THE SPECTRA OF SATURATED AND α–β UNSATURATED SIX-MEMBERED LACTAMS[1]

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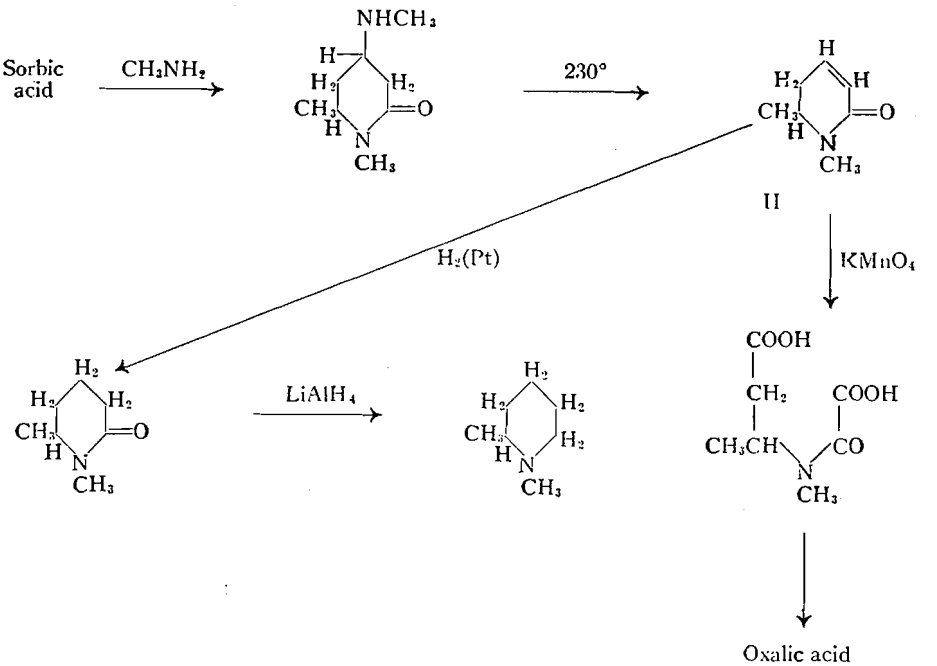
ABSTRACT

The ultraviolet and infrared spectra of some saturated and unsaturated six-membered lactams are described, and the unusual features in the 3μ and 6μ regions discussed. A comparison is made of these spectra with those previously ascribed to α–β unsaturated lactams.

On the basis of ultraviolet and infrared spectra, α–β unsaturated lactam structures have been assigned to products of Beckmann rearrangement of unsaturated oximes (8, 14) and to the alkaloid bakankosine (1). In addition an α–β unsaturated lactam structure has been considered for one of the transformation products of lycoctonine (5). It thus became of interest to examine the spectra of authentic α–β unsaturated lactams for comparison with those of the above compounds.

6-Methyl-5,6-dihydro-2-pyridone (I) and 1,6-dimethyl-5,6-dihydro-2-pyridone (II) were prepared by a method similar to that of Fischer and Schlotterbeck (7). The preparation and characterization of the latter is outlined below.



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Since hydrolysis of the oxidation product from the unsaturated lactam gave oxalic acid in 75% yield, the lactam contained at least this percentage of the α–β unsaturated isomer.[3]

The 1,2-dimethyl piperidine gave a picrate analyzing correctly, and melting at 242° (the literature gives 241° (12)).

The ultraviolet spectra of the various compounds which have been assigned α–β unsaturated lactam structures are recorded in Table I. Our observations with 6-methyl-5,6-dihydro-2-pyridone contrast with the broad band (236–251 mμ) or series of maxima recorded by Linstead and co-workers (6). The positions of the maxima of all the compounds are similar, occurring at much longer wave lengths than for acyclic α–β unsaturated amides (2). As an example of the latter we have examined N-crotonylpiperidine,[4] and find it to have only a shoulder around 235 mμ.

The intensity of the maxima of the two six-membered α–β unsaturated lactams is considerably lower than those recorded for the seven-membered analogues and the bakankosine derivatives. Indeed, the spectra of the compounds related to bakankosine are more like those of α–β unsaturated ketones except that no long wave length (300–330 mμ) maxima are recorded.

The "iso" compounds derived from the periodate cleavage products of lycoctonine (5) have λ_{max} 219 mμ, 20 mμ lower than the simple α–β unsaturated lactams which have been studied. This raises doubt as to the unsaturated lactam postulate.

The origin of the bands in the 3μ and 6μ regions in the infrared spectra of amides has been the subject of considerable controversy (9, 15, 16). The

TABLE I
ULTRAVIOLET SPECTRA IN ETHANOL

Compound	λ_{max} in mμ	ϵ_{max}	Reference
Bakankosine derivatives	236–242	12,000–18,000	1
3,5,5-Trimethyl-7-amino-2-heptenoic acid lactam	237	7,320	14
3,5-Dimethyl-7-amino-2-heptenoic acid lactam	241	—	8
6-Methyl-5,6-dihydro-2-pyridone	241	1,470	
1,6-Dimethyl-5,6-dihydro-2-pyridone	251	1,120	

strong band in the 6μ region observed with aliphatic amides has been associated with the C=O stretching vibration (9,13,15). Saturated N-alkyl six-membered lactams have a strong band near 1640 cm.$^{-1}$ when in carbon disulphide solution or in the liquid or solid state (mull). This band is displaced to near 1625 cm.$^{-1}$ in chloroform solution (Table II). The peak is often asymmetric but in the simple compounds so far examined no second band has been clearly resolved. In contrast to these the spectrum of N-crotonylpiperidine has two bands, and the spectra of the two α–β unsaturated lactams have three bands

[3]*The equilibrium between acyclic α–β and β–γ unsaturated acids and esters at moderate temperatures lies over 65% on the α–β side (11). The position of the equilibrium in the above dihydropyridone seems the same at 230° as at room temperature, since no change in ϵ_{max} was observed when I was left at room temperature in 1 N alkali for six hours.*

[4]*The authors are indebted to Dr. F. A. L. Anet for a sample of this amide.*

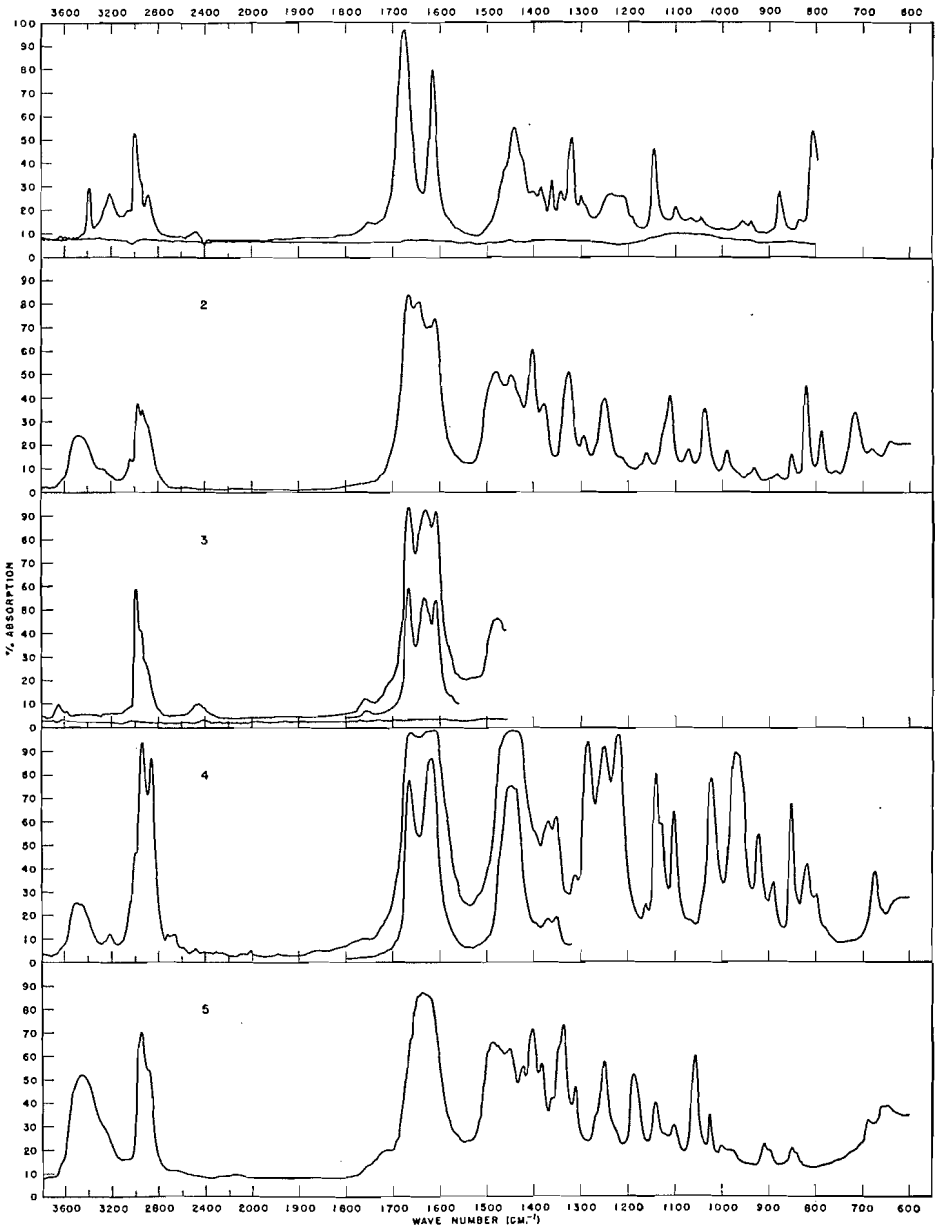

FIG. 1. Infrared spectra of: 1. 6-methyl-5,6-dihydro-2-pyridone (chloroform), 2. 1,6-dimethyl-5,6-dihydro-2-pyridone (liquid), 3. 1,6-dimethyl-5,6-dihydro-2-pyridone (chloroform), 4. N-crotonylpiperidine (liquid), 5. 1,6-dimethyl-2-piperidone (liquid). The background trace in 1 and 3 is that obtained when both cells were filled with pure chloroform.

in the 1600–1700 cm.$^{-1}$ region (Fig. 1). No bands occur in the 1500–1600 cm.$^{-1}$ region in the saturated or unsaturated lactams.

The C=C and C=O stretching bands in the α–β unsaturated amides would be expected to lie in the 1610–1630 cm.$^{-1}$ region since conjugation usually shifts

This page has been reprinted to include the correction pointed out in the Errata that appear at the end of the volume.

both toward smaller wave numbers. The C=C band should as usual be very much weaker than the C=O band. The CN band according to Letaw and Gropp (10) should lie between 1600 and 1650 cm.$^{-1}$. A possible explanation of the spectra actually found is that the three vibrations have very close to the same fundamental frequency, and that resonance between them results in split bands of higher and lower frequency with very much modified relative intensity.

The "iso" compounds derived from lycoctonine have single bands near 1650 cm.$^{-1}$ which lends no support to the unsaturated lactam suggestion.

The infrared spectra of bakankosine derivatives resemble that of N-crotonyl-piperidine more than that of 6-methyl-5,6-dihydro-2-pyridone (the 1610 cm.$^{-1}$ band is more intense than the 1670 cm.$^{-1}$ band). However, the alkaloid spectra could as readily be interpreted as that of α–β unsaturated ketones (1670 cm.$^{-1}$) with an isolated hydrogen bonded lactam (1610 cm.$^{-1}$). (See the discussion of ultraviolet spectra.)

The hydrogen on the double bonds (*cis* disubstituted in I and II) shows up in the infrared near 3040 cm.$^{-1}$ (CH stretching) and probably (3) in the strong band at 805–820 cm.$^{-1}$ (CH bending). It is interesting that the 3040 band does not appear in the spectrum of the N-alkyl lactam II taken in chloroform.

The band at 2800 cm.$^{-1}$ in 4-methylamino-1,6-dimethyl-2-piperidone can most probably be assigned to the C–H stretching of the methyl group on the basic nitrogen since the N-methyl lactams do not show it.

The 3400–3500 cm.$^{-1}$ bands in the spectra of liquid films of N-dialkyl amides have been noted by Letaw and Gropp (10). They consider them to be overtones of the 1600–1700 cm.$^{-1}$ bands. We have observed with lupanine (4) and in the present work that this band does not appear in the spectra in chloroform or carbon disulphide solutions. It is much too intense for an overtone, and in addition, it is at too high a wave number (first overtones usually appear at a wave number very close to double the parent wave number). Thus the only simple explanation of this band appears to be that in the liquid state N-alkyl lactams exist to a considerable extent as the enol. Although lupanine gave no methane in the Zerewitinoff determination, freshly distilled II and 1,6-dimethyl-2-piperidone gave close to one mole at 100°, indicating the mobility of the hydrogens α (or γ) to the carbonyls.

The two lactams with an NH (I and 2-piperidone) in chloroform solution had sharp bands near 3400 cm.$^{-1}$ (free NH) and broader bands of similar intensity near 3200 cm.$^{-1}$ (bonded NH). In the spectra of the pure substances, however, the 3400 cm.$^{-1}$ band was absent but the 3200 cm.$^{-1}$ one was much more intense.

A study of saturated N-alkyl lactams in which enolization is blocked by alkyl substitution, or which contain N^{15}, and α–β unsaturated N-alkyl lactams with the double bond carbons substituted might clarify the origin of the infrared spectra in the 3 and 6μ regions.

A summary of the position of the bands in the 1600–1700 cm.$^{-1}$ region of some saturated and α–β unsaturated six-membered lactams is given in Table II.

TABLE II

Lactam	Position of band, cm.$^{-1}$	State[a]
Saturated —CONHR		
2-Piperidone[b]	1670	Liquid film
	1665	Chloroform solution
Saturated —CONR$_2$		
3-Carbethoxy-4-quinolizidone[b]	1643	Liquid film
	1631	Chloroform solution
Lupanine[c]	1642	Liquid film
	1624	Chloroform solution
Oxysparteine[c]	1640	Carbon disulphide solution
4-Methylamino-1,6-dimethyl-2-piperidone	1637	Liquid film
1,6-Dimethyl-2-piperidone	1637	Liquid film
α-β Unsaturated —CONHR		
6-Methyl-5,6-dihydro-2-pyridone	1610, 1677	Nujol mull
	1615, 1675	$CHCl_3$ solution
α-β Unsaturated —CONR$_2$		
1,6-Dimethyl-5,6-dihydro-2-pyridone	1611, 1643, 1667	Liquid film
	1609, 1634, 1664	Chloroform solution

[a]*The concentration of the chloroform solutions was approximately 30 mgm. per ml.*
[b]*The authors gratefully acknowledge the gift of samples from Dr. L. Marion and Dr. H. J. Vipond.*
[c]*See Reference (4).*

EXPERIMENTAL

The ultraviolet spectra were taken on a Beckmann model D.U. spectrophotometer using 95% ethanol as solvent. The infrared spectra were determined on a Perkin-Elmer model 21 double-beam spectrophotometer with a sodium chloride prism. Percentage absorption is indicated in brackets after the wave number in cm^{-1}.

4-Methylamino-1,6-dimethyl-2-piperidone

Twelve grams of methylamine was condensed into a pressure tube containing 2 cc. of water and 4.0 gm. of sorbic acid. The tube was sealed and heated at 150° for 60 hr. The contents of the tube were transferred to a distilling flask and the methylamine boiled off, finally under reduced pressure. Preliminary experiments showed that only a trace of free acid was left after the 60 hr. treatment. The residual liquid was distilled and a fraction was collected at 93–94° under 0.3 mm. pressure (4.5 gm., 80%). Found: N, 17.56. Calc. for $C_8H_{15}ON_2$: N, 17.95. Infrared spectrum (liquid film): 3460 (40), 3300 (46), 2950 (56), 2800 (39), 1637 (87), 1490 (60), 1475 (58), 1458 (60), 1425 (46), 1402 (61), 1377 (55), 1330 (63), 1286 (36), 1260 (34), 1241 (42), 1170 (29), 1135 (44), 1120 (40, shoulder), 1084 (33, shoulder), 1060 (31), 1032 (25), 973 (19). The spectrum in the fingerprint region was not sharp. The amino lactam did not readily give a crystalline hydrochloride or perchlorate. It formed a crystalline picrate when picric acid in benzene was added to a benzene solution of the base. This was recrystallized from 50% ethanol–water from which it separated as long stout prisms, m.p. 187–189°. Found: C, 43.77; H, 4.78. Calc. for $C_{14}H_{19}O_8N_5$: C, 43.64; H, 4.97.

1,6-Dimethyl-5,6-dihydro-2-pyridone

When 4-methylamino-1,6-dimethyl-2-piperidone was refluxed with a solution of 3 gm. of barium hydroxide octahydrate in 20 cc. of water, methylamine was slowly evolved. However, after eight hours the bulk of the amine was recovered unchanged.

At 150° the amino lactam evolved methylamine but the conversion was very slow.

The amino lactam (17.0 gm.) was decomposed by refluxing for seven hours in a nitrogen atmosphere and then slowly distilling the product at one atmosphere. The weight loss on the refluxing was 3.0 gm. (theory for 1 mole of methylamine 3.38 gm.). The distillate was dissolved in 10 cc. of 50% sulphuric acid. Fifty grams of sodium sulphate was added, the solid broken up, and then thoroughly extracted with methylene chloride. The solvent yielded 13.0 gm. of neutral oil. This was distilled at 155–157° under 130 mm. pressure, giving 10 gm. (73%) of colorless oil with a pleasant odor. Five grams of the oil was fractionated at one atmospheric pressure giving

Cut 1, b.p. up to 225°, n_D^{26}1.4952;
Cut 2, b.p. 225–228°, n_D^{26}1.4953;
Cut 3, b.p. 228–230°, n_D^{26}1.4960.

Cut 2 had λ_{max} 251 mμ, log ε 3.05, and cut 3 had λ_{max} 251 mμ, log ε 3.12. Cut 2 was analyzed. Found: C, 66.69; H, 8.98; active hydrogen, 0.627, 0.646. Calc. for $C_7H_{11}ON$: C, 67.17; H, 8.86; one active hydrogen, 0.805. Infrared spectra (see Fig. 1). Liquid film: 3480 (24), 3040 (14), 2980 (38), 2940 (35), 1667 (84), 1643 (81), 1610 (74), 1483 (51), 1450 (50), 1403 (60), 1377 (38), 1326 (51), 1294 (24), 1250 (40), 1162 (17), 1111 (41), 1073 (18), 1038 (35), 990 (18), 931 (10), 883 (7), 853 (16), 821 (45), 788 (26), 758 (9), 715 (34), 682 (19), 692 (22). Chloroform solution, 1 mm. cell: 3660 (10), 2980 (59), 2460 (10), 1755 (12), 1666 (94), 1631 (92), 1608 (92). Cut 1 (400 mgm.) was dissolved in 1 cc. of 0.1 *N* sodium hydroxide and allowed to stand at 25° for six hours. The solution was made just acid, six grams of sodium sulphate added, and the lactam extracted with methylene chloride. The resulting oil was distilled at a bath temperature of 65–70° under 0.2 to 0.3 mm. pressure. The distillate had λ_{max} 251 mμ, log ε 3.05.

The unsaturated lactam (625 mgm.) was oxidized at 0° in aqueous solution with 2.1 gm. of potassium permanganate. After filtration and acidification the solution was extracted continuously with ether. The 1.1 gm. of thick oily acid which was extracted could not be induced to crystallize. A sample of this oil (150 mgm.) was refluxed with 4 cc. of 10% sodium hydroxide solution for six hours. The solution was cooled, acidified with hydrochloric acid, and filtered from a trace of white precipitate. A solution of 0.5 gm. of calcium chloride in 1 cc. of water was added, and the mixture made alkaline to litmus with aqueous ammonia. The white gelatinous precipitate was coagulated by boiling and collected by centrifuging. After washing by suspension in water and centrifuging again, the precipitate was dried to constant weight. Yield: 75.6 mgm. (75% of theory for calcium oxalate). The salt from hydrolysis

of 450 mgm. of oily acid was decomposed with 2 cc. of 6 *N* hydrochloric acid and the organic acid extracted into ether. The ether on evaporation left a crystalline mush. This was recrystallized from hot water after which it melted at 95–100°, resolidified, and melted at 189° (dec.). A mixture of this with oxalic acid hydrate behaved in an identical manner.

1,6-Dimethyl-2-piperidone

A solution of 130 mgm. of 1,6-dimethyl-5,6-dihydro-2-piperidone in 10 cc. of ethanol in the presence of platinum from 30 mgm. of platinum oxide (Adams') absorbed 26.1 cc. of hydrogen at 21°C. and 760 mm. pressure in 15 min. The rate of hydrogen uptake then fell off very markedly. The solution was filtered and concentrated below room temperature under reduced pressure. The residual liquid was distilled at a bath temperature of 80–85° under 1 mm. pressure. The distillate had n_D^{24}1.4802. Found: C, 66.04; H, 10.18; active hydrogen, 0.487. Calc. for $C_7H_{13}ON_2$: C, 66.10; H, 10.30; one active hydrogen, 0.792. Infrared spectrum (liquid film, Fig. 1): 3460 (52), 2950 (70), 1637 (87), 1490 (65), 1475 (64), 1451 (63), 1422 (55), 1402 (71), 1382 (57), 1337 (73), 1311 (46), 1250 (57), 1186 (52), 1140 (40), 1101 (30), 1056 (60), 1026 (35), 1000 (21), 909 (22), 850 (20), 688 (32), 657 (38), 645 (39).

1,2-Dimethylpiperidine (N-Methyl pipecoline)

The above 1,6-dimethyl-2-piperidone (300 mgm.) was dissolved in 15 cc. of anhydrous ether and 1 gm. of lithium aluminum hydride added. Fifteen cubic centimeters of dioxane was added, and the ether boiled off. The dioxane solution was then refluxed for 30 min. The excess hydride was decomposed by slow addition of methanol, following which the dioxane, methanol, and amine were distilled together under reduced pressure (boiling point around 70°). Twenty cubic centimeters of dioxane was added to the residue and this distilled. To the combined distillate was added 500 mgm. of picric acid. When this solution was concentrated to 10 cc., 600 mgm. of picrate crystallized. The picrate crystallized from ethanol as yellow feathery crystals, m.p. 242° (literature m.p. 240–241°). Found: C, 45.76; H, 5.34. Calc. for $C_{13}H_{15}N_4O_7$: C, 45.61; H, 5.30.

6-Methyl-5,6-dihydro-2-pyridone

This was prepared as described by Fischer and Schlotterbeck (7). When recrystallized from ethyl acetate – petroleum ether it separated as needles, m.p. 105–106°. Found: C, 65.02; H, 7.98. Calc. for C_6H_9ON: C, 64.84; H, 8.16. Ultraviolet spectrum: λ_{min} 235 mμ, log ε 3.15; λ_{max} 241 mμ, log ε 3.17. Infrared spectrum (nujol mull): 3180 (71), 3060 (54), 2930 (52), 1677 (90), 1660 (81, shoulder), 1610 (79), 1475 (41), 1447 (43), 1420 (67), 1381 (30), 1370 (33), 1355 (26), 1326 (77), 1300 (34), 1210 (19), 1199 (21), 1153 (42), 1100 (20), 1075 (19), 981 (11), 939 (22), 885 (34), 820 (57, shoulder), 812 (72), 757 (29), 697 (30), 655 (23). Chloroform solution (31 mgm. per ml., 0.1 mm. cell): 3400 (29), 3220 (27), 3000 (53), 2890 (27), 1675 (97), 1615 (80), 1442 (55), 1400 (28), 1385 (30), 1363 (33), 1345 (28), 1321 (51), 1300 (26), 1145 (46), 1100 (21), 878 (28), 807 (54).

N-Crotonylpiperidine

This boiled at 117–119° under 10 mm. pressure, and had n_D^{25}1.5090. Ultraviolet spectrum: log ϵ 4.04 (215 mμ); 3.82 (235 mμ). Infrared spectrum (liquid film) (see Fig. 1): 3500 (25), 3220 (12), 2940 (93), 2860 (87), 1664 (98), 1617 (99), 1449 (75), 1369 (60), 1353 (62), 1314 (37), 1285 (94), 1253 (92), 1220 (97), 1162 (25), 1140 (80), 1129 (59), 1103 (64), 1024 (78), 971 (90), 922 (54), 891 (34), 851 (68), 819 (42), 798 (29), 675 (39).

2-Piperidone

A sample of the lactam was purified by dissolving in 3 *N* sulphuric acid, salting out with anhydrous sodium sulphate, and extraction into methylene chloride. After distillation under 10 mm. pressure the compound crystallized readily. The hygroscopic solid melted at 38°. Infrared spectrum: (*a*) Thin liquid film: 3220 (45), 3090 (31), 2950 (53), 2880 (41), 1670 (89), 1500 (58), 1475 (36), 1452 (34), 1415 (44), 1356 (55), 1330 (49), 1310 (44), 1273 (23), 1182 (25), 1170 (35), 1115 (34), 1060 (17), 990 (17), 939 (28), 829 (31), 769 (30), 656 (33). (*b*) Chloroform solution (32.4 mgm. per ml., 0.1 mm. cell): 3400 (28), 3290 (18), 3220 (26), 3000 (57), 3970 (57), 2890 (34), 1665 (97), 1499 (59), 1474 (36), 1454 (32), 1416 (32), 1395 (32), 1356 (59), 1334 (47), 1309 (38), 1274 (30), 1182 (22), 1170 (40), 1106 (27), 1060 (18), 988 (18), 936 (21), 825 (17).

3-Carbethoxy-4-quinolizidone

A chloroform solution of the compound was washed with dilute acid and with sodium carbonate solution. The residual oil after removal of the chloroform was distilled under 0.2 mm. pressure (bath temperature, 130°). Found: C, 64.31; H, 8.81; N, 6.35. Calc. for $C_{11}H_{19}O_3N$: C, 63.97; H, 8.50; N, 6.22. Infrared spectrum (liquid film): 3450 (12, broad), 2940 (68), 2860 (49), 1736 (84), 1644 (90), 1470 (66), 1446 (71), 1392 (32), 1370 (56), 1351 (51), 1320 (55), 1300 (45), 1263 (69), 1219 (58), 1180 (75), 1120 (44),1100 (51), 1145 (43), 1135 (44), 985 (21), 975 (22), 916 (11), 897 (11), 850 (27).

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