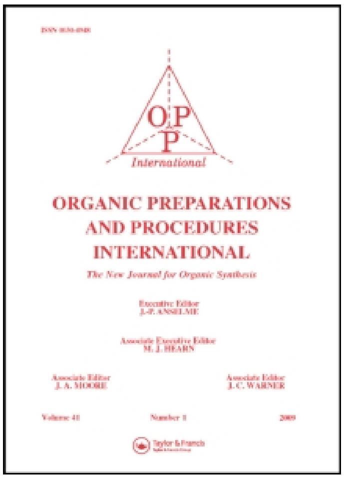

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A CONVENIENT METHOD FOR THE PREPARATION OF N-SUBSTITUTED 2(1H)-PYRIDONES

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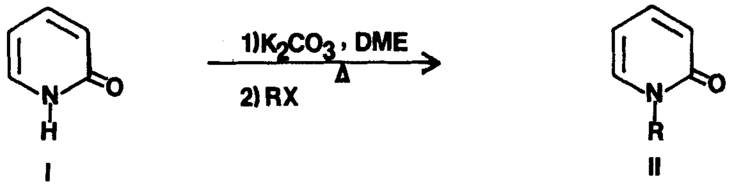
N-Alkyl-, aryl-, and aralkyl-2(1H)-pyridones have been screened for their biological activity.[1-5] Previous procedures for the preparation of the pyridone derivatives require the cumbersome use of alkali metals or of expensive silver or of toxic mercury reagents. Treatment of the sodium and potassium salts[6] of 2(1H)-pyridone with alkyl halides gave the corresponding N-alkyl-2(1H)-pyridones (IIa-f) albeit in only moderate yields. Gautier and Renault[7] extended this procedure to include the N-decyl-2(1H)-pyridone (IIg).



Hopkins and coworkers[8] employed both alkali metals and silver carbonate, in a variety of polar and nonpolar solvents, to study the effect of these reaction conditions on the alkylation of the ambident anion. Kaye and Chang[9] prepared N-alkenyl-2(1H)-pyridones using mercuric acetate to generate the ambident anion. We now report a convenient procedure for the synthesis of N-alkyl- or N-aralkyl-2(1H)-pyridones (IIa-g).

The potassium salt of 2(1H)-pyridone was generated by reacting 2(1H)-pyridone (I) with potassium carbonate in 1,2-dimethoxyethane (DME). When the mixture was treated with methyl iodide, an excellent yield (85%) of N-methyl-2(1H)-pyridone (IIa) was obtained. The product had GLC retention time, IR and ^{13}C nmr spectra identical to those of an authentic sample.[10] Similarly, in situ reactions of the ambident anion with other alkyl or aralkyl halides led to the formation of the N-substituted-2(1H)-pyridones (II) (TABLE 1). All of these pyridones have been prepared previously[6,7] and their physical properties and infrared and ^{13}C nmr spectra were consistent with the assigned structures.

TABLE 1. N-Substituted-2(1H)-pyridones (II)

II	R	Yield[1]	bp.(mp.)	$\delta^{13}C(C{=}O)$(ppm)
a	CH_3	85	$75\text{-}78^{0.5}$	162.939
b	Et	82	$95\text{-}98^{0.3}$	162.337
c	n-Pr	87	$109\text{-}112^{0.3}$	162.446
d	iso-Pr	46	$79.5\text{-}82.5^{0.1}$	162.118
e	n-Bu	86	$108\text{-}110^{0.3}$	162.446
f	$PhCH_2$	88	$144.5\text{-}147^{0.5}$(72.5-74)	162.282
g	n-Decyl	89	$173\text{-}176^{0.3}$	162.337

1) All yields are of isolated material.

EXPERIMENTAL

Melting points are corrected. Infrared spectra were measured with a Beckman Model IR-8 Grating Spectrometer; the IR bands are given in cm^{-1}. The ^{13}C nmr spectra were recorded on a JEOL PFT-100 Spectrometer, as 95% $CDCl_3$ - 5% tetramethylsilane solutions; all chemical shifts are given in the δ scale. Gas chromatographic analyses were performed on a Varian Aerograph Series 1520 Gas Chromatograph, using a 6 foot by 1/4 inch stainless steel column packed with 3% OV-1 on Gas Chrom Q (100/120 mesh).

N-Methyl-2(1H)-pyridone (IIa).--2(1H)-Pyridone (10.0g; 0.105 mole) and anhydrous potassium carbonate (29.0g; 0.210 mole) were covered with

1,2-dimethoxyethane (DME; 150 ml). To the vigorously stirred mixture, heated to reflux was added methyl iodide (62.3 ml; 141.94g; 1.0 mole) over a period of 3 hrs. The mixture was stirred at reflux for 8 hrs, filtered hot and the filter cake washed with several small portions of DME (100 ml). Removal of the solvent _in vacuo_ left a red oil which was distilled _in vacuo_, giving 9.76g (85%) of IIa, bp. 75-78° (0.5mm), lit.[6] 134-5/16mm.

IR (film): 1644.7 (C=O); ^{13}C NMR: 162.939 (C_2), 120.314 (C_3), 138.559 (C_4), 105.741 (C_5), 139.545 (C_6), 37.365 ($N-CH_3$).

Similarly, a slight excess of ethyl iodide gave 82% of N-ethyl-2(1H)-pyridone (IIb),[6] bp. 95-98° (0.3mm).

IR (film): 1644.7 (C=O); ^{13}C NMR: 162.337 (C_2), 120.752 (C_3), 137.299 (C_4), 106.069 (C_5), 139.326 (C_6), 44.652 ($N-CH_2-$).

N-_n_-Propyl-2(1H)-pyridone (IIc),[6] 87%, bp. 109-112° (0.3mm).

IR (film): 1644.7 (C=O); ^{13}C NMR: 162.446 (C_2), 120.752 (C_3), 137.846 (C_4), 105.631 (C_5), 139.216 (C_6), 51.226 ($N-CH_2-$).

N-Isopropyl-2(1H)-pyridone (IId),[6] 46%, bp. 79.5-82.5° (0.1mm). In addition, approximately 30% of 2-isopropyloxypyridine was observed.

IR (film): 1642 (C=O); ^{13}C NMR: 162.118 (C_2), 120.479 (C_3), 138.504 (C_4), 106.179 (C_5), 139.490 (C_6), 46.186 (N-CH-).

N-_n_-Butyl-2(1H)-pyridone (IIe),[6] 86%, bp. 108-110° (0.3mm).

IR (film): 1647.4 (C=O); ^{13}C NMR: 162.446 (C_2), 120.752 (C_3), 137.792 (C_4), 105.686 (C_5), 139.216 (C_6), 49.418 ($N-CH_2-$).

N-Benzyl-2(1H)-pyridone (IIf),[6] 88%, bp. 144.5-147° (0.5mm), recrystallized from carbon tetrachloride giving white needles mp. 72.5-74°C. In addition, approximately 10% of 2-benzyloxypyridine was observed.

IR (KBr): 1644.7 (C=O); ^{13}C NMR: 162.282 (C_2), 120.752 (C_3), 137.463 (C_4), 105.686 (C_5), 139.216 (C_6), 51.665 (N-CH_2-).

N-n-Decyl-2(1H)-pyridone (IIg),[7] 89%, bp. 173-176° (0.3mm).

IR (film): 1652.9 (C=O); ^{13}C NMR: 162.337 (C_2), 120.752 (C_3), 137.846 (C_4), 105.576 (C_5), 139.107 (C_6), 49.692 (N-CH_2-).

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