of <u>1a</u> (prepared by the action of diazomethane on 4,6-heptadienoyl chloride[6] in quantitative yield), (250 mg; 0.0017m) in dioxane (1 ml), was added over 20 min to a stirred mixture of silver oxide (20 mg), anhydrous sodium carbonate (50 mg), sodium thiosulfate (30 mg) in water (2 ml) at 60-65°C. After the addition was complete, the reaction mixture was stirred at 90°C for 5 hours, during which time a solution of silver oxide (20 mg), anh. sodium carbonate (50 mg) and sodium thiosulfate (30 mg) in 2 ml of water and 1 ml of dioxane was added each hour. The reaction mixture was cooled, acidified with 1N nitric acid, and extracted with methylene chloride. Evaporation yielded pure <u>3a</u> (220 mg; 94.3%); IR (neat) cm^{-1} 3300 O-H, 1700 C=O, 1642, 1595 C=C. The presence of a base proved to be essential, otherwise <u>1a</u> decomposed to give a mixture of <u>3a</u> and <u>4a</u>. Identity of <u>4a</u> was established previously[1,8] by ^{13}C-NMR - it is interesting to note that its formation occurs stereoselectively - and by its conversion to the known bicyclooctene <u>5a</u>[9].

It proved advantageous to effect the Wolff rearrangement in an alcoholic solvent to produce esters which were later hydrolyzed. The two-step sequence was experimentally faster and more facile. Thus, a solution of <u>1a</u> (7.5 g; 0.05m) in absolute methanol (75 ml) was treated with silver benzoate (1 g; 0.004m) in triethylamine (10 ml) during 30 min at room temperature. After 1 hr, the solvent was removed in vacuo, the residue taken up in ether, washed with dilute hydrochloric acid (2N), neutralized (sodium bicarbonate), dried and evaporated to give 6.27g (82%) of 2a, b. p. 31-32°/0.1mm; IR (neat) cm^{-1} 1730 C=O, 1640, 1596 C=C. Exposure of 2a to methanolic potassium hydroxide (0.1M) in water (10 ml) for 30 min at reflux, followed by acidic workup gave 90% of 3a. 3a was cautiously added to a ten-fold excess of oxalyl chloride, left standing at room temperature overnight and distilled to give 81% of corresponding acid chloride, which was converted quantitatively to 1b.

Acid	Acid Chloride	Diazo Ketone	Ester	Acid	Remarks
	81	$\sim$100	82	3a, 90	
				94	directly from 1a
 3a	70	$\sim$100	94	3b, 88	
 3b	82	$\sim$100	85	3c, 80	
 6	85	$\sim$100	/	/	Complex mixtures

All yields are based on isolated material

TABLE I

Table I summarizes the results of our experiments. In all cases, the structure of diazoketones, esters and acids was confirmed by ^{1}H-NMR, ^{13}C-NMR and mass spectrometry. It appears therefore that the decomposition pathway of α-diazoketones containing an olefinic moiety can be directed to give either cyclopropanes or Wolff-rearranged products. It is our feeling that the low yields of homologous acids reported previously[2] were in part due to cyclopropanated products formed in the absence of base, which, being neutral, escaped detection and acidic workup. Our results suggest that unsaturated or dienic acids may be homologized using Arndt-Eistert reaction, provided they are not α,β - unsaturated;[1] the only case examined in our laboratory was the decomposition of 1-diazo-3,5-hepadien-2-one[7,10] which gave complex mixtures and was therefore abandoned.

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6. W. Oppolzer and R. Hunadi, unpublished observation: 4,6-hephadienoic acid is prepared from 1,4-pentadien-3-ol and triethylorthoacetate via Claisen rearrangement, followed by base hydrolysis.
7. Prepared from commercially available (Aldrich) 2,4-hexadienoic acid.
8. 1a gives 4 quantitatively when heated in benzene in the presence of Cu(acac)$_2$.
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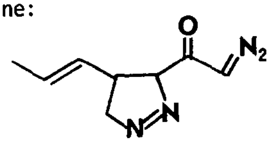

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