ically for 1.5 hr. At the end of this period 250 ml of a saturated solution of sodium carbonate was added. To this resulting solution of sodium hydroxylamine disulfonate 20.0 g (0.147 mol) of 2,3,6-trimethylphenol (mp 63.4°) and 100 ml of heptane were added. A stainless steel anode[10] (*ca.* 10 mesh/cm²) was immersed into the heterogeneous two-phase system. The cathode, in the form of a stainless steel coil, was placed into a porous pot (Soxhlet type extraction thimble), filled with water plus 2 ml of the electrolyte, and immersed to about $^3/_4$ of its length into the two-phase reaction mixture. The cold two-phase system was now stirred mechanically and electrolyzed for 5 hr at 7–8V/3A at 0–5°. The trimethylphenol dissolved slowly and the color of the hexane layer changed to yellow, then to orange, and again to lemon yellow at the end. The course of the reaction was conveniently followed by tlc (aluminum oxide plates, chloroform, phosphomolybdic acid spray). Only trace amounts of phenol could be detected at the end of the electrolysis. The water layer had a violet color and some inorganic material crystallized. The whole mixture was transferred into a 1-l. separatory funnel. The yellow heptane layer was separated and washed two times with 50 ml of 4 *N* sodium hydroxide and then with saturated sodium chloride solution until the washes were neutral. The water layers were washed twice with heptane. The heptane extracts were combined, dried over magnesium sulfate, filtered, and evaporated to dryness (rotary evaporator, 40° bath temperature). The residue, a lemon oil, crystallized under cold running water. The last traces of solvent were subsequently removed under high vacuum. This procedure gave 20.8 g (94%) of crystalline, yellow trimethylbenzoquinone (**9**), mp 29.6–31°[13] (Mettler automatic melting point apparatus) and tlc examination of this material revealed only one spot.

B. From 2,3,5-Trimethylphenol (3).—Using the same procedure described in A, **9** was obtained in 73% yield, mp 27.8°.

Trimethylhydroquinone (1).—Reduction of a sample of **9** with sodium hydrosulfite and crystallization from water yielded pure **1**, mp 170–173°.[13] Ir and uv spectra of this material were superimposable with those of an authentic sample.[11]

Registry No.—**1**, 700-13-0; **2**, 16782-79-9; **3**, 697-82-5; **4**, 20030-29-9; **5**, 2416-94-6; **6**, 20030-30-2; **7**, 34638-67-0; **9**, 935-92-2.

Acknowledgments.—Thanks are due to the staff of our Physical Chemistry Department directed by Dr. P. Bommer. In particular we are indebted to Dr. H. Wyss for ir, Dr. V. Toome for uv, Dr. T. Williams for nmr, Dr. W. Benz for mass spectra, and Dr. F. Scheidl for microanalyses.

(13) R. Nietzki and J. Schneider, *Chem. Ber.*, **27**, 1426 (1894), report mp 32° for **9** and 169° for **1**.

Notes

On the Electrophilic Substitutions and Additions to the Pyrrolidine Enamine of 1-Acetyl-3-oxopiperidine

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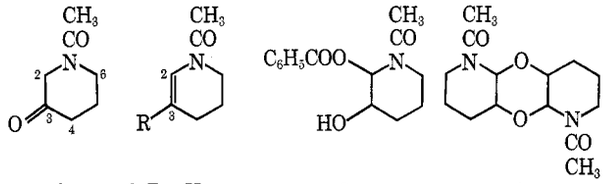
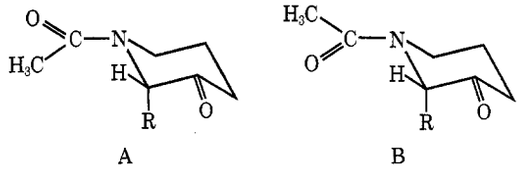
Enamine chemistry has been investigated extensively[1] since Stork's excellent application of enamines for electrophilic substitution reactions.[2] However, only a few examples have been reported of substitutions or additions to enamines of ketones bearing a methylene group flanked by a carbonyl group and a nitrogen atom.[3] In connection with research on synthesis of veratramine,[4] we have examined some reactions of the pyrrolidine enamine of 1-acetyl-3-oxopiperidine (**1**).

The starting ketone **1** was prepared as follows. Treatment of 1-acetyl-1,4,5,6-tetrahydropyridine[5] (**2**) with perbenzoic acid afforded the hydroxy derivative **3** in 50% yield, which on pyrolysis produced **1** in 72% yield along with a dimeric by-product **4**. In accordance with the structure, compound **1** exhibited a peak at *m/e* 141 (M^+) and absorption maxima at 1726 and 1642 cm^{-1} in the mass and ir spectra, respectively. The nmr spectrum of **1** was simplified by rapid ring inversion and, conversely, complicated by the presence of two conformers A and B (R = H) caused by slow rotation of the acetyl group around the C–N bond,[6] as



1 **2**, R = H **3** **4**

5, R = NC_4H_8



A B

(1) For recent reviews, see (a) G. H. Alt in "Enamines," A. G. Cook, Ed., Marcel Dekker, New York, N. Y., 1969, p 115; (b) K. Bláha and O. Červinka in "Advances in Heterocyclic Chemistry," Vol. 6, A. R. Katritzky and A. J. Boulton, Ed., Academic Press, New York, N. Y., 1966, p 147; (c) J. Szmuszkovicz in "Advances in Organic Chemistry," Vol. 4, R. A. Raphael, E. C. Taylor, and H. Wynberg, Ed., Interscience, New York, N. Y., 1963, p 1.

(2) G. Stork, R. Terrel, and J. Szmuszkovica, *J. Amer. Chem. Soc.*, **76**, 2029 (1954); G. Stork and H. K. Landesman, *ibid.*, **78**, 5128, 5129 (1956).

(3) *E.g.*, S. Danishefsky and R. Cavanaugh, *J. Org. Chem.*, **33**, 2959 (1968).

(4) (a) T. Masamune, M. Takasugi, A. Murai, and K. Kobayashi, *J. Amer. Chem. Soc.*, **89**, 4521 (1967); (b) T. Masamune, M. Takasugi, and A. Murai, *Tetrahedron*, **27**, 3369 (1971).

(5) C. Schöpf, A. Komzak, F. Braun, and E. Jacobi, *Justus Liebigs Ann. Chem.*, **559**, 1 (1948); T. Masamune and M. Takasugi, *Yuki Kagobutsu Goseiho*, **18**, 1 (1968).

(6) For recent papers concerning the slow rotation of the C–N bond, see W. E. Stewart and T. H. Siddal, *Chem. Rev.*, **70**, 517 (1970); B. U. Schlottmann, *Tetrahedron Lett.*, 1221 (1971); C. R. Narayanan and B. M. Sawant, *ibid.*, 1321 (1971).

TABLE I

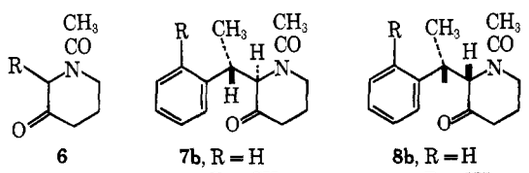
RESULTS IN ALKYLATIONS OF PYRROLIDINE ENAMINE OF 1-ACETYL-3-OXOPIPERIDINE (1)

Run	Alkylating reagents	Products	R in 6	Yield,[a,b] %
a	Benzyl chloride	6a	Benzyl	44 (53)
b	1-Phenylethyl bromide[c]	7b	1-Phenylethyl	33
		8b	1-Phenylethyl	20
c	1-(*o*-Tolyl)ethyl bromide[d]	7c	1-(*o*-Tolyl)ethyl	27
		8c	1-(*o*-Tolyl)ethyl	17
d	Allyl bromide	6d	Allyl	62 (67)
e	*n*-Butyl iodide	6e	*n*-Butyl	13 (57)
f	Phenacyl bromide	6f	Phenacyl	76 (55)
g	Bromoacetone	6g	2-Oxopropyl	40 (40)
h	Ethyl bromoacetate	6h	Ethoxycarbonylmethyl	40 (58)
i	Chloromethyl methyl ether	6i	Methoxymethyl	6 (33)
j	Ethyl acrylate	6j	2-Ethoxycarbonylethyl	48 (80)
k	Acrylonitrile	6k	2-Cyanoethyl	52 (80)

[a] Yields of isolated products. [b] The numbers in parentheses denote yields of the corresponding reactions to cyclohexanone under comparable conditions, and are cited from ref 1c. [c] H. Rupe and W. Tomi, *Chem. Ber.*, **47**, 3064 (1914). [d] See footnote 9.

revealed by *two* sharp singlets (τ 7.89 and 7.82, NCO-CH_3), *two* overlapped triplets (B, τ 6.35 and 6.29, H at C_6), and *two* singlets (A, τ, 5.97 and 5.83, H at C_2). In fact, signals A and B remained unchanged on irradiation at τ 7.52 (H at C_4), while the latter B was simplified to two singlets by irradiation at τ 7.95 (H at C_5). The by-product was assigned formula **4** on the basis of the mass (*m/e* 282, M^+) and ir spectra (ν_{max} 1650 cm^{-1} and no absorption near 3300 and 1720 cm^{-1}) as well as its facile conversion into **1** by acid treatment.

Ketone **1** was readily converted into the pyrrolidine enamine (**5**), which showed only two sharp *singlets* due to the C_2 proton at τ 4.59 and 3.79 with total intensity of one proton in the lower field of the nmr spectrum, confirming the double bond location at C_2 and C_3.[3] Electrophilic substitutions or additions of the enamine were generally carried out by heating with 1 equiv or excess of alkylating reagents in dry dioxane or acetonitrile. The reactions were continued until the starting enamine had disappeared or until the products had started to decompose, and the products after hydrolysis were separated and purified by thin layer (tlc) or column chromatographies. The results are summarized in Table I. The products listed in Table I showed satisfactory elemental analyses as well as uv, ir (ν_{max} *ca.* 1720 and 1636 cm^{-1}), and nmr spectra[7,8] consistent with the assigned structures.[9]



6 **7b**, R = H; **c**, R = CH_3 **8b**, R = H; **c**, R = CH_3

The alkylated piperidines were produced from enamine **5** in 40–76% yields except in a few cases (runs e and i). These low yields are ascribed to the parallel occurrence of N-alkylations and also of side reactions caused by extremely reactive alkylating reagents. In view of the fact that the starting ketone **1** and resulting piperidines **6** are not very stable, the present yields are regarded as moderate, as compared with those in the corresponding reactions with cyclohexanone.[1c] In summary, the result suggests that the relevant alkylations would be generally available for synthesis.[10]

Experimental Section[9]

Melting points were measured in open capillaries and are uncorrected. Homogeneity of each compound was always checked by tlc on silica gel (Wakogel B-5) and/or alumina (Merck G). The uv and ir spectra were taken in 99% ethanol and in the liquid state, unless otherwise stated. The nmr spectra were determined in deuteriochloroform at 60 and/or 100 MHz, tetramethylsilane being used as an internal reference. The abbreviations "s, d, t, q, m, do, tri, and br" in the nmr spectra denote "singlet, doublet, triplet, quartet, multiplet, double, triple, and broad," respectively.

1-Acetyl-3-oxopiperidine (1).—To a solution of perbenzoic acid (2.85 g, purity 82%) in dry ether (10 ml) was added dropwise 1-acetyl-1,4,5,6-tetrahydropyridine[5] (**2**, 2.00 g) in dry ether (5 ml) under stirring and cooling with a freezing mixture during 2 min, and the mixture was allowed to stand overnight in a refrigerator. The crystalline substance separating out was colected by decantation and washed with cold, dry ether to yield 1-acetyl-2-benzoyloxy-3-hydroxypiperidine (**3**, 2.25 g), mp 101–105°, which was used without further purification, ir (Nujol) ν_{max} 3300, 3025, 1732, 1626, 948, 890, and 715 cm^{-1}.

The hydroxypiperidine **3** (1.00 g) was heated to 140° (oil-bath temperature) under reduced pressure (2 mm) for 1 hr in a sublimation apparatus. The pyrolyzed product adhering to the cold finger was combined with those obtained in another three runs (total 4.0 g), dissolved in ether (100 ml), and mixed with powdered sodium carbonate (10 g) under vigorous stirring, and then filtered to remove the resulting benzoic acid. The filtrate was dried and evaporated to yield oxopiperidine (**1**, 0.71 g) as an oil, which showed the same ir spectrum as the analytical sample. This was distilled to give an analytical sample (550 mg): bp 118–120° (0.21 mm); mass spectrum *m/e* 141 (M^+) and 98; ir 1726 and 1642 cm^{-1}; nmr τ 7.89 and 7.82 (each s, $NCOCH_3$), 7.52 (2 H, m, H at C_3), 6.35 and 6.29 (total 2 H, each t, J = 6 and 6 Hz, H at C_6), and 5.97 and 5.83 (each 1 H, s, H at C_2).

(7) H. Paulsen and K. Todt, *Angew. Chem.*, **78**, 943 (1966); *Chem. Ber.*, **100**, 3385, 3396 (1967).

(8) R. A. Johnson, *J. Org. Chem.*, **33**, 3627 (1968).

(9) Representative nmr spectra and interpretation, details of the purification and properties of compounds **6a** to **6k** (Table I) and the preparation of 1-(*o*-tolyl)ethyl bromide will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JOC-72-2343. Remit check or money order for $4.00 for photocopy or $2.00 for microfiche.

(10) For examples of the use of enamines for alkaloid syntheses, see, E. Wenkart, *Accounts Chem. Res.*, **1**, 78 (1968); D. A. Evans, *J. Amer. Chem. Soc.*, **92**, 7593 (1970), and references cited therein.

TABLE II

REACTION CONDITIONS IN ALKYLATIONS OF PYRROLIDINE ENAMINE OF 1-ACETYL-3-OXOPIPERIDINE (1)

Run	Alkylating reagents mg	Alkylating reagents equiv[b]	Ketone 1 mg	Ketone 1 mmol	Enamine 5, mg	Solvent[a]	ml	Temp, °C	Time, hr	Products	mg[c]	%[b]
a	758	2.0	423	3.0	586	D	1.5	100	14	**6a**	301	44
b	532	1.0	424	3.0	584	D	3.0	100	10	**7b**	235	33
										8b	140	20
c	597	1.0	423	3.0	593	D	3.0	100	10	**7c**	230	27
										8c	148	17
d	721	2.0	421	3.0	590	A	2.0	70	12	**6d**	337	62
e	910	1.0	635	4.5	890	D	3.0	100	6	**6e**	120	13
f	735	1.0	517	3.6	717	D	4.2	100	0.6	**6f**	692	76
g	480	1.0	494	3.5	678	D	1.5	100	0.25	**6g**	278	40
h	1001	2.0	425	3.0	588	D	1.5	100	4	**6h**	280	40
i	445	1.1	710	5.0	960	D	5.0	25	8	**6i**	59	6
j	896	3.0	426	3.0	558	D	2.0	100	13	**6j**	334	48
k	1366	4.0	494	3.5	652	D	2.5	100	18	**6k**	352	52

[a] D, dioxane; A, acetonitrile. [b] Based on ketone 1. [c] Weights of isolated products.

Anal. Calcd for $C_7H_{11}NO_2$: C, 59.55; H, 7.85; N, 9.92. Found: C, 59.43; H, 7.98; N, 9.75.

The pyrolyzed product remaining on the bottom of the apparatus crystallized on trituration with ethanol. This (240 mg) was recrystallized from ethanol to give an analytical sample of dimer **4**: mp 262–264°; mass spectrum *m/e* 282 (M^+) and 141; ir (Nujol) ν_{max} 1650, 1072, and 986 cm^{-1}. This was scarcely soluble in chloroform, dimethyl sulfoxide, and pyridine.

Anal. Calcd for $C_{14}H_{22}N_2O_4$: C, 59.55; H, 7.85; N, 9.92. Found: C, 59.53; H, 7.77; N, 10.27.

Dimer **5** (500 mg) was suspended in chloroform (20 ml) saturated with dry hydrogen chloride and stirred at room temperature for 4 hr. After addition of sodium carbonate followed by filtration, the mixture was evaporated to leave an oily residue (518 mg). This was separated by preparative tlc and then distilled to give **1** (354 mg), which showed the same ir spectrum and retention time (vpc) as the sample obtained by pyrolysis.

General Procedure.—A solution of 1-acetyl-3-oxopiperidine (**1**) (420–710 mg, 3.5–5.0 mmol) and pyrrolidine (1–2 ml) in benzene (20–60 ml) was refluxed for 2–3 hr, water being removed by azeotropization with a Dean–Stark apparatus. The solution was then evaporated to dryness under reduced pressure to leave the enamine **5**, which showed the ir and nmr spectra superimposable over those of the analytical sample and could be used for further reactions. A part of the enamine was distilled for analysis: bp 125–128° (5 mm) (sublimation apparatus); ir ν_{max} 1640 cm^{-1}; nmr τ 8.17 (6 H, m, $CH_2CH_2CH_2CH_2$ and H at C_5), 7.95 and 7.94 (total 3 H, each s, $NCOCH_3$), 7.76 (2 H, t, J = 6 and 6 Hz, H at C_4), 7.07 (4 H, m, CH_2NCH_2), 6.59 and 6.46 (total 2 H, each t, J = 6 and 6 Hz, H at C_6), and 4.59 and 3.79 (0.6 and 0.4 H, each s, H at C_2).

Anal. Calcd for $C_{11}H_{18}N_2O$: C, 68.00; H, 9.34; N, 14.42. Found: C, 67.76; H, 9.25; N, 14.12.

A solution of the enamine **5** and alkylating reagents (1.0–4.0 equiv) in dioxane or acetonitrile was heated (usually steam-bath temperature) in a sealed tube until the starting material had disappeared or until the product had started to decompose. The reaction mixture was then treated with water (1–4 ml) at *ca.* 100° for 0.5–4.0 hr in a sealed tube and evaporated under diminished pressure. The residue was mixed with water (3–6 ml) and extracted with organic solvents (usually chloroform, 4 × 30 ml). The extracts were dried and submitted to further separation. The detailed reaction conditions were tabulated in Table II.

Registry No.—**1**, 34456-78-5; **3**, 34456-79-6; **4**, 34456-80-9; **5**, 34456-81-0; **6a**, 34456-82-1; **6d**, 34456-83-2; **6e**, 34456-84-3; **6f**, 34456-85-4; **6g**, 34456-86-5; **6h**, 34456-87-6; **6i**, 34456-88-7; **6j**, 34456-89-8; **6k**, 34456-90-1; **7b**, 34456-91-2; **7c**, 34456-92-3; **8b**, 34456-93-4; **8c**, 34456-94-5.

Acknowledgments.—The authors are grateful to Mr. S. Shimokawa for the measurement of 60-MHz nmr spectra, to Miss G. Maeda and Mrs. T. Tohma for the microanalysis, and to Miss Y. Imai for the measurement of mass spectra.

Oxidation of Bis(aroylhydrazones) of α-Dicarbonyl Compounds to 1,2,3-Triazolylisoimides. IV. Substituent Effect

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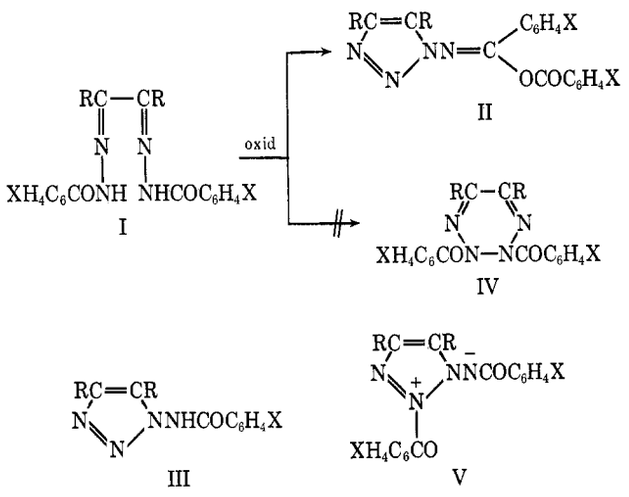
It is known[2,3] that the oxidation of bis(aroylhydrazones) of α-dicarbonyl compounds I gives, instead of the expected 1,2,3,4-tetrazines IV, 1,2,3-triazolylisoimides II.



The structure of the oxidation products was for a long time in doubt, since the zwitterionic formula V had been also proposed[4,5] as an alternative. However,

(1) Taken in part from the Ph.D. thesis of E. D. M., University of Thessaloniki.

(2) D. Y. Curtin and N. E. Alexandrou, *Tetrahedron.*, **19**, 1967 (1963).

(3) N. E. Alexandrou and E. D. Micromastoras, *Tetrahedron Lett.*, 231 (1968).

(4) Personal communication from Professor A. R. Katritzky (1963).

(5) S. Petersen and H. Heitzer, *Angew. Chem., Int. Ed. Engl.*, **9**, 69 (1970).