

A NEW SYNTHESIS OF  $\alpha,\beta$ -UNSATURATED ALDEHYDES  
INCLUDING (E)2-METHYL-2-ALKENAL

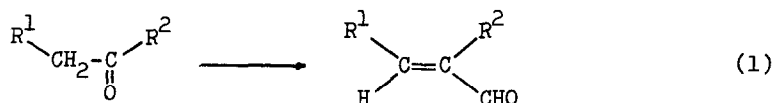
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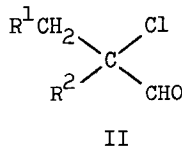
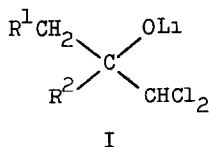
We wish to announce a novel technique for the one carbon homologation of ketones to produce  $\alpha,\beta$ -unsaturated aldehydes<sup>1</sup> (eq. 1) The direct formation of



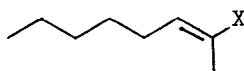
such conjugated aldehydes from simple ketones is not possible by means of preexisting synthetic methods, and consequently indirect approaches which are multistep in low over-all yields have been required.<sup>2</sup>

The complete sequence is illustrated by the transformation of cyclohexanone to 1-cyclohexenecarbaldehyde. Addition of cyclohexanone (1.00 equiv) to a THF solution of dichloromethylithium<sup>3</sup> (1.20 equiv) (-95° for 10 min, -78° for 2 hr, and -25° for 30 min) gave a colorless solution of the oxido adduct I ( $\text{R}^1, \text{R}^2 = -(\text{CH}_2)_4-$ ),<sup>4</sup> homogeneous by tlc analysis ( $R_f$  0.40,  $\text{SiO}_2$ -benzene). The solution was heated at reflux for 1 hr to produce  $\alpha$ -chloroaldehyde II ( $\text{R}^1, \text{R}^2 = -(\text{CH}_2)_4-$ ),<sup>4b,5</sup> which was concentrated in vacuo at 0°. Hexamethylphosphoric triamide (excess), lithium perchlorate (2.00 equiv.), and calcium carbonate (2.50 equiv.)<sup>6</sup> were added, and the suspension was heated at 130° for 1.5 hr to afford 1-cyclohexenecarbaldehyde<sup>2</sup> as a sole product (74% by glpc, 68% by 2,4-DNP: mp 222.5-223°, lit.<sup>7</sup> 219-220°). Similarly cyclododecanone and cyclopentanone gave 1-cyclododecenecarbaldehyde<sup>8</sup> (81% after tlc purification),

and 1-cyclopentenecarbaldehyde (50% by glpc, 2,4-DNP: mp 216-217<sup>o</sup>, lit.<sup>9</sup> 215-216<sup>o</sup>), respectively

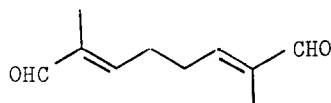


Although the simplicity and directness of this homologation procedure are appealing, even more important is the fact that the reaction of 2-octanone gave (E)2-methyl-2-octenal (IIIa)<sup>10</sup> exclusively in 74% yield (glpc). The stereochemistry of IIIa was clearly indicated by analysis of the nmr spectrum (CCl<sub>4</sub>, TMS) which revealed peaks at 1.70 (s, 3H, olefinic methyl), 6.40 (t, 1H, J = 7 Hz, olefinic proton), and 9.30 ppm (s, 1H, CHO). The chemical shifts for this product occur precisely as expected for IIIa<sup>11</sup> and contrast with those observed for the regio- and stereoisomeric olefins (Z) isomer 1.72, 6.46, and 10.11 ppm, CH<sub>2</sub>=CHRCHO 9.55 ppm.<sup>11,12</sup> The structure IIIa was further confirmed by reduction to the corresponding alcohol IIIb which showed the expected nmr properties.<sup>13</sup> Gas chromatographic analysis of the product IIIa showed the absence of detectable (<1%) amounts of the isomeric olefins



IIIa X = CHO

IIIb X = CH<sub>2</sub>OH



IV

The observed regio- and stereoselectivity of this reaction portends its broad synthetic applications in isoprenoid field. Thus, starting with the readily available 2,7-octanedione and using the same procedure as described above, the dialdehyde IV, a key intermediate for squalene synthesis,<sup>14</sup> was

obtained in a single step stereoselectively (>99%) and efficiently (68% after tlc purification)

The scope and synthetic applications of this reaction are under current investigation.

#### REFERENCES AND FOOTNOTES

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- 4 A valuable intermediate for (a)  $\alpha$ -chloro ketones and (b)  $\alpha$ -chloro aldehydes. (a) H Taguchi, H Yamamoto, and H. Nozaki, Tetrahedron Lett , 4661 (1972), J Villieras, C Bacquet, and J. F Normant, J Organometal. Chem., 40, C1 (1972), G. Kobrich and J. Grosser, Tetrahedron Lett., 4117 (1972), (b) G Kobrich and W Werner, ibid., 2181 (1969)
- 5 The intermediary chlorooxirane was found to give the same product, 1-cyclohexenecarbaldehyde, with lithium perchlorate in HMPA. unpublished results by S Tanaka For epoxide-ring opening using lithium perchlorate, see B Rickborn and R M Gerkin, J Amer Chem. Soc., 90, 4193 (1968) The delay of sequence by the isolation of the sensitive  $\alpha$ -chloro aldehyde II is therefore unnecessary.
- 6 Dehydrohalogenation of  $\alpha$ -halocarbonyl compounds using lithium salts R Joly J. Warnant, G Nomine, and D. Bertin, Bull. Soc Chim. Fr , 366 (1958) At least in the case studied, the combination of  $\text{LiClO}_4$ - $\text{CaCO}_3$ -HMPA was found

to be the best conditions for the dehydrochlorination of  $\alpha$ -chloroaldehydes.

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8. Mass m/e 194 ( $M^+$ ), ir (neat) 1685 and 1635  $\text{cm}^{-1}$  (conjugated aldehyde); nmr ( $\text{CCl}_4$ , TMS)  $\delta$  6.29 (t, J = 8 Hz, olefinic proton), 9.20 (s, CHO) 2,4-DNP mp 197.5-198 $^\circ$ .
9. I. Heilbron, E. R. H. Jones, J. B. Toogood, and B. C. L. Weedon, ibid., 1827 (1949).
10. Mass m/e 140 ( $M^+$ ), ir (neat) 1688 and 1640  $\text{cm}^{-1}$  (conjugated aldehyde), homogeneous by tlc analysis. 2,4-DNP: mp 95-96 $^\circ$
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14. U. T. Bhalerao and H. Rapoport, ibid , 93, 5311 (1971).