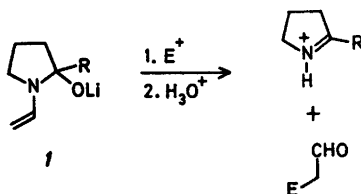


## A New Acetaldehyde Anion Equivalent\*

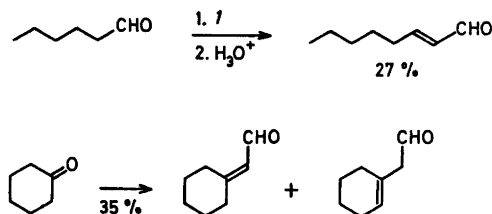
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Cyclic imines can be synthesized by the reaction of *N*-vinylactams with organolithium reagents followed by hydrolysis with dilute acid.<sup>1</sup> With *N*-vinylpyrrolidone (NVP) as starting material, the initial reaction product should be the addition compound **1**. A study of the reactions of **1** with various electrophiles has been undertaken and we here report the results of experiments with a number of  $\alpha,\beta$ -unsaturated ketones and two saturated carbonyl compounds. The structures of the new compounds formed demonstrate that **1** is synthetically equivalent to the enolate anion of acetaldehyde.



In the investigation of the reactions of **1** with various types of  $\alpha,\beta$ -unsaturated ketones, preparatively useful reactions were encountered only for compounds containing the cinnamoyl moiety (Table 1) and the only products found were those derived from 1,4-additions to the enone systems. Simple aliphatic enones, e.g. 5-methyl-3-hexen-2-one, invariably gave negligible yields of  $\delta$ -ketoaldehydes. The reactions between **1** ( $R = C_6H_5$ ) and saturated carbonyl compounds gave low to moderate yields of  $\alpha,\beta$ -unsaturated aldehydes.



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Table 1. Yields of  $\delta$ -ketoaldehydes in the reactions of **1** ( $R = n$ -Bu) with enones of the type  $Ar-CH=CH-CO-R'$

	Product		Yield/ %
	$H-C-CH_2-CH-CH_2-C-R'$		
	$\begin{array}{c} \parallel \\ O \end{array}$	$\begin{array}{c}   \\ Ar \end{array}$	$\begin{array}{c} \parallel \\ O \end{array}$
	Ar		R'
2	$C_6H_5$	$C_6H_5$	66
3	$C_6H_5$	<i>t</i> -Bu	57
4	$p-(CH_3O)C_6H_4$	<i>i</i> -Bu	55

Several methods have been described for the preparation of  $\alpha,\beta$ -unsaturated aldehydes from saturated aldehydes or ketones containing two carbon atoms less,<sup>2-13</sup> but only a few methods, all copper-based, have been reported for the addition of the elements of acetaldehyde across the carbon-carbon double bond of  $\alpha,\beta$ -unsaturated ketones to obtain  $\delta$ -ketoaldehydes.<sup>2a,12-16</sup> Enamines of aldehydes larger than acetaldehyde have been used in order to achieve 1,4-addition, but not enamines of acetaldehyde itself, probably because of difficulties associated with the instability of the latter compounds.<sup>17,18</sup> The enolate anion of acetaldehyde can be obtained in an essentially quantitative yield from butyllithium and THF,<sup>19</sup> but no condensation reactions with it have been reported.

The advantages of the present technique lie in the greater ease with which the acetaldehyde anion equivalent is prepared and the low cost of the starting materials.

**Experimental.** NVP (Fluka) was distilled before use. Reaction products were distilled using a Nester-Faust NFT-51 spinning band column.  $^1H$  and  $^{13}C$  NMR spectra of the products were in accord with the structures given.  $^{13}C$  NMR spectra were run in deuteriochloroform at 25.05 MHz using a JEOL JNM-FX 100 spectrometer and with TMS as internal reference. Single-frequency off-resonance (SFOR) spectra were obtained by irradiating at 400 Hz upfield from TMS in the proton spectrum. A long-range coupling, ascribed to an interaction between C-2 and H-1, was used in assigning the signals to the C-2 carbons of compounds 2-4 (Table 1). When the one-bond residual splittings were 33 and 31 Hz in the SFOR spectra of 2 and 3, additional two-bond splittings of 11 and 10 Hz, respectively, were obtained. The corresponding signal from 4 was only a broad triplet.

**Procedure for reaction of 1 with hexanal and cyclohexanone.** A solution of NVP (15.0 g, 135 mmol) in ether (100 ml) was added dropwise to a stirred and cooled solution (0.7 M) of phenyllithium (125 mmol) in ether, keeping the temperature at  $-15$  to  $-10^\circ C$ . After one h at the same temperature, the carbonyl com-

pound (100 mmol) dissolved in ether (50 ml) was added and the temperature was allowed to rise to (a)  $-5^{\circ}\text{C}$  during 40 min (hexanal) or (b)  $+20^{\circ}\text{C}$  during 30 min (cyclohexanone). Oxalic acid dihydrate (50 g) in 300 ml of water was added and the resulting mixture was subjected to steam distillation. The crude  $\alpha,\beta$ -unsaturated aldehydes were taken over in ether (salting out with NaCl) and the ethereal layer dried ( $\text{MgSO}_4$ ). Removal of the solvent followed by distillation afforded the  $\alpha,\beta$ -unsaturated aldehydes.

(E)-2-Octenal (> 99 % purity, GLC) was obtained in a 27 % yield; b.p.  $70-71^{\circ}\text{C}$  (1.6 kPa); lit.<sup>20</sup> b.p.  $75-78^{\circ}\text{C}$  (1.7 kPa). The  $^1\text{H}$  NMR spectrum of the *trans* enal moiety was indistinguishable from the published spectrum.<sup>21</sup>

Cyclohexylideneacetaldehyde was obtained together with 1-cyclohexenylacetaldehyde in a combined yield of 35 % with the former predominating (57:43). No attempt was made to suppress the formation of the latter isomer by using a smaller amount of oxalic acid.<sup>22</sup> As found previously, a separation of the isomers could be achieved by distillation ( $58-84^{\circ}\text{C}$ , 1.3 kPa).<sup>23</sup> Parts ( $\approx 50$  %) of both compounds were obtained in a purity exceeding 97 % (GLC).

*Procedure for reaction of 1 with  $\alpha,\beta$ -unsaturated ketones.* A solution of NVP (4.4 g, 40 mmol) in toluene (20 ml) was added fairly rapidly to a stirred solution ( $-60^{\circ}\text{C}$ ) of butyllithium (38 mmol) in ether (30 ml) and toluene (20 ml). After 5 min, a solution of the enone (36 mmol) in toluene (20 ml) was added dropwise, and the cooling bath was removed. When the mixture had been stirred for 15 min, it was again cooled to about  $-60^{\circ}\text{C}$  and then hydrolyzed with a mixture of 4 M hydrochloric acid (25 ml), water (10 ml), and THF (80 ml) with efficient stirring. The cooling bath was removed after the acid had been added and the stirring was continued for 30 min at  $22^{\circ}\text{C}$ . The major part of the THF was evaporated under reduced pressure and the residue partitioned between water and ether. Three extractions with ether were carried out and the combined organic layers dried ( $\text{Na}_2\text{SO}_4$ ). After filtration and evaporation of the solvent, the crude reaction product was purified by chromatography on silica gel ( $4 \times 40$  cm) using a light petroleum-ethyl acetate (4:1) solvent system. The yields given in Table 1 refer to these chromatographically purified products.

5-Oxo-3,5-diphenylpentanal (2) was obtained on crystallization from light petroleum ( $85-110^{\circ}\text{C}$ ); m.p.  $69-70^{\circ}\text{C}$ .  $^{13}\text{C}$  NMR: 201.1 (C-1), 198.0 (C-5), 143.2-126.9 (aromatic carbons), 49.6 (C-2), 44.9 (C-4), and 35.4 ppm (C-3).

6,6-Dimethyl-5-oxo-3-phenylheptanal (3) was obtained as a colourless liquid, b.p.  $85-86^{\circ}\text{C}$  (7 Pa).  $^{13}\text{C}$  NMR: 213.2 (C-5), 201.0 (C-1), 143.8, 128.8, 127.7, and 126.9 (aromatic carbons), 49.3 (C-2), 43.9 (C-6), 43.1 (C-4), 35.1

(C-3), and 26.0 ppm (C-7). The aldehyde was fairly easily oxidized in air to the corresponding carboxylic acid, which was recrystallized from cyclohexane; m.p.  $122-125^{\circ}\text{C}$ , lit.<sup>24</sup> m.p.  $124^{\circ}\text{C}$ .

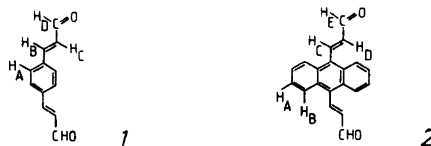
3-(4'-Methoxyphenyl)-7-methyl-5-oxo-octanal (4) was obtained after distillation at  $135^{\circ}\text{C}$  (0.8 mPa).  $^{13}\text{C}$  NMR: 209.0 (C-5), 201.5 (C-1), 158.5, 135.2, 128.4, and 114.2 (aromatic carbons), 55.2 ( $\text{O}-\text{CH}_3$ ), 52.3 (C-2), 49.7 and 49.5 (C-4 and C-6), 34.3 (C-3), 24.4 (C-7), and 22.4 ppm (C-8).

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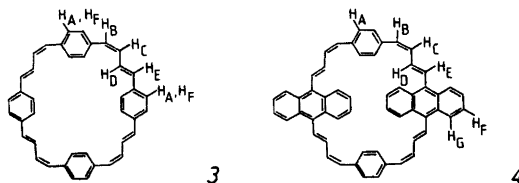
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The structure of 3, [4.4.4.4]paracyclophane-*cis,trans,trans,cis,cis,trans,trans,cis*-octaene or, according to IUPAC nomenclature; pentacyclo-[28.2.2.2.2<sup>6-9</sup>.2<sup>14-17</sup>.2<sup>22-25</sup>]tetraconta-2,4,6,8,10,-12,14,16,18,20,22,24,26,28,30,32,33,35,37,39-eicosaene, follows from its mass and NMR spectra. The mass spectrum shows the molecular ion as parent peak and little fragmentation.



The <sup>1</sup>H NMR spectrum showed two sharp singlets for the two types of benzene rings and an ABMX-pattern for the olefinic protons. Spin decoupling and simulation gave the shifts and coupling constants. The large coupling constant  $J_{CD} = 12$  Hz indicates that the molecule is relatively planar with *S-trans* orientation of the butadiene bridges. *S-cis* orientation would lead to a more compact, but less planar, structure due to steric interaction between the inner protons. The benzene rings rotate fast on the NMR time scale. No coalescence of the signals was observed on cooling the sample down to  $-110$  °C.

[4.4.4.4]Paracyclophaneoctane, 3, can be regarded as a [16]annulene with four benzene rings inserted into four single bonds in a symmetrical way. The corresponding isomer of [16]annulene with *cis,cis,trans,trans,cis,cis,trans,trans* orientation of the double bonds is not the one observed in the crystalline state<sup>4</sup> nor one of the major isomers in solution.<sup>5</sup> It is noteworthy that 3 (and 4) which contains eight double bonds, four *cis* and four *trans*, is, in contrast to the annulenes, rather stable and can be isolated as one single isomer.

The UV spectrum of 3 is much simpler than that of the annulenes.<sup>6</sup> It shows two absorption bands at 345 nm ( $\epsilon$  74 000) and 360 nm ( $\epsilon$  75 000 in cyclohexane).

The  $\pi$  electron system of 3 contains 40 electrons of which 32 can be considered as conjugated in a macrocyclic ring, and therefore the compound is formally an anti-Hückel system. Ring current effects on the chemical shifts are small. Although the shift difference between the internal and external protons H<sub>C</sub> and H<sub>D</sub> is 1.54 ppm which is *ca.* 1/3 of the value for [16] annulene at  $-110$  °C, the corresponding difference in the closely related open chain

## Synthesis of [4.4.4.4]Cyclophanes

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We have previously reported that multiple Wittig reactions provide an efficient synthetic route to cyclophanes with ethylene bridges between the aromatic rings.<sup>1,2</sup> Although the overall yields are often low (< 15 %), the simple starting materials and procedure for separation and isolation of the products make this one-step synthesis an easy route to a large number of cyclophanes and bicyclophanes<sup>3</sup> and their derivatives.

We now report the synthesis, by four-fold Wittig reactions, of cyclophanes in which four aromatic rings are bridged by butadienes of known conformations.

1,4-Benzenedicarbaldehyde and 9,10-anthracenedicarbaldehyde were converted to the vinylogous dialdehydes 1, 1,4-benzenedipropenal, and 2, 9,10-anthracenedipropenal. The dialdehydes 1 and 2 were reacted with the bis-triphenylphosphonium salt from 1,4-bis(bromomethyl)benzene in *N,N*-dimethylformamide at  $-40$  °C in the presence of lithium ethoxide to give *ca.* 2 % yield of the [4.4.4.4]cyclophane-octaenes 3 and 4, respectively.