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ADDUCTS OF DIMETHYLKETENE WITH C=N CONTAINING COMPOUNDS

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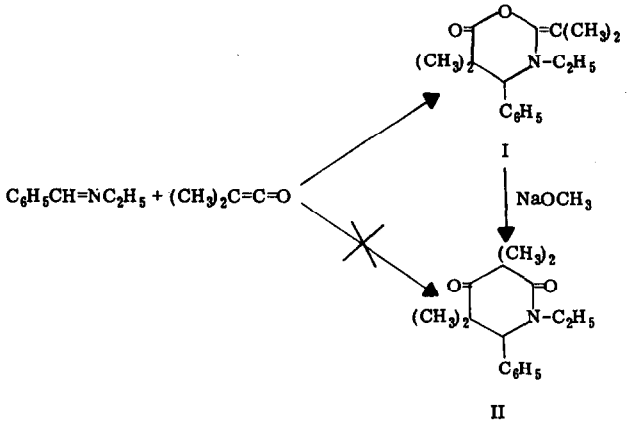
Staudinger and co-workers (1) first reported the cycloadditions of ketoketenes to C=N compounds and assigned piperidinedione structures, such as II and VII, to the products. Apparently other workers in this field have accepted the correctness of these structural assignments. (2, 3) Because of the ready hydrolysis of these cycloaddition products to amido acids, we doubted the correctness of the piperidinedione structures. Therefore, we reinvestigated the products of the interaction of dimethylketene with two C=N compounds, N-benzylideneethylamine and quinoline. We chose these two products because they represent decidedly different C=N compounds, and also because they had received careful attention by previous workers. We found that I is the correct structure for the N-benzylideneethylamine adduct, and that VI is the correct structure for the quinoline adduct.



I on treatment with a catalytic amount of sodium methoxide rearranged to the authentic piperidinedione II. With compounds I and II in hand it was simple to make the proper structural assignments because it is obvious that the dihydrooxazinone I will hydrolyze much more readily than the piperidinedione II. I with 10% aqueous sodium carbonate hydrolyzed rapidly to the amido acid IIIa; whereas II was recovered after prolonged refluxing with the same reagent.

Dimethylketene and N-benzylideneethylamine react in benzene or, more rapidly, in acetonitrile to give 95% and 83%, respectively, of 3-ethyldihydro-2-isopropylidene-5, 5-dimethyl-4-phenyl-2H-1, 3-oxazin-6(5H)-one (I), m.p. 101.5-104°.*

Anal. Calcd. for $C_{17}H_{23}NO_2$: C, 74.7; H, 8.5; N, 5.1. Found: C, 74.9; H, 8.2; N, 5.1. Infrared spectrum: $\lambda_{max.}^{CCl_4}$ 5.72 and 5.92 μ. N.M.R. spectrum (CCl_4): singlets at 1.04, 3H and 1.07, 3H (gem-dimethyl group), singlets at 1.78, 3H and 1.85, 3H (isopropylidene group), triplet at 0.98, 3H and multiplet at 2.80, 2H (N-ethyl group), singlet at 4.07, 1H (benzal proton), and singlet at 7.43 p.p.m. δ, 5H (aromatic protons).

Treatment of I with a catalytic amount of sodium methoxide gave 92% of 1-ethyl-3, 3, 5, 5-tetramethyl-6-phenyl-2, 4-piperidinedione (II), m.p. 89.5-91.0°.

Anal. Calcd. for $C_{17}H_{23}NO_2$: C, 74.7; H, 8.5; N, 5.1. Found: C, 74.7; H, 8.7; N, 5.1. Infrared spectrum: $\lambda_{max.}^{cyclohexane}$ 5.87 and 6.10 μ. N.M.R. spectrum (CCl_4): singlets at 0.83, 3H, 1.43, 6H, and 1.50, 3H (gem-dimethyl groups), triplet at 1.08, 3H and multiplets at 2.78, 1H and 3.81, 1H (N-ethyl group), singlet at 4.25, 1H (benzal proton), and multiplet at 7.14 p.p.m. δ, 5H (aromatic protons).

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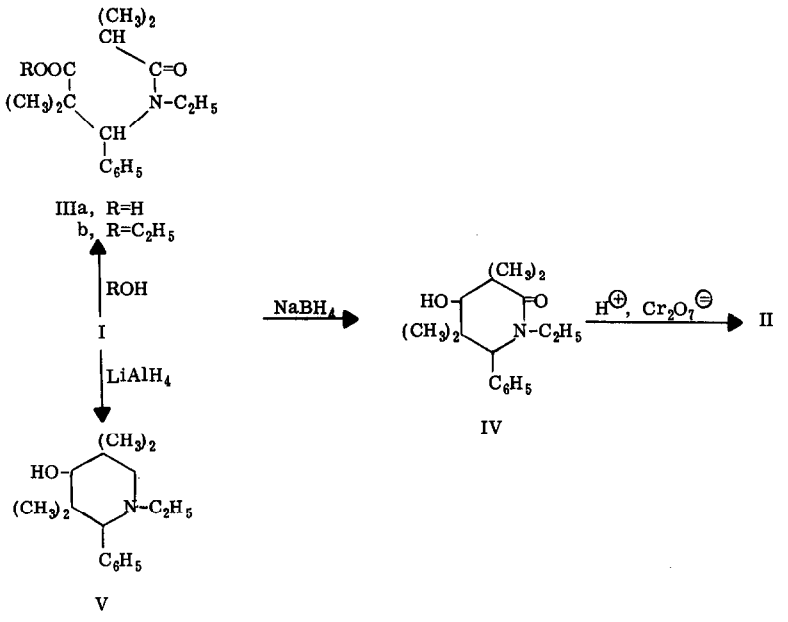
*Ballard, Melstrom, and Smith (2) reported a melting point of 89-90° for their sample of I, but by their own admission and analysis it was impure.



Treatment of I with excess ethanol at 25° for 1 hr. resulted in a quantitative conversion to ethyl 3-(N-ethyl-2-methylpropionamido)-2, 2-dimethyl-3-phenylpropionate (IIIb), b.p. 128-130° (0.4 mm.), m.p. 44-45°.

Anal. Calcd. for $C_{19}H_{29}NO_3$: C, 71.4; H, 9.2; N, 4.4. Found: C, 71.7; H, 9.5; N, 4.3. Infrared spectrum: $\lambda_{max.}^{KBr}$ 5.84 and 6.12 μ.

On refluxing with aqueous 10% sodium carbonate solution for 30 min. and after acidification and recrystallization, I gave 82% of 3-(N-ethyl-2-methylpropionamido)-2, 2-dimethyl-3-phenylpropionic acid (IIIa), m.p. 120-121° (reported (2) 114-114.5°).

Anal. Calcd. for $C_{17}H_{25}NO_3$: C, 70.1; H, 8.6; N, 4.8. Found: C, 70.4; H, 8.5; N, 5.0. Infrared spectrum: $\lambda_{max.}^{KBr}$ 5.82 and 6.22 μ.

We showed that II was stable to refluxing ethanol and aqueous sodium carbonate solution.

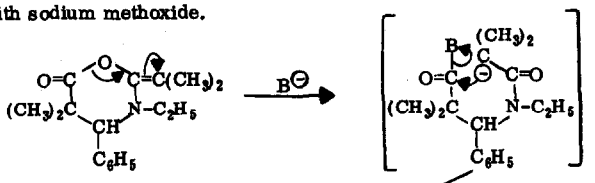
On treatment with sodium borohydride in tert-butyl alcohol, I gave 22% of 1-ethyl-4-hydroxy-3, 3, 5, 5-tetramethyl-6-phenyl-2-piperidinone (IV) as a mixture of isomers, m.p. 188-198°.

Anal. Calcd. for $C_{17}H_{25}NO_2$: C, 74.1; H, 9.1; N, 5.1. Found: C, 74.4; H, 8.8; N, 4.9. Infrared spectrum: $\lambda_{max.}^{KBr}$ 2.93, 6.22 and 9.40 μ.

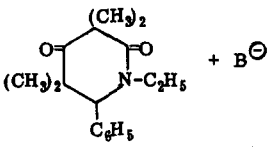
On treatment with lithium aluminum hydride, I gave 73% of 1-ethyl-3, 3, 5, 5-tetramethyl-2-phenyl-4-piperidinol (V) as a mixture of isomers, b.p. 115° (0.5 mm.), m.p. 81-86°.

Anal. Calcd. for $C_{17}H_{27}NO$: C, 78.1; H, 10.4; N, 5.4. Found: C, 78.3; H, 10.5; N, 5.7.

These hydride reductions are examples of rearrangement-reductions. In each case the basicity of the reducing agent brings about the same rearrangement of I observed with sodium methoxide.

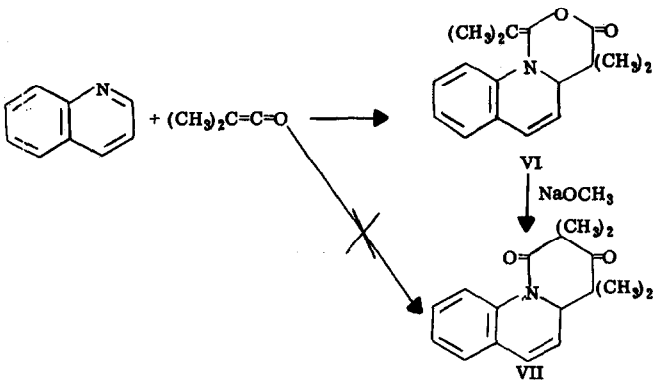


I



II

Treatment of IV with a sulfuric acid-dichromate mixture gave 95% of II.



VI

VII

Quinoline and dimethylketene react in acetonitrile to give 92% of 4, 4a-dihydro-1-isopropylidene-4, 4-dimethyl-1H-1, 3-oxazino[3, 4-a]quinolin-3-one (VI), b.p. 143° (0.1 mm.), m.p. 82-83.5° (reported (1) m.p. 81-82°).

Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.8; H, 7.1; N, 5.2. Found: C, 75.9; H, 7.2; N, 4.9. Infrared spectrum: $\lambda_{max.}^{CCl_4}$ 5.75 and 5.92 μ. N.M.R. spectrum (CCl_4): singlet at 1.18, 6H (gem-dimethyl group), singlets at 1.49, 3H and 1.83, 3H (isopropylidene group), doublet at 4.27, 1H (4a proton), pair of doublets at 5.55, 1H (5 proton), and multiple peaks from 6.30 to 7.10 p.p.m. δ, 5H (aromatic protons and 6 proton).

Treatment of VI with a catalytic amount of sodium methoxide effected a rearrangement to give 4, 4a-dihydro-2, 2, 4, 4-tetramethyl-1H-benzo[c]quinolizine-1, 3-(2H)-dione (VII), m.p. 84-86°, in 76% yield. A mixture of VI and VII had a melting range of 58-76°.

Anal. Calcd. for $C_{17}H_{19}NO_2$: N, 5.2. Found: N, 5.3. Infrared spectrum: $\lambda_{max.}^{cyclohexane}$ 5.92 and 6.00 μ. N.M.R. spectrum (CH_2Cl_2): singlets at 1.13, 3H, 1.28, 3H, 1.32, 3H, and 1.38, 3H (gem-dimethyl groups), triplet at 4.38, 1H, J=2.4 c.p.s. (4a proton), pair of doublets at 5.82, 1H, J=9.8 and 2.4 c.p.s. (5 proton), pair of doublets at 6.55, 1H, J=9.8 and 2.4 c.p.s. (6 proton), and multiplets at 7.07, 1H and 7.73 p.p.m. δ, 3H (aromatic protons).

Our preliminary evidence shows that a large number of products prepared by reaction of ketoketenes with C=N compounds have been erroneously assigned the piperidinedione structure. Our work in this field is continuing, and we will publish a more complete description at a later date.

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