Short Communications

Reactions of Some Enamines with 1-Acetyl-1-cyclohexene LARS H. HELLBERG* and MORROW F. STOUGH, III

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Numerous enamines (A) of ketones have been alkylated with acyclic alkyl vinyl ketones to yield, after aldol-like cyclization and pyrrolidine loss and re-addition, dienamines (B). These usually have been hydrolyzed to the corresponding ketones (\tilde{C}) .^{1,2} In contrast, A and either α -alkylidene cyclanones sa or their Mannich bases sb

have been observed to give alkylation only to 1,5-diketones (with one exception ³²). More recently, Leonard and Musliner have caused 2-cyclohexenone to react with its own pyrrolidine dienamine to yield a bisenamine which was hydrolyzed to a tricyclic diketone.4 In this communication we describe some reactions of enamines I (n = 0, 1) with yet another structural type of a, B-unsaturated ketone, 1-acetyl-1-cyclohexene (II), to yield tricyclic derivatives.

A solution of II⁵ (0.109 mole) and I $(n = 1)^1$ (0.109 mole) in 30 ml xylene was refluxed for 46 h under nitrogen using a water trap (1.4 ml water). One-half of the reaction mixture was vacuum-evaporated, then hydrolyzed in refluxing aqueous acetic acid-sodium acetate solution.1 Rapid chromatography of 1.0 g of the hydrolyzate (9.0 g) on acid-washed alumina using benzene as eluent gave crude solid which, on recrystallization from methanol-water, gave 0.57 g of IV (n = 1) (46 % yield overall): m.p. 85-87°C, $v_{\rm max}^{\rm KBr}$ 1660 vs and 1619 m cm⁻¹; $\lambda_{\text{max}}^{\text{ethanol}}$ 238 m μ (ϵ 9 300); NMR (in CCl₄) singlet (in appearance, presumably due to virtual coupling as half-band width ~3.8 c/s) at τ 4.35 (vinyl H α to carbonyl) and strong, complex absorption at τ 7.3-9.3. The solid IV (n = 1) was probably identical to that prepared earlier in 32-35 % yield from II and cyclohexanone in cold ether with sodium amide:6,7 m.p. 89°C , $^{6}\lambda_{\max}^{\text{ethanol}}$ 238 m μ (ε 13 800), 7 viaa Michael-aldol sequence. A 2,4-dinitrophenylhydrazone of IV (n = 1) was prepared: m.p. 224-225°C. An undetermined % of β , γ unsaturated ketone V (n = 1) accompanied IV (n = 1), as a rapid IR of an early chromatographic fraction showed carbonyl absorptions in the regions expected for IV (n = 1) and V (n = 1).

The dienamine III (n = 1) (probably a mixture 2) was shown to be present in the original reaction mixture; concentrating and then distilling the second half of it gave a small amount of liquid, b.p. 156-165°C (0.5 mm), with a large quantity of material (tars?) remaining undistilled (a later preparation gave 33 % of largely III (n = 1), b.p. 156-160°C (0.25 mm)). The fraction of b.p. 156-165°C (0.5 mm) was III (n = 1), contaminated with some IV (n = 1) and V (n = 1) (observed previously 2). This was shown by its IR: $v_{\text{max}}^{\text{neat}}$ 1710 s (presumably V, n = 1), 1665 vs (\overline{IV} , n = 1), 1625 s, 1597 s and 1580 s cm⁻¹ (III,

n=1, $C=\overset{\cdot}{C}-\overset{\cdot}{C}=\overset{\cdot}{C}-N$ absorptions), lit.1,2 $v_{\max}^{CCl_4}$ for the pyrrolidine dienamine from

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I (n=1) and methyl vinyl ketone: 1628 and 1600 cm⁻¹; its NMR (in CDCl₃) singlet at τ 4.25 (vinyl H α to carbonyl of IV, n=1, impurity), singlet at τ 5.21 (vinyl α -H of III, n=1) and a broad peak at τ 4.86 (vinyl γ -H of III, n=1) (see Ref. 2 for basis of assignments); and its UV spectrum: $\lambda_{\text{max}}^{\text{cyclohexane}}$ 283 m μ (ε 27 400), lit. 8 $\lambda_{\text{max}}^{\text{cther}}$ 280 – 282 m μ (ε 22 700 – 24 100) for some pyrrolidine dienamines of Δ^6 -3-keto steroids.

The usefulness of enamines in synthesis was again demonstrated in the successful preparation of the previously unknown IV (n = 0); earlier synthesis of IV (n = 0) by reaction of cyclopentanone (VI) and II in the presence of various bases had failed, VI undergoing selfcondensation instead.9 This difference in reactivity in the Michael reaction between VI and its enamine had been noted earlier.1 After refluxing 0.104 mole each of I (n = 0) and II in 35 ml of xylene for 24 h under a water trap (1.9 ml water) and then vacuum-evaporating the xylene, distillation gave three lower-boiling fractions (total 1.5 g) followed by 3.8 g of impure III (n = 0), b.p. $170-180^{\circ}$ C (2.0 mm): $\lambda_{\text{max}}^{\text{neat}}$ 1710 m (presumably V, n = 0), 1665 vs (presumably IV, n = 0), 1623 s, 1595 s and

1575 vs cm⁻¹ (III, n = 0, C = C - C = C - N absorptions). Presumably IV (n = 0) and V (n = 0) were formed because the pyrrolidine evolved was removed from the flask due to the high reaction temperature before being able to reform III (n = 0) (see Ref. 1 for a mechanism that suggests this possibility).

Hydrolysis of the enamine III (n = 0) in aqueous acetic acid-sodium acetate 1 gave 3.0 g of a mixture of ketones. Rapid chromatography (as above) of 0.90 g of this mixture gave two fractions. The first, 0.58 g of an oil, was largely (80 % as a minimum from NMR) V (n = 0): $v_{\text{max}}^{\text{neat}}$ 1710 vs and 1665 vs cm⁻¹ (IV, n = 0, impurity), and NMR (in CDCl₃) small peak at τ 4.22 (vinyl H α to carbonyl of IV, n=0, present), small, poorly resolved triplet ($J\sim2.2$ c/s) at 7 4.52 (assigned to vinyl H of that isomer of V, n = 0, having such an H) and strong, complex absorption at τ 6.9-9.2 (analysis indicated that apart from the IV, n=0, present, approximately 80 % of the V, n = 0, was that isomer having a tetrasubstituted olefinic bond). The second fraction was 0.09 g of an oil: $v_{\text{max}}^{\text{neat}}$ 1710 w (trace of V, n=0) and 1660 vs cm⁻¹, which, when recrystallized from aqueous methanol at 0°C, gave 0.01 g IV (n = 0): m.p. 61-63°C, $v_{\text{max}}^{\text{KBr}}$ 1710 vw and 1660 vs cm⁻¹.

Earlier, in another enamine III (n=0) preparation, pure IV (n=0) crystallized from a distillation fraction: m.p. $65-66^{\circ}$ C, $\nu_{\rm max}^{\rm KBr}$ 1660 vs and 1610 vw, sh cm⁻¹; $\lambda_{\rm max}^{\rm ethanol}$ 238 m μ (ε 12 700); NMR (in CCl₄) doublet $(J=\pm 1.9$ c/s) at τ 4.28 (vinyl H α to carbonyl) and strong, complex absorption at τ 7.2-9.2. From IV (n=0) was prepared a 2,4-dinitrophenyl-hydrazone, m.p. $209-210^{\circ}$ C.

Spectral data were obtained on Perkin-Elmer No. 621 (IR), Perkin-Elmer No. 337 (IR of enamines and of liquid ketone mixtures), Cary No. 14 (UV) and Varian A-60 (NMR) spectrophotometers. Satisfactory carbon-hydrogen analyses were obtained on IV (n=0), IV (n=1), and their 2,4-dinitrophenylhydrazones (C. F. Geiger, Ontario, California).

Refinements of these procedures and extensions to other systems are under way. We are grateful to the San Diego State College Research Foundation for financial support of MFS and to Professor Arne Fredga for discussion and facilities made available to LHH. We thank the American-Scandinavian Foundation for a grant-in-aid to LHH.

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Influence of Magnesium Purity on the Addition of Grignard Reagents to α.β-Unsaturated Esters JYTTE HILDEN and (the late) JON MUNCH-PETERSEN

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In earlier papers we have treated the conjugate addition of butylmagnesium bromide to a variety of α,β -unsaturated esters.1-18 During the years we have occasionally repeated the addition of butylmagnesium bromide to sec-butyl crotonate and have found some unexpected variations in the yield of sec-butyl 3-methylheptanoate, although we at any given time, with the particular samples of reagents (Mg, ester etc.) used at that time, were able to reproduce our results with a good accuracy (1-2% deviations).

In checking a variety of factors, which could cause these deviations, we have finally settled on the purity of the magnesium employed in the preparation of the Grignard reagent. Table 1 shows an analysis of six magnesium samples; I is a high purity magnesium (triply sublimed) yielding clear, colorless Grignard reagents, while II-VI are samples of commercial grade "Grignard magnesium" yielding the well known dark colored Grignard reagents containing colloid impurities. The last column shows the yield of sec-butyl 3-methylheptanoate obtained after preparation of butylmagnesium bromide from the sample and subsequent addition of sec-butyl crotonate.* The yield of sec-butyl 3-methylheptanoate shows a decrease with an increase in the combined iron and manganese contents in the magne-

Table 1. Yields of sec-butyl 3-methylheptanoate obtained by reaction of sec-butyl crotonate with butylmagnesium bromide prepared from magnesium of varying purity.

Magnesium sample	Impurities (ppm)									Yield
	Fe	Mn	Si	Cu	Zn	Pb	Al	Ni .	Ca	%
I a	10	<10	20	5	10	<5_	_<5_	_<5_	<40	80
II p	245	130	170	15	35	100	110	25	<40	65
III p	295	695	75	20_	_50	<5_	45	20	<40	57
IV b	340	60	30	5	20	30	20	10	<40	68
ν,	160	160	200	20			120_	10	10	65
VI b	380	350	130	30	_	_	100	10	10	56

^a Triply sublimed. ^b Commercial grade "Grignard magnesium".

^{*} The yields are based on sec-butyl crotonate. The sec-butyl crotonate not accounted for in sec-butyl 3-methylheptanoate gives rise to a byproduct, di-sec-butyl α-(1-methylpentyl)-βmethylglutarate.12