TABLE I

COMPARISON OF ABSORBANCES OF PURIFIED *vs.* UNPURIFIED HYDROCARBON SOLVENTS AT SPECIFIC WAVELENGTHS[a,b]

Hydrocarbon	Wavelength, mμ								
	210	220	230	240	250	260	270	280	300
Cyclohexane		2	0.55	0.24	0.31	0.32		0.13	0.02
		0.25	0.12	0.034	0.010	0.005		0.003	0.001
Hexane	>2		>2		>2		2	0.36	0.10
	0.18		0.032		0.008		0.003	0.003	0.001
Pentane	>2	>2	>2	0.55		0.10		0.05	0.033
	0.065	0.03	0.018	0.012		0.006		0.003	0.002
3-Methylpentane	1.15	1.25		0.32		0.25		0.17	0.07
	0.15	0.055		0.012		0.005		0.003	0.002
2,2,4-Trimethyl-pentane		0.40		0.10		0.05		0.03	0.02
		0.08		0.015		0.005		0.002	0.001
Methylcyclo-hexane		0.57	0.35	0.22		0.065		0.025	0.015
		0.2	0.010	0.035		0.007		0.003	0.001

[a] The upper number for a specific wavelength in the series of numbers following a given hydrocarbon is the absorbance of the unpurified hydrocarbon, and the lower number is the absorbance of the hydrocarbon after one pass through a silver nitrate on alumina column. [b] Absorbances were obtained on the unpurified hydrocarbons in a 1.0-cm cell while those for the purified liquids were obtained in a 10-cm cell; in order to make comparisons, the latter values were divided by 10 for inclusion in this table.

spectroscopically pure cyclohexane, hexane, pentane, 3-methylpentane, 2,2,4-trimethylpentane, and methylcyclohexane. The exceptional efficiency of this method is reflected in the specific data summarized for each hydrocarbon in Table I. A 90-cm length of the silver nitrate–alumina in a 16-mm (i.d.) column was found to remove effectively the impurities from as much as 6 l. of cyclohexane.

Experimental Section

The silver nitrate–alumina column material was prepared in the following way. A sample of alumina (360 g) was mixed thoroughly with 500 ml of 2 *M* nitric acid. This slurry was filtered through a coarse sintered-glass funnel and the solid was washed with water until the filtrate was neutral to Hydrion paper. Reagent grade silver nitrate (40 g) was dissolved in 20 ml of distilled water and the resulting solution was diluted with 350 ml of reagent grade methanol. This solution was used to wash the damp alumina from the filter into a 2-l. flash evaporator flask. After removal of the solvent by means of the flash evaporator, the solid was poured from the flask and air dried at 140° for 24 hr. The silver nitrate–alumina column material prepared by this procedure is white in contrast to the brown material obtained by Barbour.[6]

A 13-mm (i.d.) column was packed to a depth of 25 cm with the silver nitrate–alumina for the survey experiments reported here. The solvent to be purified was dried over phosphorus pentoxide and then decanted into a reservoir on the top of the column. The column was evacuated with an aspirator before the solvent was allowed to flow; the flow of liquid through the column was then adjusted to approximately 1 drop/sec. One hundred milliliters of solvent was collected and its spectrum was recorded in a 10-cm cell using a Cary Model 14 spectrophotometer.

Registry No.—Silver nitrate, 7761-88-8; cyclohexane, 110-82-7; hexane, 110-54-3; pentane, 109-66-0; 3-methylpentane, 96-14-0; 2,2,4-trimethylpentane, 540-84-1; methylcyclohexane, 108-87-2.

Synthesis of 1-Azatricyclo-[7.2.1.$0^{6,11}$]dodecan-12-one

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In previous work[2] it was found that 7-carboxytetrahydrobenzazepine (**1**) underwent facile cyclization to tricyclic lactam **2** on hydrogenation over ruthenium at 160°. It was thought of interest to determine whether this reaction would be useful in producing other lactams as well.

Homodihydrocarbostyril[3] (**3**) was reduced with lithium aluminum hydride and converted to N-acyltetrahydrobenzazepine (**4**). In contrast to the ultraviolet spectrum of acetanilide [λ_{max} 238 mμ (ε 10,500)][4] the spectrum of **4** had λ_{max} at 226 and 265 mμ. The latter peak had an extinction coefficient of 450 and was in the form of a typical benzene fingerprint. The appearance of the benzenoid fine structure indicated a nearly complete lack of conjugation between the amide group and the aromatic ring caused, presumably, by an interaction between the *peri* hydrogen and the amide carbonyl.

Because of this lack of conjugation it was felt that electrophilic attack would most likely take place on C-8 of the benzazepine.[5] Friedel–Crafts acylation of **4** gave

(1) Supported by Grant MH-10107 from the National Institutes of Health. This support is gratefully acknowledged.

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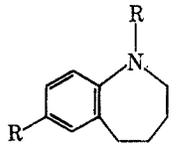
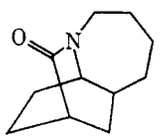
(3) E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *J. Amer. Chem. Soc.*, **74**, 5153 (1952).

(4) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Inc., Englewood Cliffs, N. J., 1965, p 18.

(5) N. P. Buu-Hoi, P. Jacquignon, and M. Marty, *Compt. Rend.*, **251**, 2978 (1960).



1, R = H; R′ = CO_2H
7, R = Ac; R′ = Et



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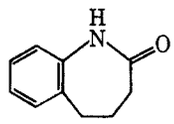

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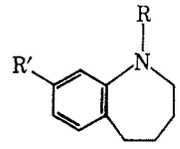
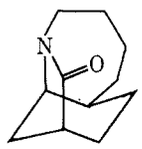
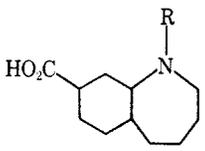


4, R = Ac; R′ = H
5, R = Ac; R′ = Ac
6, R = Ac; R′ = Et
8, R = Ac; R′ = CO_2H
9, R = H; R′ = CO_2H



10



11, R = Ac
12, R = H

a 50% yield of a ketone which had infrared and nmr spectral characteristics of a 1,2,4-trisubstituted benzene.[6] Further spectral characterization was, however, ambiguous. Catalytic hydrogenolysis of this ketone gave an ethyltetrahydrobenzazepine which was different from the 7-ethyl isomer **7** previously obtained.[2] Thus, the hydrogenolyzed material must be the 8-ethyl compound **6** and the ketone, 8-acylbenzazepine (**5**).

Sodium hypobromite oxidation of **5** gave the carbocyclic acid **8**, which on acid hydrolysis readily formed the amino acid **9** in good yield. Catalytic hydrogenation of **9** over ruthenium on carbon at 160° gave the tricyclic lactam **10** in 75% yield. The infrared spectrum of **10** showed a strong band at 1680 cm^{-1}, considerably higher than the lactam absorption reported for substituted isoquinuclidones such as **2**.[2,7]

In order to establish the ease with which this hydrogenative cyclization occurred **10** was prepared from **8** by an alternate route. Hydrogenation of **8** gave the saturated amido acid **11**, which was hydrolyzed to the amino acid **12**. Heating **12** at 260° for a short time[8] gave **10** in 9% over-all yield from **8**. It appears, therefore, that the direct hydrogenative cyclization of substituted aminobenzoic acids over ruthenium is a useful method for the preparation of lactams such as **2** and **10**.

Experimental Section[9]

1-Acetyl-2,3,4,5-tetrahydro-1H-1-benzazepine (4).—A solution of 20 g of **3**[3] in 300 ml of dry tetrahydrofuran was slowly added with stirring, over a 30-min period, to a refluxing mixture of 12 g of lithium aluminum hydride in 200 ml of tetrahydrofuran. The mixture was stirred and refluxed for 14 hr and, after slow addition of 100 ml of ethyl acetate, cooled and carefully hydrolyzed with 50 ml of water. The precipitated alumina was removed by filtration and washed thoroughly with ether and with methylene chloride. The combined filtrate was evaporated to a turbid yellow oil which was dissolved in methylene chloride, dried over potassium carbonate, filtered through a pad of Norit, and evaporated. The residual oil was dissolved in *n*-hexane and filtered through Norit and the solvent was removed by distillation to give 17.5 g of the crude amine as a light yellow oil.

The amine was dissolved in 150 ml of acetic anhydride and allowed to stand at room temperature for 2 days. After warming on a steam bath for 2 hr, the solvent was removed and the residual oil was dissolved in ether and washed with 5% hydrochloric acid, 5% sodium bicarbonate solution, water, and saturated brine. After drying over sodium sulfate, the solution was filtered through a pad of Norit and the ether was removed *in vacuo* to leave a yellow, crystalline mass which, after recrystallization from *n*-hexane, gave 19.67 g (84%) of white crystals, mp 79–81°. Further recrystallization from *n*-hexane followed by sublimation at 50° (0.5 mm) gave pure **4**: mp 80–81°; infrared spectrum (Nujol), C=O at 1634 cm^{-1}; ultraviolet spectrum, λ_{max} 226 mμ (ε 6900) and 265 (450). The 265-mμ peak had the form of a benzene fingerprint.[4] *Anal.* Calcd for $C_{12}H_{15}NO$: C, 76.15; H, 7.99; N, 7.40. Found: C, 76.18; H, 8.22; N, 7.65.

1,8-Diacetyl-2,3,4,5-tetrahydro-1H-1-benzazepine (5).—A mixture of 42.8 g of anhydrous aluminum chloride, 250 ml of carbon disulfide, and 10 g of **4** was stirred and refluxed while 13 ml of acetyl chloride was added over a 10-min period. After 20 hr of stirring and refluxing, 150 ml of the solvent was distilled from the reaction mixture. The residual, red oil was added to 550 g of ice and the resulting precipitate was extracted into methylene chloride. The extract was washed with water and saturated brine and dried over sodium sulfate. After filtration through a pad of Norit, the methylene chloride was removed and the residual, viscous, amber oil was dissolved in 75 ml of cyclohexane. Scratching induced the crystalline product to separate slowly. After standing at room temperature for 2 days, the reddish crystals were collected. The crude product was dissolved in methanol, boiled with Norit, and filtered and the solvent was removed. Recrystallization from cyclohexane gave 6.13 g (50.2%) of the tan, crystalline product, mp 105.5–108°. Further recrystallizations from cyclohexane gave pure, white **5**: mp 107–108.5°; infrared spectrum (Nujol), ketone at 1680, amide at 1650, and C–H bending at 874 and 828 cm^{-1}; ultraviolet spectrum, λ_{max} 234 mμ (ε 14,420), 248 (14,770) and 284 (1250, sh); nmr spectrum, CH_3 at δ 1.87 (singlet, 3) and at 2.59 (singlet, 3), aromatic CH at 7.39 (doublet, 1, J = 8 Hz), 7.78 (singlet, 1.5), and at 7.92 (doublet, 0.5, J = 2 Hz). *Anal.* Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.98; H, 7.31; N, 5.97.

1-Acetyl-8-ethyl-2,3,4,5-tetrahydro-1H-1-benzazepine (6).—A mixture of 465 mg of **5**, 100 mg of 10% palladium on carbon, and 25 ml of 95% ethanol was stirred under hydrogen at 1 atm for 6 hr. Removal of the catalyst followed by evaporation of the solvent gave 440 mg of colorless oil which crystallized on standing. Recrystallization from *n*-hexane gave 350 mg (80.5%) of white, crystalline **6**: mp 58–58.5°; infrared spectrum (Nujol), C=O at 1655 cm^{-1}; ultraviolet spectrum, λ_{max} 266 mμ (ε 460) and 208 (25,180, sh). *Anal.* Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.40; H, 8.71; N, 6.28.

1-Acetyl-2,3,4,5-tetrahydro-1H-1-benzazepine-8-carboxylic Acid (8).—A solution of 5 g of **5** in 25 ml of dioxane was slowly added to a cold (0–5°), stirred solution of sodium hypobromite (prepared from 7.20 g of sodium hydroxide, 75 ml of water, and 10.4 g of bromine). After stirring in an ice bath for 90 min, the mixture was acidified with concentrated hydrochloric acid and diluted with 100 ml of acetone. When the solution became colorless, evaporation *in vacuo* to a small volume caused white crystals to separate. Filtration and drying gave 4.77 g (94.5%) of the crude acid, mp 231–232°. Recrystallization from aqueous acetone gave pure **8**: mp 233.5–234°; infrared spectrum (Nujol), acid OH at 2580, acid C=O at 1712, and amide C=O at 1600 cm^{-1}; ultraviolet spectrum, λ_{max} 223 mμ (ε 18,610) and 276 (950). *Anal.* Calcd for $C_{13}H_{15}NO_3$: C, 66.93; H, 6.48; N, 6.01. Found: C, 66.65; H, 6.37; N, 6.02.

2,3,4,5-Tetrahydro-1H-1-benzazepine-8-carboxylic Acid (9).—A solution of 2.0 g of **8** in 100 ml of 6 *N* hydrochloric acid was refluxed for 50 hr, cooled, and allowed to stand at room temperature for 2 days. Filtration and drying gave 2.06 g of the hydrochloride salt of **9** as white needles, mp 307–312° dec. The salt was dissolved in 75 ml of hot water and the acidity of the solution was adjusted to pH 3 by addition of ammonium hydroxide. The white precipitate which formed on cooling was filtered and dried. Recrystallization from acetonitrile, with hot filtration

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(7) M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *J. Amer. Chem. Soc.*, **80**, 126 (1958); J. W. Huffman, C. B. S. Rao, and T. Kamiya, *J. Org. Chem.*, **32**, 697 (1967).

(8) L. H. Werner and S. Ricca, *J. Amer. Chem. Soc.*, **80**, 2733 (1958).

(9) Boiling points and melting points are uncorrected. Melting points were measured in open capillary tubes on a Mel-Temp apparatus. The infrared spectra were obtained on a Beckman IR 10 recording double-beam infrared spectrophotometer. Nuclear magnetic resonance spectra were obtained in deuteriochloroform using tetramethylsilane as the internal standard. Spectra were recorded on a Varian Associates Model A-60A spectrometer. The spectra data are reported in units of δ and the multiplicity of the resonance signal and the number of protons integrated for the peak are given in parentheses. Ultraviolet spectra were measured in methanol on a Beckman DB spectrophotometer.

through Norit, gave 1.11 g (68%) of crude **9**, mp 176.5–178°. Further recrystallizations from acetonitrile and from water gave pure **9**: mp 186–187°; infrared spectrum (Nujol), N–H at 3200 and C=O at 1680 cm^{-1}; ultraviolet spectrum, λ_{max} 218 mμ (ε 25,800) and 294 (2150). *Anal.* Calcd for $C_{11}H_{13}NO_2$: C, 69.10; H, 6.85; N, 7.33. Found: C, 69.52; H, 6.88; N, 7.30.

1-Azatricyclo[7.2.1.0^{6,11}]dodecan-12-one (10). Method A. From 9.—A solution of 950 mg of **9** in 100 ml of 95% ethanol was stirred in the presence of 1.5 g of 5% ruthenium on carbon under 2000 psig of hydrogen at 160° for 43 hr in a stainless steel autoclave. The catalyst was removed by filtration. Evaporation of the solvent gave 800 mg of colorless oil. The oil was dissolved in 30–60° petroleum ether and filtered through a pad of Norit and the solvent was removed by evaporative distillation to give 760 mg (75.4%) of crude **10** as a coloress oil. Distillation *in vacuo* in a Hickman still gave pure **10**: bp 82° (0.05 mm); infrared spectrum (film), C=O at 1680 cm^{-1}. *Anal.* Calcd for $C_{11}H_{17}NO$: C, 73.70; H, 9.56; N, 7.81. Found: C, 73.40; H, 9.54; N, 7.97.

Method B. From 8.—A solution of 2.33 g of **8** in 200 ml of 95% ethanol containing 1 g of 5% rhodium on carbon was stirred under 1500 psig of hydrogen at 100° for 80 hr in a stainless steel reaction vessel. After cooling and filtering, the solvent was distilled *in vacuo* and the residual oil was dissolved in methylene chloride, washed with saturated brine, dried over sodium sulfate, filtered through a pad of Norit, and evaporated to 1.33 g of colorless gum. The gum was refluxed with 50 ml of concentrated hydrochloric acid for 42 hr, cooled, and filtered to remove 440 mg of **9** hydrochloride, mp 306–309°, which had separated as white needles on standing at room temperature overnight. The aqueous filtrate was evaporated *in vacuo* to a moist gum which was dissolved in 10 ml of water, neutralized to pH 4 with ammonium hydroxide, and evaporated to a white paste. The paste was boiled with methylene chloride and the solvent was separated by decantation; the product was dried and evaporated to give 460 mg of a white froth.

The crude amine was heated under nitrogen for 10 min at 250°, dissolved in methylene chloride, filtered through a pad of Norit, and washed with 5% sodium bicarbonate solution, water, and saturated brine. After drying with sodium sulfate, the solvent was evaporated and the residual yellow oil was dissolved in 30–60° petroleum ether, filtered through a pad of Norit, and evaporated to give 185 mg of colorless oil. Short-path distillation in a bulb-to-bulb distilling tube at 0.04 mm (bath temperature 120°) gave 166 mg (9.25%) of pure **10**, which was identical with the product obtained from **9** by method A.

Registry No.—**4**, 19886-89-6; **5**, 19886-87-4; **6**, 19886-90-9; **8**, 19886-88-5; **9**, 19886-91-0; **10**, 19922-51-1.

Effect of pH on ^{31}P–^{1}H Coupling Constants and ^{1}H Chemical Shifts in Methyl Phosphates[1]

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The effect of pH on the chemical shift of methyl groups bonded to phosphorus has been reported[3] for substituted phosphine oxides, phosphinic acids, and phosphinate esters. The pK values for these compounds were determined by measuring the chemical shift (δ) as a function of sulfuric acid concentration. However, there are no data available on the change in the coupling constant (J_{P-H}) as a function of pH. This report describes the effect of pH on both δ and J_{P-H} for monomethyl and dimethyl phosphates. Both δ and J_{P-H} are pH dependent for monomethyl phosphate (I) and pH independent for dimethyl phosphate (II). The change in δ and J_{P-H} for I occurs between pH 4 and 8 and is due to the ionization of the second proton of the phosphate group.

The spectrum obtained from either I or II consists of two peaks which are due to the splitting of the proton peak of the methyl group by ^{31}P. Below pH 5, the spectra of the two compounds are similar, but, as the pH is raised, the spectrum of II remains unchanged while that of I shifts to higher field and shows a decreased J_{P-H}. Figure 1 shows the dependence of δ and J_{P-H} on pD[4] for both I and II. Tsubori, *et al.*,[5] reported a J_{P-H} of 10.3 Hz for the disodium salt of I and 10.5 Hz for the barium salt of II. They did not report the pH at which their measurements were made and did not investigate the effect of pH on J_{P-H}. Their reported values are somewhat at variance with the values reported here.

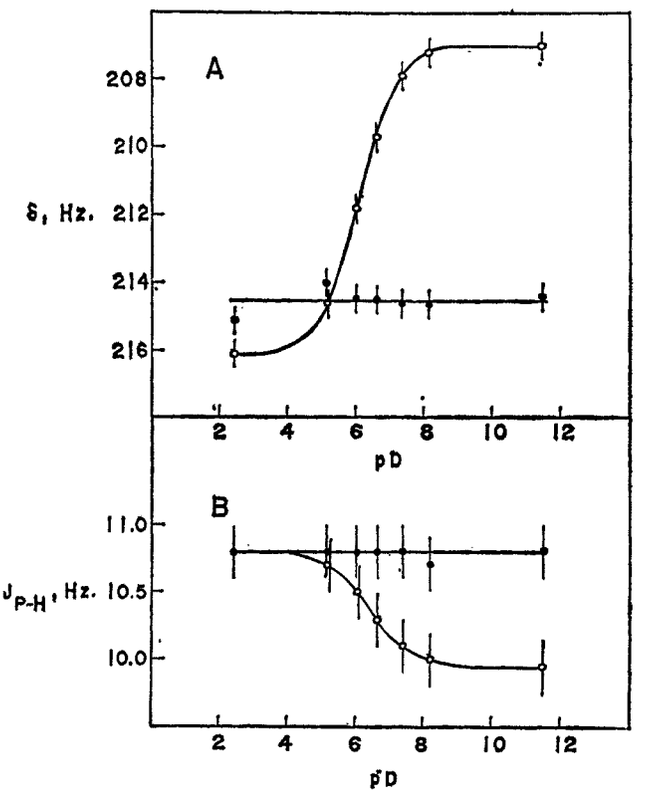

Figure 1.—Dependence of chemical shift and coupling constant on pD. Curve A gives chemical shifts and curve B gives coupling constants for monomethyl phosphate (—○—) and dimethyl phosphate (—●—). Each point represents an average of several determinations at each pH.

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(2) Supported from NIH Training Grant No. GM-255, Sept 1965–Sept 1967. NASA Predoctoral Fellow, 1967–present. This report is from a dissertation to be submitted in partial fulfillment of the requirement for the degree of Doctor of Philosophy in the Faculty of Pure Science, Columbia University.

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