A Convenient Synthesis of *m*-Aminophenols by Mercury(II) Acetate Oxidation of 3-Amino-2-cyclohexenones

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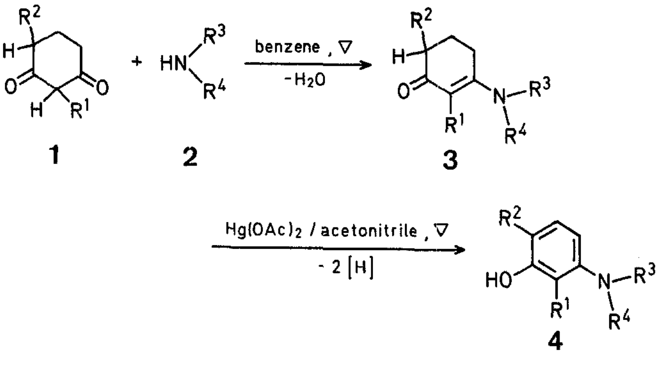
Both abilities to interact readily with soft nucleophiles and to act as oxidizing agent are significant properties of compounds containing mercury, thallium, and lead. Such compounds have been utilized in a wide variety of synthetic processes, and this has also led to a better knowledge of the interesting chemistry of these metals[1]. Mercury(II) salts with oxidizing ability have been extensively used as versatile dehydrogenating agents, in particular, for the dehydrogenation of tertiary amines[2]. However, the reaction of enamines with mercury(II) salts such as mercury(II) acetate has only been little studied; the reaction involves the introduction of an oxygen functionality into the β-position with respect to the amino group, thus giving rise to an acetoxyiminium salt[3,4].

In continuation of our work on conjugated enamines[5], we have now studied the behavior of 3-amino-2-cyclohexenones (cyclic 3-oxoenamines) towards mercury(II) acetate. Contrary to our expectation, no oxygenated product was obtained in any case but aromatization took place to give *m*-aminophenols which are important as intermediates in the synthesis of rhodamine dyes.

The 3-amino-2-cyclohexenones (**3**) are readily available by condensation of 1,3-cyclohexanediones (**1**) with primary or secondary amines (**2**) in boiling benzene with azeotropic removal of water. On treatment of the aminoenones **3** thus obtained with equimolar amounts of mercury(II) acetate in boiling acetonitrile, oxidative aromatization occurs to give the corresponding 3-aminophenols (**4**). Compounds **4** were characterized by microanalyses and by their spectral data which were fully consistent with the assigned structures.

The present method compares favorably with known procedures[6,7] for the synthesis of *m*-aminophenols because of the ease of performance and the ready availability of the 1,3-cyclohexanediones[8] used as starting materials.



Melting points were obtained with a Yanagimoto micro apparatus and are uncorrected. Mass spectra were obtained using a Hitachi KMU-7L double-focusing spectrometer at 70 eV. I.R. spectra were determined on a Hitachi 215 spectrophotometer. ^{1}H-N.M.R. spectra were recorded on a Varian T-60 spectrometer.

3-Propylamino-2-cyclohexenone (3b); Typical Procedure:

A mixture of 1,3-cyclohexanedione (**1**; $R^1=R^2=H$; 2.24 g, 20 mmol) and propylamine (**2**; $R^3=H$, $R^4=n\text{-}C_3H_7$; 1.18 g, 20 mmol) in benzene (200 ml) is heated under reflux with azeotropic removal of water using a Dean-Stark apparatus for 5 h. The solvent is then evaporated and the residue distilled under vacuum to give **3b** as a colorless oil; yield: 2.35 g (87%); b.p. 159-161 °C/0.07 torr; the product solidifies on standing; m.p. 61-63 °C.

$C_9H_{15}NO$	calc.	C 70.55	H 9.87	N 9.14
(153.2)	found	70.37	9.82	8.99

I.R. ($CHCl_3$): $\nu=3420$, 1605 (C=O); 1580 cm^{-1} (C=C).

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta=0.95$ (t, 3H, $J=6$ Hz); 1.45-2.53 (m, 8H); 3.05 (q, 2H, $J=6$ Hz); 5.08 (s, 1H); 6.60 ppm (br s, 1H).

6-Methyl-3-pyrrolidino-2-cyclohexenone (3g):

Prepared in an analogous manner; yield: 68%; b.p. 179-180 °C/0.45 torr.

$C_{11}H_{17}NO$	calc.	C 73.70	H 9.56	N 7.81
(179.3)	found	73.55	9.61	7.87

I.R. film: $\nu=1600$ (C=O); 1550 cm^{-1} (C=C).

3-Aminophenols (4); General Procedure:

A mixture of the 3-amino-2-cyclohexenone **3** (1 mmol) and mercu-

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Table 1. Preparation of 3-Aminophenols (**4**) from 3-Amino-2-cyclohexenones[a] (**3**)

4	R¹	R²	R³	R⁴	Reaction time [h]	Yield[b] [%]	m.p. or b.p./torr [°C]	Molecular formula[c] or Lit. data [°C]	M.S. *m/e* (relative intensity, %)
a	H	H	H	H	20	56	m.p. 121–122°	m.p. 122°[6]	
b	H	H	H	*n*-C_3H_7	10	78	b.p. 117–118°/2.4	$C_9H_{13}NO$ (151.2)	151 (M^+, 34); 122 (100)
c	H	H	H	—CH_2—C_6H_5	16	75	b.p. 174–176°/2	$C_{13}H_{13}NO$ (199.3)	199 (M^+, 42); 91 (100); 85 (35); 83 (63)
d	H	H	H	—C_6H_4—OCH_3(3)	20	35	[d]	$C_{13}H_{13}NO_2$ (215.3)	215 (M^+, 100)
e	H	H	H	—C_6H_4—OCH_3(4)	20	32	[d]	$C_{13}H_{13}NO_2$ (215.3)	215 (M^+, 22); 200 ($M^+ - 15$, 100)
f	H	H	—$(CH_2)_4$—		12	73	m.p. 134°[e]	$C_{10}H_{13}NO$ (163.2)	163 (M^+, 74); 162 ($M^+ - 1$, 100); 107 (41)
g	H	CH_3	—$(CH_2)_4$—		14	68	m.p. 160–161°[e]	$C_{11}H_{15}NO$ (177.2)	177 (M^+, 88); 176 ($M^+ - 1$, 100); 121 (40)
h	CH_3	H	—$(CH_2)_4$—		14	61	[d]	$C_{11}H_{15}NO$ (177.1154)[f]	177 (M^+, 74); 176 ($M^+ - 1$, 100); 148 (53); 134 (25); 113 (37)

[a] Ketones **3** are known compounds except for **3b** and **3g**.
[b] Yield of isolated product. All products are pure according to T.L.C. analysis (silica gel, benzene/chloroform).
[c] The microanalyses were in satisfactory agreement with the calculated values: C, ±0.22; H, ±0.18; N, ±0.21.
[d] A liquid purified by column chromatography on silica gel using benzene and then benzene/chloroform (75/25, v/v) as eluents.
[e] Purified by column chromatography on silica gel using the same solvent system as above followed by sublimation.
[f] High resolution mass spectrometry; −0.0014.

Table 2. I.R.- and ¹H-N.M.R.-Spectral Data of Compounds **4**

4	I.R. ($CHCl_3$) ν [cm^{-1}]	¹H-N.M.R. ($CDCl_3$/TMS) δ [ppm]
b	3570, 3400, 1610, 1585	0.94 (t, 3H, $J=7$ Hz); 1.25–1.74 (m, 2H); 3.00 (t, 2H, $J=7$ Hz); 6.09–7.12 (m, 3H_{arom})
c	3570, 3380, 1610, 1585	4.10 (s, 2H); 7.19 (s, 5H_{arom}); 6.01–7.03 (m, 4H_{arom})
d	3570, 3400, 2820, 1585	3.68 (s, 3H); 6.34–7.28 [m, 10H (8H_{arom}, and OH and NH)]
e	3570, 3400, 2825, 1595	3.76 (s, 3H); 6.17–7.12 (m, 8H_{arom})
f	3565, 3300, 1605, 1565	1.83–2.06 (m, 4H); 3.12–3.33 (m, 4H); 6.05–7.18 (m, 4H_{arom})
g	3575, 3320, 1610, 1560	1.81–2.04 (m, 4H); 2.13 (s, 3H); 3.08–3.29 (m, 4H); 6.02–6.69 (m, 3H_{arom})
h	3575, 3350, 1600, 1575	1.72–2.09 (m, 4H); 2.18 (s, 3H); 2.99–3.53 (m, 4H); 6.10–7.00 (m, 3H_{arom})

ry(II) acetate (1 mmol) in acetonitrile (70 ml) is heated under reflux for the time indicated in Table 1. After cooling to room temperature, the mixture is filtered through Celite and the filtrate evaporated under reduced pressure to remove the solvent. The residue is purified either by distillation in vacuo or by column chromatography on silica gel to give the product **4**.

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[1] E. Negishi, *Organometallics in Organic Synthesis*, Vol. 1, John Wiley & Sons, New York, 1980, p. 455.

[2] L. F. Fieser, M. Fieser, *Reagents for Organic Synthesis*, Vol. 1, John Wiley & Sons, New York, 1967, p. 647.

[3] N. J. Leonard, L. A. Miller, P. D. Thomas, *J. Am. Chem. Soc.* **78**, 3463 (1956).

[4] In similar reaction, lead(IV) acetate works less satisfactorily as oxidizing agent to give a complex mixture of acetylated products [F. Corbani, B. Rindone, C. Scolastico, *Tetrahedron* **29**, 3253 (1973)], whereas the analogous oxidation with thallium(III) acetate is preparatively useful and leads to the formation of α-acetoxyketones [M. E. Kuehne, T. J. Giacobbe, *J. Org. Chem.* **33**, 3359 (1968)].

[5] Preceding paper: H. Iida, Y. Yuasa, C. Kibayashi, *J. Chem. Soc. Chem. Commun.* **1981**, 114.

[6] For the preparation of 3-aminophenol (**4a**), see: A. R. Forrester, J. L. Wardell, *Rodd's Chemistry of Carbon Compounds*, 2nd Edn., S. Coffey, Ed., Vol. III/A, Elsevier, Amsterdam, 1971, p. 354; and references cited therein.

[7] For a recent convenient method for the preparation of substituted *m*-aminophenols, see: H. Böhme et al., *Justus Liebigs Ann. Chem.* **1980**, 394.

[8] For the preparation of substituted cyclic β-diketones, see:
For 2-substituted cyclohexane-1,3-diones: A. B. Mekler, S. Ramachandran, S. Swaminathan, M. S. Newman, *Org. Synth. Coll. Vol.* V, 743 (1973).
For 4-substituted cyclohexane-1,3-diones: E. G. Meek, J. H. Turnbull, W. Wilson, *J. Chem. Soc.* **1953**, 811.
For 5-substituted cyclohexane-1,3-diones: V. Kvita, J. Weichet, *Chem. Listy* **51**, 380 (1957); *C. A.* **51**, 9502 (1957).

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