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LACTAMS. XXI.[1] SPECTROSCOPIC CHARACTERIZATION OF 3-, 4-, 5-, AND 6-TERT-BUTYL-1-METHYL-2(1H)-PYRIDONES

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Abstract —— 4-*tert*-Butyl-1-methyl-2(1*H*)-pyridone (II), its 6-*tert*-butyl isomer (IV), and 4-*tert*-butyl-1-(3,4-dimethoxyphenethyl)-2(1*H*)-pyridone (V) were prepared by the alkaline ferricyanide oxidation of the corresponding 1-substituted 4- and 6-*tert*-butylpyridinium ions (X, XI, and XII). Infrared and ultraviolet spectroscopic analysis was found to be a convenient diagnostic method for distinguishing between the four possible positional isomers (I—IV) of *tert*-butyl-1-methyl-2(1*H*)-pyridone.

Of the four possible positional isomers of *tert*-butyl-1-methyl-2(1*H*)-pyridone, the 3-*tert*-butyl (I) and the 5-*tert*-butyl isomer (III) were recently synthesized in our laboratory[2] by the alkaline ferricyanide oxidation of 3-*tert*-butyl-1-methylpyridinium iodide (IX). The 4-*tert*-butyl (II)[3] and the 6-*tert*-butyl isomer (IV)[4] have also been prepared in other laboratories by the ferricyanide oxidation of the corresponding quaternary pyridinium ions [X (sulfate for I^-) and XI] under slightly different conditions, but they were poorly characterized. In addition, the literature[3] in the former case has not described any experimental details. In order to characterize these two isomers fully, we first tried to synthesize them from the corresponding quaternary salts according to our standardized oxidation procedure.[2,5] Treatment of X,[6] prepared by quaternization of 4-*tert*-butylpyridine with MeI, with potassium ferricyanide and KOH at 32°C ± 0.1°C for 5 h furnished II in 81% overall yield (from the pyridine base). A similar oxidation of XI[4,6] gave IV in 64% yield. When 4-*tert*-butyl-1-(3,4-dimethoxyphenethyl)pyridinium bromide (XII), synthesized from 4-*tert*-butylpyridine by quaternization with 3,4-dimethoxyphenethyl bromide, was likewise oxidized, V was produced in 48% overall yield (from 4-*tert*-butylpyridine).

TABLE 1. Nuclear Magnetic Resonance Spectra of Pyridones

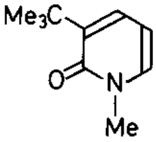
2-Pyridone		Chemical shift (δ)a)						Coupling constant (Hz)				
No.	C-Substituent	C(3)-H	C(4)-H	C(5)-H	C(6)-H	NMe	CMe_3	$J_{3,4}$	$J_{3,5}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$
I b)	3-CMe_3	——	7.25 (d-d)	6.08 (d-d)	7.20 (d-d)	3.52 (s)	1.36 (s)	——	——	7.1	2.0	6.8
II	4-CMe_3	6.65 (d)	——	6.29 (d-d)	7.29 (d)	3.55 (s)	1.24 (s)	——	2.0	——	——	7.1
III c)	5-CMe_3	6.53 (d)	7.42 (d-d)	——	7.09 (d)	3.54 (s)	1.24 (s)	9.5	——	——	3.0	——
IV	6-CMe_3	6.49 (d-d)	7.25 (d-d)	6.23 (d-d)	——	3.69 (s)	1.46 (s)	9.0	1.5	7.3	——	——
V	4-CMe_3	6.54 (d)	——	6.04 (d-d)	6.79 (d)	——	1.22 (s) d)	——	2.1	——	——	7.2

a) Measured in $CDCl_3$ at 4% (w/v) concentration and expressed in ppm downfield from internal Me_4Si. The letter in parentheses designates the multiplicity of the signal with the abbreviations appeared at the top of "Experimental".

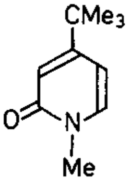
b) The previously reported nmr data[2] of I should be superseded by the present ones.

c) From ref. 2.

d) In addition, signals at δ 2.99 (2H, t, J = 7.0 Hz, $ArCH_2$), 3.78 and 3.86 (3H each, s, MeO's), 4.08 (2H, t, J = 7.0 Hz, NCH_2), and 6.5–6.9 (3H, m, aromatic protons) were observed.



I



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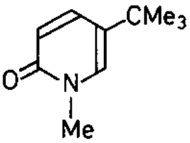

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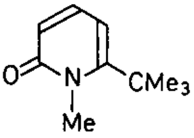

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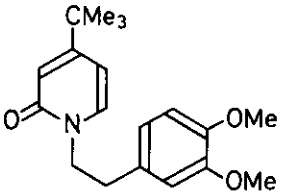

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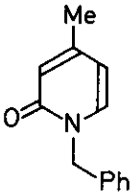

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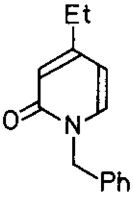
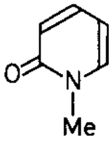


VII



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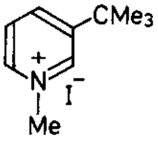
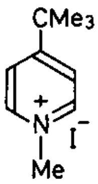
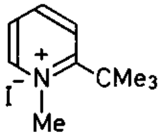


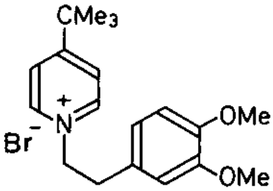
IX



X



XI



XII

The structures of the pyridones thus obtained were confirmed on the basis of their nmr spectral data assembled in Table 1.

Now that all the four possible positional isomers (I–IV) are available, we are able to examine whether any convenient diagnostic method exists for distinguishing between them. It may be seen from Table 2 that the 3-tert-butyl (I) and the 6-tert-butyl isomer (IV) are unique in that their C=O stretching vibrations are lowered from the ν_{CO} of VIII[7] by ca. 10 cm^{-1}. The 6-tert-butyl isomer (IV) is then differentiated from the 3-tert-butyl isomer (I) by a bathochromic shift of the long-wavelength uv band of IV by 6 nm relative to the 303 nm band of VIII and by a hypsochromic shift of that of I by 2 nm. Since the 4-tert-butyl (II) and the 5-tert-butyl isomer (III) undergo similar hypsochromic and bathochromic shifts, this sets up a convenient distinction between them. 4-Methyl- (VI)[1] and 4-ethyl-1-benzyl-2(1H)-pyridone (VII)[8] are found to embody the same spectroscopic feature as the 4-tert-

TABLE 2. Ultraviolet and Infrared Spectra of Pyridones

2-Pyridone		Ultraviolet spectrum[a]					Infrared spectrum[b] [ν_{max} (cm^{-1})]	
		Short-wavelength band		Long-wavelength band				
No.	C-Substituent	λ_{max} (nm)	log ε	λ_{max} (nm)	log ε	$\Delta\lambda_{max}$[c] (nm)	C=O	$\Delta\nu_{CO}$[d]
I[e]	3-CMe_3	233	3.75	301	3.83	−2	1650	−11
II	4-CMe_3	230.5	3.77	298	3.72	−5	1658	−3
III[e]	5-CMe_3	230	3.96	309	3.75	+6	1663	+2
IV	6-CMe_3	230	3.78	309.5	3.89	+6.5	1652	−9
V	4-CMe_3	230.5	4.12	301	3.75[f]	−2	1658	−3
VI	4-Me	232 (sh)	3.74	301	3.73	−2	1664[g]	+3
VII	4-Et	232 (sh)	3.71	301	3.71[h]	−2	1660	−1
VIII	——	229	3.82	303	3.71	0	1661	0

a) Measured in abs. EtOH. *b*) Determined in $CHCl_3$ solution at 0.2 M concentration. *c*) Deviation of λ_{max} from that of VIII. *d*) Deviation of ν_{CO} from that of VIII. *e*) From ref. 2b. *f*) In addition, a medium-wavelength band was observed at 287 nm (log ε 3.82). *g*) From ref. 1. *h*) Data obtained in 95% aq. EtOH was reported in ref. 8.

butyl analogues II and V do. It is also noteworthy that on tlc analysis using alumina or silica gel and various solvent systems the mobility decreases in going through the series 3- (I) >> 6- (IV) > 4- (II) ≥ 5-*tert*-butyl isomer (III). Thus, the above spectroscopic and chromatographic features may find ways to be utilized as criteria for distinguishing between 1,3-, 1,4-, 1,5-, and 1,6-dialkyl-2(1*H*)-pyridones.

EXPERIMENTAL

General Notes —— All melting points are corrected; boiling points are uncorrected. Unless otherwise noted, see ref. 1 for details of instrumentation and measurements. The following abbreviations are used: d = doublet, d-d = doublet-of-doublets, m = multiplet, s = singlet, sh = shoulder, t = triplet. Microanalyses were performed by

Mr. Y. Itatani and his associates at Kanazawa University.

4-(1,1-Dimethylethyl)-1-methylpyridinium Iodide (X) —— A solution of 4-*tert*-butylpyridine (1.37 g, 10 mmol) and MeI (2.9 g, 20 mmol) in dry benzene (4 ml) was stirred at room temp. for 6 h. The reaction mixture was extracted with H_2O (50 ml), and the aqueous extracts were washed with benzene and concentrated *in vacuo* to leave X as a yellowish thick oil (lit.[6] mp 124–125°C). The oil was directly used in the next oxidation step without purification.

1-(3,4-Dimethoxyphenethyl)-4-(1,1-dimethylethyl)pyridinium Bromide (XII) —— A stirred solution of 4-*tert*-butylpyridine (1.08 g, 8 mmol) and 3,4-dimethoxyphenethyl bromide (2.16 g, 8.8 mmol) in dry benzene (10 ml) was heated under reflux for 20 h. The reaction mixture was worked up as described above for X, giving XII as a yellowish thick oil. The oil was directly used in the next oxidation reaction without purification.

4-(1,1-Dimethylethyl)-1-methyl-2(1*H*)-pyridone (II) —— The total amount of the crude salt X described above was oxidized with potassium ferricyanide and KOH at 32°C ± 0.1°C for 5 h according to the previously reported[2,5] standard procedure, and II (81% yield from 4-*tert*-butylpyridine) was obtained as a hygroscopic solid, bp 131°C (4 mmHg); MS *m/e*: 165 (M^+); other spectra (see Tables 1 and 2).

6-(1,1-Dimethylethyl)-1-methyl-2(1*H*)-pyridone (IV) —— The quaternary salt XI[6] was oxidized in a manner similar to that described above for II, producing IV (64% yield) as a colorless solid, mp 47–48°C; bp 120°C (bath temp.) (1 mmHg); MS *m/e*: 165 (M^+); other spectra (Tables 1 and 2). *Anal*. Calcd. for $C_{10}H_{15}NO$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.41; H, 9.24; N, 8.45.

1-(3,4-Dimethoxyphenethyl)-4-(1,1-dimethylethyl)-2(1*H*)-pyridone (V) —— The total amount of the crude salt XII described above was oxidized as described above for II. The pyridone V obtained in 48% yield (from 4-*tert*-butylpyridine) was recrystallized from AcOEt–hexane (1 : 3, v/v) to afford an analytical sample as colorless scales, mp 118–119°C; nmr, uv, and ir spectra (Tables 1 and 2). *Anal*. Calcd. for $C_{19}H_{25}NO_3$: C, 72.35; H, 7.99; N, 4.44. Found: C, 72.33; H, 7.74; N, 4.30.

Chromatographic Behavior of the Pyridones I–IV —— On tlc analysis using Al_2O_3 and AcOEt–hexane (2 : 1, v/v), AcOEt–ether (1 : 1, v/v), AcOEt–benzene (1 : 1, v/v), $CHCl_3$–EtOH (20 : 1, v/v), or benzene–EtOH (20 : 1, v/v), the mobilities of the pyridones were found to decrease in the order of I >> IV > II ≥ III. The same mobility order was observed when the pyridones I–IV were run on a silica gel tlc plate with AcOEt–EtOH (20 : 1, v/v), $CHCl_3$–EtOH (20 : 1, v/v), ether–EtOH (10 : 1, v/v), benzene–MeOH (10 : 1, v/v), ether–AcOH (20 : 1, v/v), or AcOEt.

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