Vinylogous Amides of 2-Methylaminoethanol and Their Behavior with Lithium Aluminum Hydride. Vinylogous Urethanes of Ethanolamines and Their Acetylation

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Received February 19, 1962

The crystalline hydroxyeneamino ketones, I and II, obtained by reaction of hydroxymethyleneacetophenone and 1-hydroxymethylene-1-phenyl-2-propanone, respectively, with β-methylaminoethanol, are typical vinylogous amides. They are reduced with lithium aluminum hydride to corresponding hydroxyamino ketones, III and IV, respectively. Spectral aspects of vinylogous amides, which are exceptionally clear in I and II, are discussed and a few similar unsaturated derivatives of other ethanolamines are also described, together with their acetyl derivatives.

Vinylogous amides[1-3] and amidines[4] are now well recognized as classes of substances quite different from other basic ketones and their derivatives. The principle of altered functional character[1,3-5] and spectral shift[2,5-8] caused by π-p conjugate interaction between the two parts of what may be thought of as a π-electron-elongated functional group applies just as well to cyclic[9-13] as to open-chain compounds of this general type, and extends logically to vinylogous urethanes,[11,14] vinylogous cyanamides,[15] etc. Nearly all studies of the spectra of vinylogous amides have been carried out upon NH group-containing compounds, and recent n.m.r. measurements have led to the conclusion[16] that, while they may in some cases exist as a mixture of both chelated tautomers,[2] the eneaminocarbonyl form[1] definitely predominates. The hydride reduction of vinylogous amides also has been a focal point of considerable interest,[4,11,13,17-19] and the conclusion in this matter until recently has been that lithium aluminum hydride preferentially affects the carbonyl (enol) rather than the eneamine (imino) portion of the molecule; this analogy with the reduction of simple amides and electronically uncomplicated amino ketones seems logical and holds good as long as one deals with compounds in which the carbonyl moiety is more exposed geometrically and/or more reactive than the eneamine part (which in many instances has been part of a ring system, often itself resonance-stabilized), or when the eneamine group is one containing associated hydrogen atom(s), which render it capable of salt or complex formation. In other cases without these factors it seems likely that the eneamine moiety might be reduced in preference to the carbonyl, and in fact reduction of this sort has been reported recently,[20] serving as an alternative to direct Mannich base synthesis. This paper presents other cases in which the "reverse" of the hitherto accepted course of events occurs.

Recently it was found[4] that crystalline, nonchelated, borohydride-reducible vinylogous amidines were formed from indole-3-aldehyde with various β-hydroxyamines. In attempting to obtain similar, well characterized derivatives from two typical β-dicarbonyl compounds, the hydroxymethylene derivatives of acetophenone and phenylacetone,[14,21] it was found that these enols reacted smoothly with β-methylaminoethanol, giving nicely crystalline aminomethylene compounds, I and II, respectively. Similar reactions with other amines did not provide crystalline products. Analysis and positive ferric chloride tests having confirmed these formulas, further evidence favoring structures I and II, and excluding oxazolidines or other cyclic forms, was found in the infrared spectra, which

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(1) S. A. Glickman and A. C. Cope, *J. Am. Chem. Soc.*, **67**, 1017 (1945).

(2) N. H. Cromwell, F. A. Miller, A. R. Johnson, R. L. Frank, and D. J. Wallace, *ibid.*, **71**, 3337 (1949).

(3) N. F. Albertson, *ibid.*, **74**, 249 (1952).

(4) G. N. Walker and M. A. Moore, *J. Org. Chem.*, **26**, 432 (1961), and references cited therein.

(5) N. H. Cromwell and J. C. David, *J. Am. Chem. Soc.*, **82**, 2046 (1960).

(6) K. Ueno and A. E. Martell, *J. Phys. Chem.*, **59**, 998 (1955).

(7) H. F. Holzclaw, J. P. Collman, and R. M. Alire, *J. Am. Chem. Soc.*, **80**, 1100 (1958).

(8) J. Weinstein and G. M. Wyman, *J. Org. Chem.*, **23**, 1618 (1958).

(9) J. Romo and A. R. de Vivar, *J. Am. Chem. Soc.*, **81**, 3446 (1959).

(10) K. Kotera, *Yakugaku Zasshi*, **80**, 1275 (1960).

(11) N. A. Nelson, *et al.*, *J. Org. Chem.*, **26**, 2599, 3086 (1961).

(12) C. L. Bell, C. N. V. Namburg, and L. Bauer, *ibid.*, **26**, 4923 (1961).

(13) See D. R. Liljegren and K. T. Potts, *ibid.*, **27**, 377 (1962), and earlier references therein to other 3-acylindoles.

(14) G. N. Walker and B. N. Weaver, *ibid.*, **26**, 4441 (1961); it should be noted that the spectra of nonchelated vinylogous urethanes (1,4-dihydrobenzo[*f*]quinoline-2,6-dicarboxylic esters) mentioned in this paper also show strong peaks at 6.51 and 6.65 μ, not previously reported, in addition to those at 3.05, 5.84, and 6.08 μ.

(15) S. Baldwin, *ibid.*, **26**, 3288 (1961).

(16) G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, **83**, 2099, 3914 (1961).

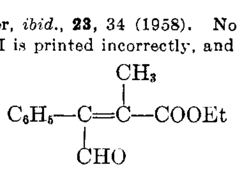
(17) (a) N. G. Gaylord, *Experientia*, **10**, 166 (1954). (b) See also same author, "Reduction with Complex Metal Hydrides," Interscience Publishers, New York, N. Y., 1956, pp. 979–985.

(18) N. A. Nelson, J. E. Ladbury, and R. S. P. Hsi, *J. Am. Chem. Soc.*, **80**, 6633 (1958).

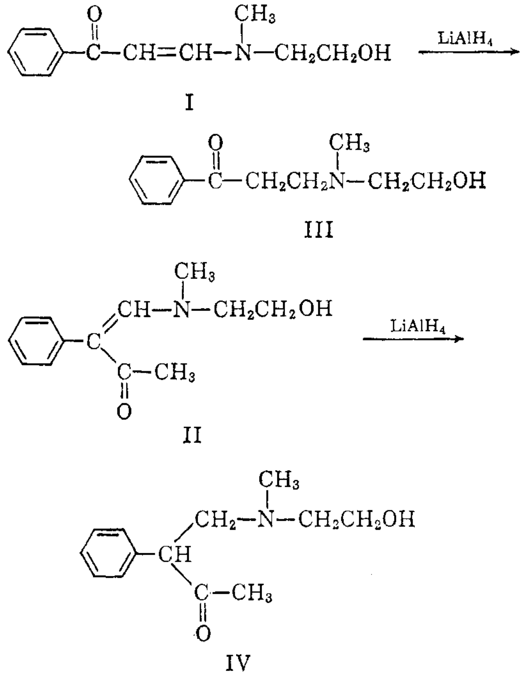
(19) C. H. Eugster and P. G. Waser, *Helv. Chim. Acta*, **40**, 888 (1957).

(20) G. deStevens and A. Halamandaris, *J. Org. Chem.*, **26**, 1614 (1961).

(21) G. N. Walker, *ibid.*, **23**, 34 (1958). Note that in this paper the structure of VIII is printed incorrectly, and should be:



$$C_6H_5-\underset{\displaystyle CHO}{C}=\overset{\displaystyle CH_3}{C}-COOEt$$



showed strong, bonded hydroxyl bands (in the solid state) at 3.05 and 3.06 μ, respectively (shifted to 2.77 μ and lowered in intensity in solution indicating that the bonding is intermolecular[4,22]), moderately weak, sharp benzene peaks at 6.29 and 6.22 μ, vinylogous amide-I peaks at 6.10 and 6.14 μ, and intense peaks at 6.54 and 6.41 μ, respectively, also characteristic of substances of this type.[2,5,7–11,14,23] The n.m.r. spectra not only provided additional evidence for structures I and II but also showed clearly that the *trans* configuration is the preferred one,[24] in respect to carbonyl and amino groups.

The vinylogous amide bands in the infrared spectra of I and II are influenced only slightly by phenyl conjugations, and thus, as in other compounds of this type, there is present an electron delocalization strong enough to override all other, weaker effects,[15] even though chelating protons are not present.

It would appear from these exceptionally clear examples that electronic shifts alone are resonsible for the development of amide-like spectra in vinylogous amides (and presumably in other "vinylogous-carboxyl" derivatives as well) and that chelation or other effects associated with mobile hydrogen, if it is present, are of secondary importance. This view contradicts some earlier ones which have been held, at least tentatively, concerning the importance of chelation, but, as pointed out previously,[7] is in agreement with the indisputable fact that wave length of C═N absorption *per se* is not affected appreciably by coordination with extramolecular agents.[25]

Reduction of compounds I and II with sodium borohydride in methanol, as well as hydrogenation in the presence of palladium catalyst, resulted in fragmentation into neutral and basic components in each case. This indicates a not surprising lack of stability of the compounds under alkaline and hydrogenolytic conditions, which presumably may be ascribed to β-elimination in these environments. However, reduction of I and II with lithium aluminum hydride gave compounds III and IV, respectively, in good yields.[26]

The infrared spectra of the hydrochlorides of III and IV, besides showing enhanced hydroxyl absorption (very strong peak at 3.03 μ in each case), expected ‘zwitterionic" bands (3.70–3.85 μ), and unsubstituted phenyl (6.18 and 6.21 μ, respectively, and *ca.* 700 cm.$^{-1}$ in each case), also demonstrated the presence of the preserved ketone group[27] (5.93 and 5.80 μ, respectively), now no longer particularly involved, electronically, with the nitrogen. Furthermore, in the spectra of III and IV, both the vinylogous amide bands, aforementioned in I and II, were absent.

Whereas the eneamino group of compounds I and II, and of a similar *tert*-eneaminomethylene ketone,[20] are reduced in preference to the carbonyl group, the reverse is true in a more complex example.[19] However in the latter case, lithium aluminum hydride reduces the carbonyl group only as far as the carbinol stage, and it seems likely that the additional tetrahydropyranoxy group, appended to this molecule at the same unsaturated carbon atom to which the *t*-amino group is also attached, gives this group the equivalent of amide-like stability within itself, and leaves the C═O group with less vinylogous amide—*i.e.*, more genuine ketonic—character, so rendering it susceptible to lithium aluminum hydride attack in the usual sense (see equation, top of col. 1, p. 4229).

It is now clear that vinylogous tertiary amides derived from β-ketoaldehydes (hydroxymethylene ketones) are more susceptible to reductive attack at the aminomethylene end, than at the carbonyl

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(22) M. Nakamichi and G. L. Webster, *J. Org. Chem.*, **22**, 159 (1957).

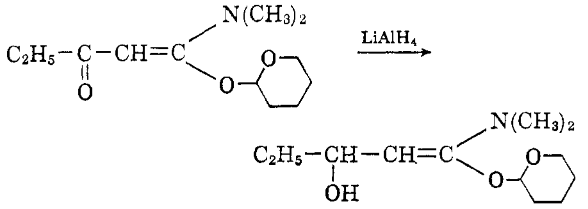
(23) This band falls in the so-called amide-II region (see L. J. Bellamy, "Infrared Spectra of Complex Molecules," Methuen and Co., Ltd., London, 1958, pp. 217–220) where normally primary and secondary acyclic and macrocyclic amides absorb, and, being present in all vinylogous amides studied so far, irrespective of chelation or presence of —NH—, probably arises from "transoid" electron delocalization within the π-electron elongated, π-p conjugated "amide" group, *as a unit.* We believe this view, though perhaps somewhat oversimplified, at present is more useful than earlier ones which call upon various "combined" vibrations and/or contributing effects from chelation.

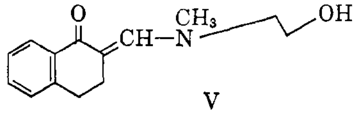
(24) The following pertinent data were obtained, from the n.m.r. spectra in $CDCl_3$ solution, on vinyl protons; compound I: 7.80 (J = 12.5) and 5.65 (J = 12.5); compound II: 7.67 (J = 7.5).

(25) B. D. Sarma and J. C. Bailar, *J. Am. Chem. Soc.*, **77**, 5476 (1955).

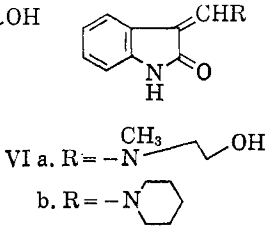
(26) Contrast the mixtures of products and low yields usually obtained in reduction of hydroxymethylene ketones and β-keto esters with lithium aluminum hydride: A. S. Dreiding and J. A. Hartman, *J. Am. Chem. Soc.*, **75**, 939 (1953); and R. Vonderwahl and H. Schinz, *Helv. Chim. Acta*, **35**, 2368 (1952).

(27) Acetophenone and phenylacetone absorb at 5.95 and 5.85 μ, respectively; see ref. 20 for a similar demonstration of return of the ketone group band after conversion of hydroxymethylene derivatives of these ketones to ethyleneacetals.



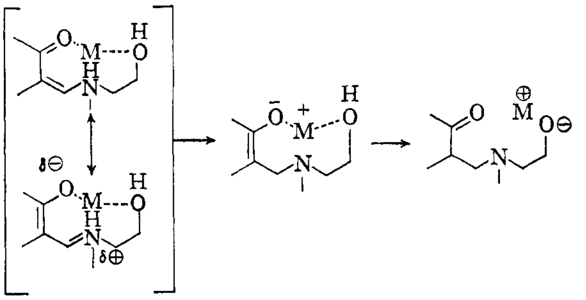


V



VI a.
b.

end, of the molecule. While exact mechanistic considerations should be avoided in the absence of additional data, there is an obvious parallel here between the nitrogen derivatives and the parent hydroxymethylene ketones in which the "aldehyde" group is considerably more reactive than the "ketone" moiety, provided that additional complicating factors are not present. It may be that the appended hydroxy group contributes its effect to stopping reduction of I and II cleanly at the stage of III and IV simply by helping to promote formation of *noncyclic*, insoluble metallic complex salts of these products, resulting in their precipitation—*i.e.*, removal from the scene where further attack by hydride might progress. This visualization of events taking place in the reaction vessel is not incompatible with a cyclic 1,4-addition of metallohydride to a *cisoid* form, such as has been postulated[17] to occur in hydride reductions of various 1,3-dicarbonyl and -imino systems; in the reduction of I and II, however, temporary formation of a metal-enolate may come into significant play:



Compounds V and VI (a) and (b), prepared by reaction of the hydroxymethylene derivatives of α-tetralone and oxindole, respectively, with the appropriate amines, resemble compounds I and II in having exceptionally strong, sharp infrared peaks at 6.56, 6.33, and 6.35 μ, respectively, as well as (again intermolecularly) bonded hydroxyl bands in V and VIa (3.06 and 2.98 μ, respectively, in solid state, shifting wholly or in part to 2.72 μ in solution). The intense vinylogous amide peak of compound V is in the usual location (6.11 μ), but those of compounds VIa (5.96 μ) and VIb (5.97 μ) show an upfield shift due to incorporation of the carbonyl in an oxindole ring. Compounds such as VI may be regarded as "vinylogous ureas."

Attempts to reduce compounds V and VI with lithium aluminum hydride were not successful; V is rather unstable, and the reduction product even more so, and compounds VI evidently form very insoluble complexes with the reagent. The stability, crystallinity, etc., of various eneaminocarbonyl compounds reflects those same properties of their carbonyl precursors. Although methylaminoethanol and a number of other amines were tried, there was no success in attempts to obtain crystalline eneamino compounds from the hydroxymethylene derivatives of phenylacetonitrile and methyl phenylacetate, nor could any crude (presumed) eneaminomethylene compounds so obtained be reduced with lithium aluminum hydride without apparent cleavage.

Finally, mention should be made of the spectral properties and certain reactions of some β-hydroxyalkylaminomethyleneoxazolones (p. 4230).

Some compounds of the type VIII, which form with exceptional ease, have been prepared[28] and their characteristic spectra noted. The anhydride-like, five-membered cyclic lactone carbonyl of VIIa (5.55 μ) or VIIb (5.59 μ) becomes involved as part of a vinylogous urethane in compounds VIII (infrared shift downfield to 5.70, 5.84, and 5.75 μ, respectively for a, b, and c), while the conjugated benzimino chromophore of VIIa (6.22 and 6.34 μ, electron-delocalized) or VIIb (5.95 μ; C=N double bond fixed) invariably becomes a single peak, in VIII (5.99, 6.09, and 6.00 μ, respectively for a, b, and c). Upon treatment with acetic anhydride, compounds VIIIa and c are *O,N*-diacetylated, and the infrared spectra of the products, IX, show the (5.56–5.57 μ) lactone no longer involved electronically with an eneamine and so returned to its original position, as well as eneamine acetate (5.73–5.75 μ), acetoxy (5.82–5.86 μ) and the benzimino (6.05–6.08 μ) bands. Thus, as expected, the acetates VIII no longer have the characteristics of π-p electron-delocalized systems, any more than enol ethers or acetates of 1,3-dicarbonyl compounds have any remaining acidic properties. These reactions, and the *N*-acetylation of a similar thiol to produce X which was also carried out, provide an additional, and perhaps exceptionally clear, demonstration, *via* crystalline derivatives, of the futility attending any effort to convert oxazolones such as VIII or similar thiols to penicillin analogs. Although this question of possible functional group exchanges has

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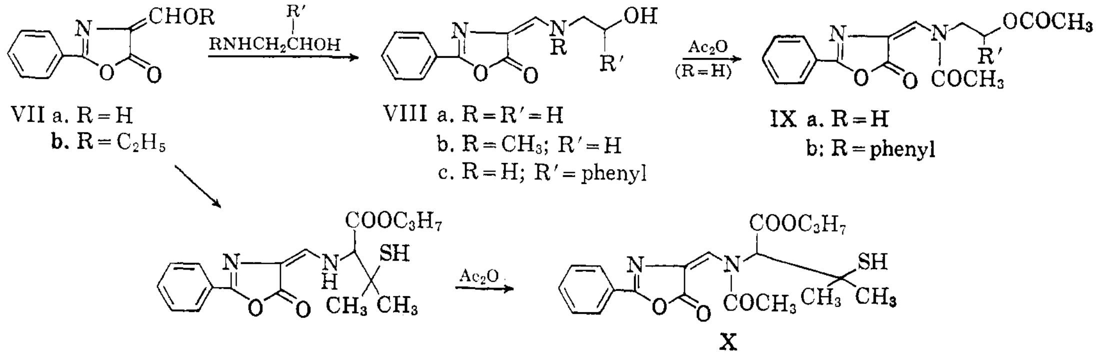
[28] See "Chemistry of Penicillin," H. T. Clarke, J. R. Johnson, and Sir R. Robinson, ed., Princeton University Press, Princeton, N. J., 1949, pp. 387–388 and 747–753.



VII a. R = H
b. R = C_2H_5

VIII a. R = R′ = H
b. R = CH_3; R′ = H
c. R = H; R′ = phenyl

IX a. R = H
b: R = phenyl

X

long since been settled in other ways,[29] it seemed possible, *a priori*, that acetic anhydride might provoke an oxazolidine ring closure in VIII and attendant or subsequent acyl transfer from azlactone-O to the eneamine nitrogen, somewhat in analogy with acyl-oxazolidine ring closures disclosed previously.[4] The failure of oxazolidine ring closure here no doubt is due to the lack of possible eneamine⇌imine shift once the exocyclic N has become acetylated, in contrast to the earlier examples[4] in which acetylation of N at either end of a β-diimino system leaves a reactive group or positive charge on one of the end carbon atoms, capable of interacting with the hydroxyl group.

Experimental

1-[*N*-Methyl-*N*-(β-hydroxyethyl)amino]-2-benzoylethylene (I).—A solution of 20 g. (0.135 mole) of benzoylacetaldehyde in 100 ml. of benzene was treated with a solution of 10 g. (0.133 mole) of β-methylaminoethanol in 100 ml. of benzene. The bright red, two-phase mixture which resulted was refluxed under a Dean-Stark trap for 1.5 hr. until collection of water (2.4 ml.) was complete. Subsequent partial evaporation of the solution and cooling resulted in formation of crystals, which were collected and washed with benzene; the yield of light yellow product, m.p. 117–120°, was 24.8 g. (91%). Recrystallization from benzene gave a nearly colorless sample of crystals, m.p. 118–121°.

Anal. Calcd. for $C_{12}H_{15}O_2N$: C, 70.22; H, 7.37; N, 6.82. Found: C, 70.11; H, 7.35; N, 6.80.

The infrared spectrum (Nujol) had peaks at 3.05 (mod.), 6.10 (int., sharp), 6.29 (mod., sharp), and 6.54 μ (intense). The spectrum in chloroform solution had bands at 2.77 and 3.01 μ and intense peaks at 6.10, 6.31, and 6.45–6.49 μ. The ultraviolet spectrum (C_2H_5OH) showed λ_{max} 243 and 344 mμ (log ε 4.052 and 4.368, respectively).

The compound gave a deep red-purple ferric chloride test. It was cleaved by treatment with sodium borohydride in methanol and by hydrogenation (in ethyl acetate solution) in the presence of palladium-charcoal.

α-Acetyl-β-[*N*-methyl-*N*-(β-hydroxyethyl)]styrene (II).—A solution of 26.4 g. (0.163 mole) of 1-hydroxymethylene-1-phenyl-2-propanone in 250 ml. of benzene was treated with a solution of 12.8 g. (0.171 mole) of β-methylaminoethanol, and the water was removed as in the preceding experiment. Evaporation of the benzene left a slowly solidifying, red oil. The crude material was recrystallized from cyclohexane–ethyl acetate, using just enough of the latter solvent to dissolve the bulk of the yellow, oily material, and decanting the hot solution away from residual dark, resinous material, the yield of yellow crystals was 14.8 g. (41%); m.p. 94–97°; raised, on further ethyl acetate recrystallization, to 101–102.5°. The pure sample was colorless.

Anal. Calcd. for $C_{13}H_{17}O_2N$: C, 71.20; H, 7.82; N, 6.39. Found: C, 71.18; H, 7.87; N, 6.40.

The infrared spectrum (Nujol) had peaks at 3.06 (mod.), 6.14 (mod. int. very sharp), 6.22, and 6.41 (intense) μ. The spectrum in chloroform solution displayed no peak *ca.* 3.1 μ, had bands at 2.77, 6.10 (mod.), and 6.47 μ (intense) and shoulders at 6.28 6.30 μ. The ultraviolet spectrum (C_2H_5OH) had λ_{max} 280 and 317 mμ (log ε 3.792 and 4.275, respectively).

The compound gave a deep purple color with ferric chloride solution. It did not yield a crystalline acetate, and was destroyed by refluxing with acetic anhydride, with sodium borohydride–methanol solution, other bases and acids, and by attempted reduction in the presence of palladium (2 molecular equivalents of hydrogen consumed, and picrate of β-methylaminoethanol subsequently isolated).

β-[*N*-Methyl-*N*-(β-hydroxyethyl)amino]propiophenone (III).—A stirred suspension of 14.2 g. of compound I in 1200 ml. of dry ether was treated with 9 g. of lithium aluminum hydride (in three to four portions); the mixture was stirred and refluxed gently for 2 hours, cooled, and cautiously treated with 27 ml. of water. When hydrolysis was complete, as indicated by conversion of the initially grey mixture to a uniform, light-colored suspension, the filtered solution was dried (potassium carbonate) and evaporated. The crude base (light yellow oil) did not crystallize. Treatment of an ether solution of the product with a slight excess of alcoholic hydrogen chloride provided the *hydrochloride* as 9.0 g. (53%) of colorless crystals, m.p. 149–152°, raised by recrystallization (ethanol) to 151–153°.

Anal. Calcd. for $C_{12}H_{18}O_2NCl$: C, 59.13; H, 7.44; N, 5.75. Found: C, 58.57; H, 7.63; N, 5.86.

The infrared spectrum (Nujol) had intense peaks 3.03 and 5.93 μ, as well as bands in the "zwitterion" region and sharp phenyl absorption at 6.22–6.25 μ.

3-Phenyl-4-[*N*-methyl-*N*-(β-hydroxyethyl)amino]-2-propanone (IV).—Reduction of 17.5 g. of compound II with 9 g. of lithium aluminum hydride by the same procedure as described in the preceding experiment gave 16.2 g. of oily, pale yellow, crude base, which was converted to the *hydrochloride:* 16.2 g. (79%) of colorless crystals, m.p. 136–137°; raised by recrystallization from alcohol to m.p. 137–138°.

Anal. Calcd. for $C_{13}H_{20}O_2NCl$: C, 60.57; H, 7.82; N, 5.44. Found: C, 60.66; H, 7.84; N, 5.91.

The infrared spectrum (Nujol) had strong peaks at 3.03 and 5.80 μ, as well as a series of dipolar bands and sharp phenyl peaks 6.21 and 6.25 μ.

2-[*N*-Methyl-*N*-(β-hydroxyethyl)aminomethylene]-1-tetralone (V).—A solution of 10 g. (0.0575 mole) of 2-hydroxymethylene-1-tetralone and 4.7 g. (0.0626 mole) of β-methylaminoethanol in 250 ml. of toluene was refluxed under a water-separator for 0.7 hr. Evaporation of the solvent gave a dark brown oil which solidified on standing overnight. Trituration with a small quantity of ethyl acetate provided

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(29) See ref. 28, pp. 758–761 and pp. 851–891.

5.5 g. (41%) of yellow crystals. Recrystallization from ethyl acetate (Norit) gave a pure sample, m.p. 88–91°.

Anal. Calcd. for $C_{14}H_{17}O_2N$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.90; H, 7.62; N, 6.04.

The infrared spectrum (Nujol) had peaks at 3.06, 6.11, 6.23, and 6.56 μ (all strong). The crystalline compound deteriorated very gradually into a dark resin, on standing. Attempted reduction of this compound with lithium aluminum hydride did not afford a recognizable product. The pure, crystalline sample gave a strong ferric chloride test.

3-[*N*-Methyl-*N*-(β-hydroxyethyl)aminomethylene]oxindole (VIa).—An exothermic reaction occurred when a solution of 16.1 g. (0.10 mole) of 3-hydroxymethylene oxindole[30] in 250 ml. of toluene was treated with 8.0 g. (0.107 mole) of β-methylaminoethanol. The two-phase mixture was refluxed under a water trap for 2.5 hr., until the water had been driven off and the solution was homogeneous. Evaporation of the toluene and trituration of the semicrystalline, residual red oil with ether–ethyl acetate provided 3.5 g. (16%) of yellow crystals, m.p. 150–153°. Recrystallization from benzene–ethyl acetate raised the m.p. to 157–159°.

Anal. Calcd. for $C_{12}H_{14}O_2N$: C, 66.03; H, 6.47; N, 12.84. Found: C, 66.35; H, 6.46; N, 12.5.

The infrared spectrum (Nujol) had a moderately strong peak at 2.98 μ, weaker bands *ca.* 3.03–3.3 μ, and intense peaks 5.96 and 6.33 μ; in chloroform solution, the hydroxyl absorption was shifted to 2.72 and 2.91 μ, although the carbonyl peak was changed very little (6.02 μ) and the 6.3 μ peak also remained. The ultraviolet spectrum (C_2H_5OH) showed λ_{max} 274, 319–324 and 345 mμ (ϵ 14,180, 12,240, and 15,220, respectively).

3-(1-Piperidylmethylene)oxindole (VIb).—Similar condensation of 3-hydroxy(or ethoxy)methyleneoxindole with piperidine (see preceding experiment) gave a low yield of pale yellow crystals, m.p. 161.5–162.5° after recrystallization from benzene.

Anal. Calcd. for $C_{14}H_{16}ON_2$: C, 73.65; H, 7.06; N, 12.27. Found: C, 73.65; H, 7.09; N, 12.43.

The infrared spectrum (Nujol) had a weak band *ca.* 3.20 μ and intense peaks 5.97 and 6.35 μ. The ultraviolet spectrum (C_2H_5OH) had λ_{max} 275, 319–325 and 349 mμ (ϵ 17,340, 12,750–13,095, and 16,950, respectively).

Attempted lithium aluminum hydride reduction of compounds VIa and VIb resulted in return of most of the starting material.

2-Phenyl-4-[*N*-(β-hydroxyethyl)aminomethylene]-5-oxazolone (VIIIa).—When a solution of 2.8 g. of 2-phenyl-4-ethoxymethylene-5-oxazolone[31] in 50 ml. of benzene was treated with 1 g. of ethanolamine, there was formed initially a red, oily phase, and then very rapidly a mass of crystals. After being collected and washed with benzene, these weighed 2.6 g. and had m.p. 134–136°. Recrystallization from ethyl acetate gave pale yellow needles, m.p. 139–140°.

Anal. Calcd. for $C_{12}H_{12}O_3N_2$: C, 62.06; H, 5.21; N, 12.06. Found: C, 62.10; H, 5.28; N, 12.12.

Spectra.—λ_{max}^{Nujol} 3.03 (bonded), 5.70 and 5.99 μ; $\lambda_{max}^{C_2H_5OH}$ 237, 281–294, and 350 mμ (ϵ 10,510, 7,250 and 32,850, respectively), with shoulders 248, 320, and 362 mμ.

The same compound was also formed when the enol acetate[32] corresponding to VII was used in the same reaction.

2-Phenyl-4-[*N*-methyl-*N*-(β-hydroxyethyl)aminomethylene]-5-oxazolone (VIIIb).—A solution of 6.9 g. (0.0318 mole) of 2-phenyl-4-ethoxymethylene-5-oxazolone in 60 ml. of benzene was treated with a solution of 2.8 g. (0.0374 mole) of β-methylaminoethanol in 80 ml. of benzene. After 15 min. standing, the solution, on scratching, rapidly deposited crystals, which were collected and washed with benzene; yield 6.2 g. (79%). Recrystallization from ethyl acetate gave pale yellow crystals, m.p. 142–143°.

Anal. Calcd. for $C_{13}H_{14}O_3N_2$: C, 63.40; H, 5.73; N, 11.38. Found: C, 63.55; H, 5.84; N, 11.21.

Spectra.—λ_{max}^{Nujol} 2.94, 5.84, 6.09, 6.23–6.26, and 6.35 μ; $\lambda_{max}^{C_2H_5OH}$ 240, 286–297, 353, and 372 mμ (ϵ 11,000, 7,020, 35,730, and 27,560, respectively, with shoulders at 250, 312, 322, 327, 336, 340 mμ); λ_{max}^{chf} 2.76, 2.94 (broad), 5.8–5.85 (broad, intense), 6.05 (broad, very intense), and 6.20 μ (intense).

2-Phenyl-4-[*N*-(β-hydroxy-β-phenylethyl)aminomethylene]-5-oxazolone (VIIIc).—After mixing solutions of 2.2 g. of VIIb and 1.5 g. of β-hydroxy-β-phenylethylamine, each in *ca.* 70 ml. of benzene, crystals appeared within a few minutes and rapidly increased in quantity. After 10 min. they were collected, washed with benzene, and air dried; 2.6 g. yield of very slightly discolored material. Recrystallization from ethyl acetate gave colorless crystals, m.p. 177–179°.

Anal. Calcd. for $C_{18}H_{16}O_3N_2$: C, 70.11; H, 5.23; N, 9.09. Found: C, 69.84; H, 5.27; N, 8.96.

Spectra.—λ_{max}^{Nujol} 3.04, 5.75, 6.00 μ; $\lambda_{max}^{C_2H_5OH}$ 234, 281–290, and 351 mμ (ϵ 10,920, 7,160, and 35,570, respectively), with shoulders 251, 269, and 370 mμ.

Compound IXa.—Compound VIIIa (1 g.) and 50 ml. of acetic anhydride were refluxed for 1.3 hrs. Evaporation of the excess reagent and crystallization of the residue from, first cyclohexane–ethyl acetate and then cyclohexane–benzene, gave lemon-yellow crystals, m.p. 108–110°.

Anal. Calcd. for $C_{16}H_{16}O_5N_2$: C, 60.75; H, 5.10; N, 8.86. Found: C, 61.09; H, 5.27; N, 8.94.

Spectra.—λ_{max}^{Nujol} 5.56, 5.74, 5.82, 6.05, and 6.25 μ; $\lambda_{max}^{C_2H_5OH}$ 229, 237, 252, 272–276, 332, 347, and 365 mμ (ϵ 8,970, 9,020, 13,270, 3,250, 31,210, 43,590, and 31,960, respectively).

Compound IXb.—Similar acetylation of compound VIIIc, refluxing 0.5 hr., and crystallization from ethyl acetate, afforded pale yellow, small crystals, m.p. 168.5–170°.

Anal. Calcd. for $C_{22}H_{20}O_5N_2$: C, 67.33; H, 5.14; N, 7.14. Found: C, 67.64; H, 5.10; N, 6.87.

Spectra.—λ_{max}^{Nujol} 5.57, 5.62, 5.75, 5.86, 6.08, and 6.25 μ; $\lambda_{max}^{C_2H_5OH}$ 227, 253, 333–337, 349, and 367 mμ (ϵ 11,480, 13,270, 29,830, 40,180, and 31,620, respectively).

Compound X.—(A) Condensation of VIIb with DL-penicillamine *n*-propyl ester was carried out in benzene solution, as in preparation of compounds VIII, except that the solution was boiled for 1 hr. Evaporation of the solvent gave a very bright red oil, which gave a strong green ferric chloride test; the infrared spectrum of this crude material had peaks at 2.96–3.05, 5.76, 6.02, and 6.24 μ.

(B) The crude material from (A) (1 g.) was treated with 50 ml. of acetic anhydride, and the red solution was refluxed for 0.8 hr. Evaporation of the reagent gave a brown oil which gradually crystallized in the presence of ethyl acetate; trituration with this solvent gave nearly colorless crystals, ferric chloride test negative, and recrystallization afforded a sample, m.p. 169–170°.

Anal. Calcd. for $C_{20}H_{24}O_5N_2S$: C, 59.4, H, 5.98; N, 6.93. Found: C, 59.47; H, 6.3; N, 6.67.

Spectra.—λ_{max}^{Nujol} 3.01, 5.58, 5.78, 6.01, and 6.11 μ; $\lambda_{max}^{C_2H_5OH}$ 225, 233, 239, 263, 291–296, 347, 361, and 377 mμ (ϵ 7,360, 8,410, 8,810, 13,520, 2,580, 25,630, 35,630, and 30,830, respectively).

Acknowledgment.—G.N.W. is indebted to Mrs. Ruth Ann MacAllister and Miss Barbara N. Weaver for assistance in preparation of compounds in this work, to Mr. George Robertson, Mr. Rudolf

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(30) Prepared by the method of H. Beringer and H. Weissauer, *Ber.*, **85**, 774 (1952).

(31) See ref. 28, p. 803.

(32) See ref. 28, p. 823.

Oeckinghaus, Mrs. Louise Porter, Miss Natalie Cahoon, Mrs. Margaret Mulligan, and Miss Jan Siragusa for analytical and spectrophotometric data; and to Mr. Louis Dorfman for the benefit of a number of stimulating discussions on amide infrared spectra.

Some Reactions of Triphenyltinlithium and Triphenylleadlithium

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Received February 23, 1962

Homogeneous solutions of triphenyltin- and triphenylleadlithium have been prepared from the corresponding chloride and lithium in tetrahydrofuran. Hexaphenylditin has been cleaved to give good yields of the tin-lithium derivative. This triphenyltinlithium reacted with water and carbon dioxide to give only hexaphenylditin. In contrast to the benzoic acid obtained from carbonation of the triphenylleadlithium prepared from lead dichloride and phenyllithium in ether, benzoic acid was not formed from carbonation of the lead-lithium compound prepared from triphenyllead chloride in tetrahydrofuran. Refluxing a tetrahydrofuran solution of triphenyltinlithium has been found to give tetraphenyltin.

In order to compare the reactions and reactivity of the lithium derivatives of the triaryl Group IV-B elements (Ar_3MLi, where M is Si, Ge, Sn, or Pb) under similar conditions,[1] it was essential that triphenyltin-[2] and triphenylleadlithium be prepared under similar conditions in tetrahydrofuran as triphenylsilyl-[3,4] and triphenylgermyllithium.[1,4] It was also of interest to investigate the existence of an equilibrium system with triphenylleadlithium in tetrahydrofuran, a condition which has been proposed to exist with triphenylleadlithium in diethyl ether.[5,6]

$$(C_6H_5)_3PbLi \rightleftharpoons (C_6H_5)_2Pb + C_6H_5Li$$

In this case the triphenylleadlithium, prepared from lead (II) chloride and phenyllithium, was postulated to be 20[5] and 50%[6] dissociated. A similar dissociation was proposed for triphenyltinlithium (22% dissociated),[6] but evidence for such an equilibrium could not be detected by carbonation[7] and other experiments.[8] However, tri-*n*-butyltinlithium was recently postulated to be dissociated.[9] Also, the presence of tetraphenyltin in many of the reactions of triphenyltinlithium, prepared from tin(II)chloride and phenyllithium,[7-10] led us to repeat some of these reactions using the triphenyltinlithium prepared directly from triphenyltin chloride.

Triphenyltinlithium has previously been prepared from phenyllithium and diphenyltin in an ether–benzene mixture,[11] from phenyllithium and tin(II) chloride in ether,[10] and from triphenyltin bromide and lithium in liquid ammonia.[11] Triphenylleadlithium was obtained in good yields from lead (II) chloride and phenyllithium in ether.[5] Since phenyllithium has been observed to be unstable in tetrahydrofuran,[12] the addition of a tetrahydrofuran solution of phenyllithium to tin(II) chloride or lead(II) chloride did not appear promising for the preparation of the tin- and lead-lithium derivatives, although this was not investigated. However, the recently reported[4] preparation of triphenylsilyl- and triphenylgermyllithium from chlorotriphenylsilane and bromotriphenylgermane, respectively, in tetrahydrofuran suggested the utilization of triphenyltin chloride and triphenyllead chloride in the same solvent. Subsequently, by allowing tetrahydrofuran (THF) solutions of these halogen compounds to react with lithium at room temperature, homogeneous solutions of the lithium derivatives were obtained. The triphenyltin- and triphenylleadlithium were characterized by reaction with benzyl chloride to give the known compounds benzyltriphenyltin and benzyltriphenyllead, in yields of approximately 75%.

$$(C_6H_5)_3MCl + Li \xrightarrow{THF} (C_6H_5)_3MLi \xrightarrow{C_6H_5CH_2Cl} (C_6H_5)_3MCH_2C_6H_5$$

$$M = Sn \text{ or } Pb$$

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