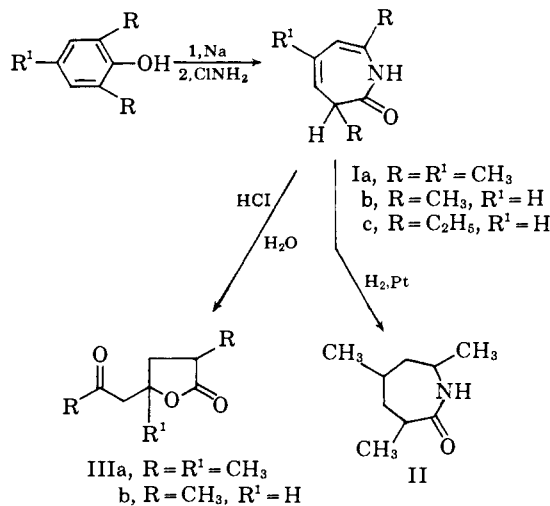


little known heterocyclic class⁶ (which may be alternatively named dihydroazatropones).

Addition of a cold (-70°) ethereal solution of chloramine⁷ in a thin stream to a rapidly stirred solution of sodio 2,4,6-trimethylphenoxide in excess 2,4,6-trimethylphenol at $120-150^{\circ}$ affords on appropriate workup^{8a} a 50–55% yield of a fluffy white solid [m.p. 132° ; *Anal.* Calcd. for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.68; H, 8.47; N, 9.16; ν_{\max}^{Nujol} 3200 (N–H) and 1695 cm.^{-1} (amide carbonyl); λ_{\max}^{EtOH} 252 $m\mu$ (6,050)]. The n.m.r. spectrum⁸ is fully compatible with the 3,5,7-trimethyl-1,3-dihydro-2H-azepin-2-one formulation (Ia); a low field singlet at 334.5 cps. was assigned to the proton at position 6, a doublet centered at 292.5 cps. ($J = 5$ cps.) to the proton at position 4 and a 5-line pattern centered at 148 cps. ($J = 6$ cps.) to the ring proton at 3, the pattern suggesting splitting with an adjacent methyl group and ring hydrogen atom. In addition, the absorption peaks of the various methyl groups were located at 120 cps. (singlet, 7-methyl), at 107.5 cps. (triplet, $J = 1.5$ cps., 5-methyl) and at 80.2 cps. (doublet, $J = 6.5$ cps., 3-methyl).

Catalytic reduction of Ia with platinum oxide in ethanol proceeded with the uptake of two moles of hydrogen to give 3,5,7-trimethylhexahydroazepin-2-one (II), m.p. $73-75^{\circ}$, in 72% yield. An authentic sample of II was prepared by the Beckmann rearrangement of 2,4,6-trimethylcyclohexanone oxime.⁹ Comparison of the spectral and m.p. properties of II with the lower melting isomer¹⁰ from this sequence showed them to be identical.



Acid hydrolysis of Ia yielded the keto-lactone IIIa (84%) [b.p. 90° (0.25 mm.) $n_{\text{D}}^{24.5}$ 1.4528;

(6) E. Vogel and R. Erb, *Angew. Chem.*, **74**, 76 (1962), have described recently a five-step synthesis of this previously unknown ring system.

(7) G. H. Coleman and H. L. Johnson, "Inorganic Syntheses," Vol. I, p. 59.

(8) Spectra were determined by Dr. George Slomp on dilute solutions in deuteriochloroform with a Varian 4300-2 Spectrometer operating at 60 mc. The spectra were calibrated by the audiofrequency side-band technique against internal tetramethylsilane standard (TMS = 0 c.p.s.).

(9) This sequence has been described previously by H. E. Ungnade and A. D. McLaren, *J. Am. Chem. Soc.*, **66**, 118 (1944); *J. Org. Chem.*, **10**, 29 (1945).

(10) A higher melting isomer, m.p. 95° , also was isolated.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.32; H, 8.51; ν_{\max}^{neat} 1770 (lactone carbonyl) and 1720 cm.^{-1} (ketone carbonyl); λ_{\max}^{EtOH} 274 $m\mu$ (197)].

In a similar manner, 2,6-dimethylphenol and 2,6-diethylphenol were transformed to Ib and Ic, respectively. IIIb was produced readily when Ib was submitted to acidic hydrolysis.

Further extensions of this novel reaction and the chemical and photochemical transformations of the 1,3-dihydro-2H-azepin-2-ones as well as the mechanism of their formation will be described in forthcoming publications.

Acknowledgment.—The author is indebted to Mr. Douglas B. Hooker for the preparation of the chloramine and to Dr. R. W. Rinehart and staff of the Physical and Analytical Chemistry Department of the Upjohn Company for the microanalytical and spectral determinations.

DEPARTMENT OF CHEMISTRY
THE UPJOHN COMPANY
301 HENRIETTA STREET
KALAMAZOO, MICHIGAN

LEO A. PAQUETTE

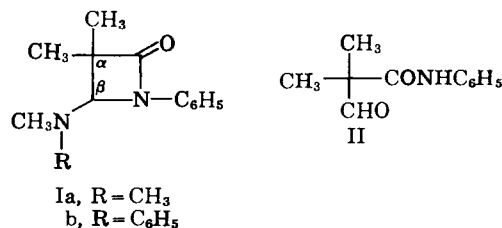
RECEIVED NOVEMBER 16, 1962

AN ENAMINE SYNTHESIS OF β -AMINO- β -LACTAMS (4-AMINO-2-AZETIDINONES)

Sir:

The cycloaddition of ketenes to Schiff bases was the original preparative method for β -lactams.¹ The present report, concerning the reaction of β,β -disubstituted enamines with aryl isocyanates, constitutes the first β -lactam synthesis in which the carbonyl to C_{α} and nitrogen to C_{β} bonds are formed simultaneously.² The only other β -lactam synthesis known to the authors which utilizes an isocyanate is the phenyl isocyanate-diazomethane synthesis of Sheehan.³

The combination of equimolar quantities of N,N-dimethylisobutylamine⁴ and phenyl isocyanate causes a spontaneous exothermic reaction. The infrared spectrum of the resulting oil shows no absorption at $4.4-4.5\ \mu$, which is characteristic of the isocyanate, but has an intense peak at $5.71\ \mu$. The structure Ia (1-phenyl-3,3-dimethyl-4-dimethylamino-2-azetidinone) which we propose for this reaction product is consistent with the infrared spectrum and further supported by n.m.r. results.



(1) Staudinger, "Die Ketene," F. Enke, Stuttgart, 1912.

(2) "The known syntheses of β -lactams that create two bonds all entail simultaneous formation of the same two bonds, i.e., carbonyl to nitrogen and C_{α} to C_{β} ": J. C. Sheehan and E. J. Corey, "Organic Reactions," Vol. IX, John Wiley and Sons, Inc., New York, N. Y., 1957, p. 390.

(3) J. C. Sheehan and P. Izzo, *J. Am. Chem. Soc.*, **70**, 1985 (1948); **71**, 4059 (1949).

(4) K. C. Brannock, A. Bell, R. D. Burpitt and C. A. Kelly, *J. Org. Chem.*, **26**, 625 (1961).

In addition to the five aromatic hydrogens at low field, single peaks are observed at 5.61 τ ($1C_{\beta}$ -H) and 7.55 τ ($1N$ - CH_3). Rather surprisingly, the C_{α} -gem-dimethyls appear nearly equivalent with a peak at 8.74 τ . The n.m.r. spectrum of the crude reaction product further indicates that Ia is obtained in excess of 95% yield. Although Ia is stable for months when stored in a tightly stoppered flask, it decomposes upon contact with water to give α -formylisobutyranilide (II) in 93% yield,⁵ m.p. 57–60° (ether–petroleum ether), (*Anal.* Calcd. for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.69; H, 7.10; N, 7.18; infrared: CHO, 5.83 μ ; CONH, 5.95 μ). The n.m.r. spectrum of II is consistent with the structure shown.

The mode of decomposition of Ia, rupture of the C_{β} to amide-N bond with formation of the transient dimethylimine cation of II, suggests that delocalization of the free electron pair on the amino nitrogen would stabilize the ring system. This was, in fact, realized by replacing one of the N-methyls in Ia by a phenyl group.

Phenyl isocyanate and N-methyl-N-phenylisobutenylamine⁶ do not react at room temperature, but after 48 hours at 80° the reaction mixture is free of phenyl isocyanate absorption in the infrared region, and shows the desired 5.71 μ β -lactam band. The resulting dark oil crystallizes upon standing. Recrystallization of the product from ether–petroleum ether affords the white solid, Ib [1-phenyl-3,3-dimethyl-4-(N-methylamino)-2-azetidinone], m.p. 113–115° (*Anal.* Calcd. for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 77.33; H, 7.31; N, 10.11; λ_{max}^{EtOH} 248 (28,000); with added acid λ_{max}^{EtOH} 243 (14,200)]. In addition to the ten low field aromatic protons detectable in the n.m.r. spectrum of Ib, peaks occur at 4.71 τ ($1C_{\beta}$ -H), 7.12 τ (N - CH_3) and at 8.49 τ and 8.83 τ ($1 > C$ - CH_3 each). The increased stability of Ib *vs.* Ia is demonstrated by the fact that an ethereal solution of the compound not only survives washings with water, but also *N* acid and *N* base. Upon several days of exposure to moist air, however, Ib also decomposes to II.

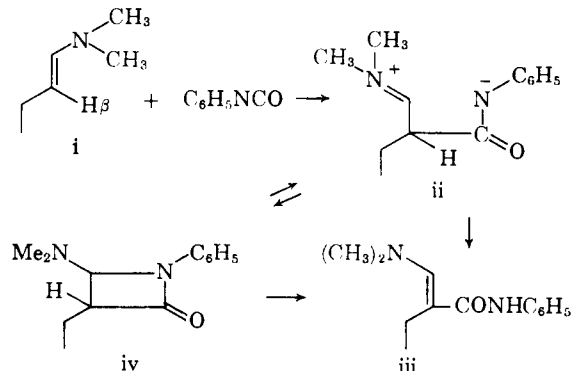
Since previously reported^{8,9} reactions of enamines and isocyanates have given, after hydrolysis, β -carbonylcarboxamides analogous to II, it seemed necessary to consider the possibility that labile β -lactams, although present, had been overlooked by previous workers before hydrolysis of their reaction products. We therefore studied the reaction of phenyl isocyanate and N,N-dimethyl-1-butenylamine.⁹ In order to moderate the very exothermic reaction and minimize decomposition of any potential β -lactam intermediate, the enamine is stirred in an ice bath and phenyl isocyanate is added drop-

wise so as to keep the temperature of the mixture below 30°. Immediately upon completion of the addition (5–10 minutes), a sample withdrawn for infrared studies shows no isocyanate or β -lactam absorption. Amide carbonyl and N–H absorption is quite strong, however, and subsequent hydrolysis of the product gives α -formyl-*n*-butyranilide as reported by Hünig, *et al.*^{9,10}

Continuing work on this enamine reaction indicates that structural requirements are very specific. Details of this work and of some further products derived from Ia will be published in the near future.

Acknowledgment.—The authors wish to acknowledge the assistance of Mr. Paul Landis in obtaining and discussing the n.m.r. spectra.

(10) The enamines of previous workers^{8,9} have in common the presence of a β -H (*e.g.*, i). Thus, the intermediate ii can alternatively be



stabilized by cyclization to β -lactam **iv** or by abstraction of the β -H to yield **iii** as suggested by infrared. Although we prefer the direct route ($i \rightarrow ii \rightarrow iii$), the possibility cannot be excluded, of course, that the initial reaction product is **iv** which rapidly decomposes to **iii** by abstraction of the C_{β} -H, or reverts to **ii** by participation of the amino nitrogen's free pair of electrons. If **iv** does, in fact, ever exist, decomposition *via* **ii** seems most likely. By selecting an enamine possessing no β -H, (*e.g.*, N,N-dimethylisobutenylamine) one obtains an intermediate (similar to **ii**) incapable of stabilization by a route other than lactam formation. In addition, the mode of decomposition of the lactam is restricted to the reverse reaction (analogous to $iv \rightarrow ii$, but excluding $iv \rightarrow iii$).

THE LILLY RESEARCH LABORATORIES
ELI LILLY AND COMPANY
INDIANAPOLIS, INDIANA

MEL PERELMAN
STEVE A. MIZSAK

RECEIVED OCTOBER 4, 1962

ON THE ORIGIN OF HYDROGEN IN METAL HYDRIDE COMPLEXES FORMED BY REACTION WITH ALCOHOLS

Sir:

We wish to report some observations on the origin of hydrogen in transition metal hydride complexes obtained from the system of metal halide, triphenylphosphine, and an alcohol (or related solvents). Of the several reactions we have investigated,¹ the one leading to an iridium monohydride complex, $[IrHCl_2(Ph_3P)_3]$ (I)² (Table I), emerged as most intriguing in view of the mild conditions (25°) under which it can be obtained.²

In order to determine the source of hydrogen giving rise to a metal–hydrogen bond in (I), we have carried out comparative experiments with deuterated aqueous³ ethanols which gave these results.

(1) L. Vaska, *Chem. and Ind.*, 1402 (1961), references quoted therein, and unpublished data.

(2) L. Vaska, *J. Am. Chem. Soc.*, **83**, 756 (1962).

(3) Water was required to dissolve K_2IrCl_6 .

(5) This instability of Ia to traces of moisture and to the common methods of purification did not allow the preparation of an analytical sample.

(6) E. Benzing, *Angew. Chem.*, **71**, 521 (1959).

(7) The yields of Ib vary from 65–90% depending upon the purity of the reactants and the care taken to exclude moisture and air from the reaction vessel.

(8) S. Hünig, *Angew. Chem.*, **71**, 312 (1959). D. Clemens and W. Emmons, *J. Org. Chem.*, **26**, 767 (1961). G. Berchtold, *ibid.*, **26**, 3043 (1961).

(9) S. Hünig, K. Hübner and E. Benzing, *Ber.*, **95**, 926 (1962).