Tetrahedron Letters,Vol.23,No.35,pp 3591-3594,1982 0040-4039/82/353591-04$03.00/0
Printed in Great Britain

ONE-STEP SYNTHESIS OF 4-AMINODIHYDROBENZOFURANS AND 4-HYDROXYINDOLES VIA DEHYDROGENATION-HETEROMERCURATION OF 2-ALLYL-3-AMINOCYCLOHEXENONES USING MERCURY(II) ACETATE

Hideo Iida, Yoshifumi Yuasa, and Chihiro Kibayashi*

Tokyo College of Pharmacy, Horinouchi, Hachioji, Tokyo 192-03, Japan

Summary: On treatment of the 2-allyl-3-aminocyclohexenones with mercury(II) acetate, either sequence, dehydrogenation–oxymercuration or dehydrogenation–aminomercuration, occurred depending on the nature of the amino group in the substrate to yield the dihydrobenzofurans or indoles, respectively.

Mercury(II) salts, such as $Hg(OCOCH_3)_2$ and $Hg(OCOCF_3)_2$, react directly with olefins in the presence of active hydrogen compounds (HY) to produce a wide variety of β-heterosubstituted organomercurials (eq 1).[1] This type of reactions valuable for the Markownikoff functionalization of olefins has been referred to as "solvomercuration" and can be rationalized as involving electrophilic attack of mercury(II) on the double bond generating the positively charged species (*vide infra*) followed by trapping by nucleophilic attack by HY.

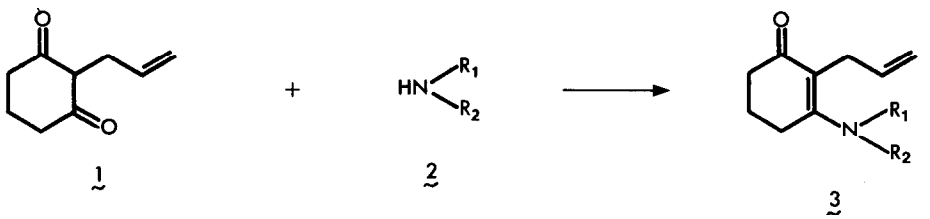
$$RCH_2{=}CH_2 + HgX_2 + HY \longrightarrow \overset{Y}{\underset{|}{}}RCHCH_2HgX + HX \qquad (1)$$

Alternatively, the oxidation potential for Hg(II) indicates that these salts can act as good oxidizing agents.[1b] Thus mercury(II) salts have been extensively used as versatile dehydrogenation agents particularly for the dehydrogenation of tertiary amines.[2]

In continuation of our work on organometallic chemistry of enaminones aimed toward the synthesis of heterocyclic compounds,[3,4] we wish to report here a new, general one-step procedure providing nitrogen- and oxygen-containing heterocycles from 2-allylated cyclic enaminones using mercury(II) acetate, which combines both significant features associated with mercury(II) salts as described above.

For the preparation of the cyclic enaminones with the 2-allyl group as substrates, a solution of 2-allylcyclohexane-1,3-dione (1) and the primary or secondary amine 2 in benzene was heated at reflux for 3–6 h to give the 2-allylenaminone 3 (Table I).

Treatment of the tertiary enaminone 3a with mercury(II) acetate (2.5 equiv) in acetonitrile (reflux, 20 h), followed by purification by column chromatography (silica gel, chroloform) afforded the mercurated dihydrobenzofuran 4 (mp 112–113 °C) in 76% yield.

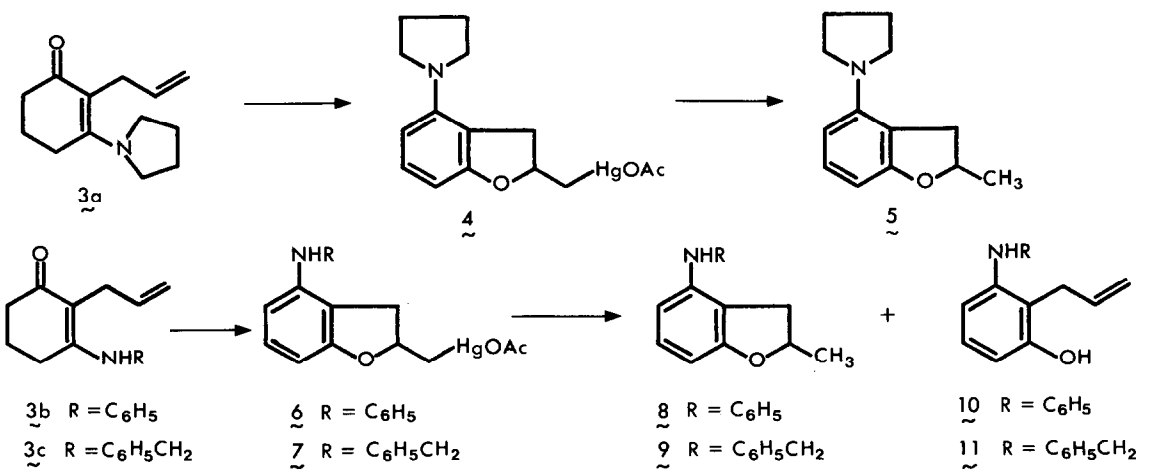


1 + 2 → 3

Table I. Preparation of N-Substituted 2-Allyl-3-aminocyclohex-2-en-1-ones

compound	R_1	R_2	% yield	bp, °C/mm or mp, °C
3a		$-(CH_2)_4-$	79	bp 136–138°/0.3
3b	H	C_6H_5	77	mp 116–117°
3c	H	$C_6H_5CH_2$	90	mp 97–99°
3d	H	C_2H_5	80	mp 95–96°
3e	H	n-C_3H_7	95	bp 118–120°/0.12
3f	H	3,4-$(CH_3O)_2C_6H_3(CH_2)_2$	92	mp 104–105°

Demercuration of 4 with $NaBH_4$ in 3*M* sodium hydroxide furnished the dihydrodibenzofuran 5 (oil) in 42% yield. Similar treatment of the N-phenyl- or N-benzylenaminones (3b or 3c) with mercury(II) acetate gave the corresponding mercurated dihydrobenzofuran 6 (mp 106–108 °C) or 7 (mp 136–140 °C) in 71 or 75% yield, respectively. When 6 was treated with $NaBH_4$ in similar manner for 4, the dihydrobenzofuran 8 (mp 86–88 °C) was obtained in 36% yield along with the allyl compound 10 (oil) in 30% yield. Similarly, treatment of 7 with $NaBH_4$ gave 9 (oil) and 11 (oil) in 38 and 32% yield, respectively.

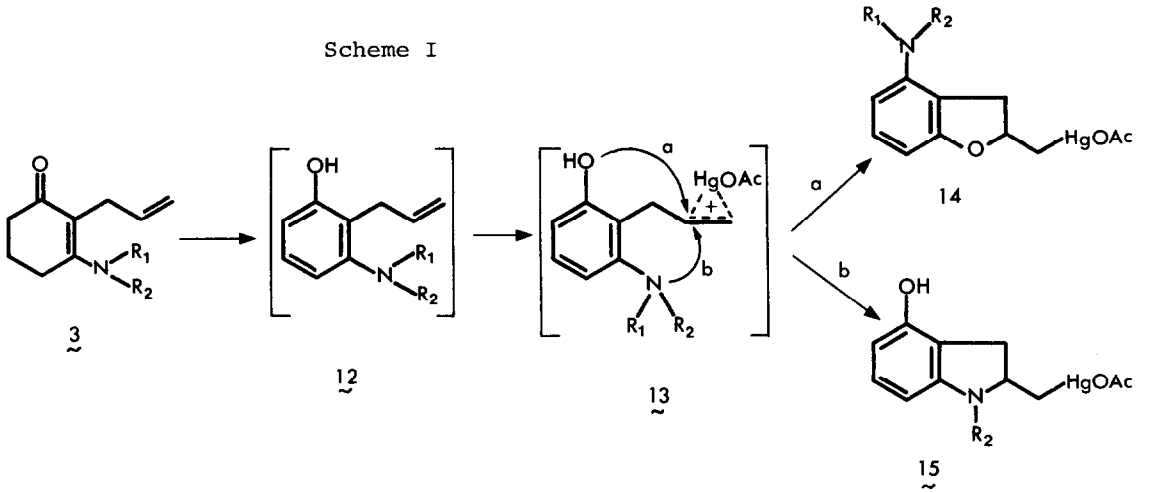


3a → 4 → 5

3b R = C_6H_5; 3c R = $C_6H_5CH_2$ → 6 R = C_6H_5; 7 R = $C_6H_5CH_2$ → 8 R = C_6H_5; 9 R = $C_6H_5CH_2$ + 10 R = C_6H_5; 11 R = $C_6H_5CH_2$

These results indicate that the allylenaminone 3 initially undergoes dehydrogenation to generate the *m*-aminophenol 12 which is rather unexpected since in the case of enamines, hydroxylation has been recognized on treatment with mercury(II) acetate.[5] Subsequent electrophilic attack of Hg(II) at the double bond in 12 forms mercurinium ion intermediate 13 which is subject to oxymercuration (path a in Scheme I) producing the mercurial 14.

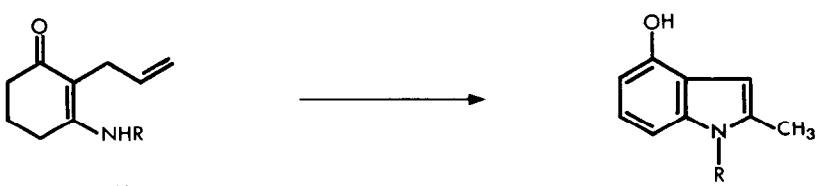
Scheme I



3 12 13

In view of the above discussion, there is an alternative possibility that the mercurinium ion 13 (R_1 = H) can be subject to nucleophilic capture by the neighboring amino group (path b) leading to the formation of the indole derivative 15. Such a pathway via aminomercuration is expected to be predominant in competition with oxymercuration, when the less hindered secondary (or primary) amino group with enhanced nucleophilisity is employed.

Thus the enaminones prepared with aliphatic primary amines, such as ethyl-, propyl-, and 3,4-dimethoxyphenylethylamines, were used as substrates. On treatment of these enaminones 3d, 3e, and 3f with mercury(II) acetate in the same manner as described above for 3a, the corresponding 2-methyl-4-hydroxyindoles 16 (mp 101–103 °C), 17 (oil), and 18 (mp 100–101 °C) were obtained in 78, 81, and 54% yield, respectively.



3d R = C_2H_5

3e R = C_3H_7

3f R = 3,4-$(CH_3O)_2C_6H_3(CH_2)_2$

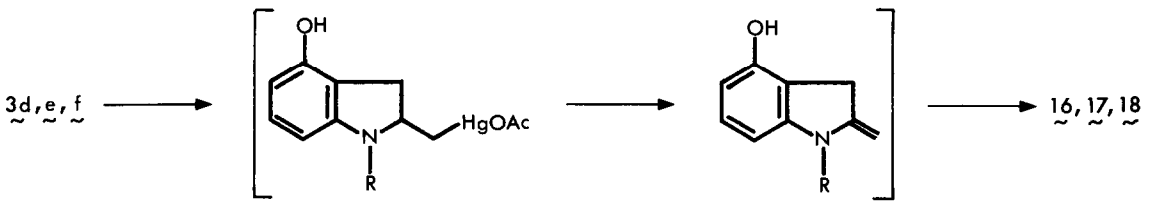
16 R = C_2H_5

17 R = C_3H_7

18 R = 3,4-$(CH_3O)_2C_6H_3(CH_2)_2$

These reactions apparently proceed via predominant pathway involving aminomercuration (path b) outlined in Scheme I rather than oxymercuration (path a). Subsequently, the resultant mercurated dihydroindole should undergo in situ β-elimination presumably via an *E2* type oxydative demercuration process[6] followed by spontaneous isomerization to effect aromatization to the indoles (Scheme II).

Scheme II



In conclusion, the reaction of the allylenaminones with the mercury(II) salt provides a versatile one-step procedure for the formation of the dihydrobenzofuran and indole derivatives, unlike the previous work[7] on similar reactants using a palladium(II) salt.

References

1. For recent reviews, see: (a) R. C. Larock, *Angew. Chem. Int. Ed.*, 1978, *17*, 27. (b) E. Negishi, "Organometallics in Organic Synthesis", Vol. 1, Wiley, New York, 1980, p 455.
2. L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley, New York, 1967, p 647.
3. H. Iida, Y. Yuasa, and C. Kibayashi, *J. Org. Chem.*, 1980, *45*, 2938.
4. H. Iida, Y. Yuasa, and C. Kibayashi, *J. Chem. Soc. Chem. Commun.*, 1981, 114.
5. N. J. Leonard, L. A. Miller, and P. D. Thomas, *J. Am. Chem. Soc.*, 1956, *78*, 3463.
6. M. F. Grundon, D. Stewart, and W. E. Watts, *J. Chem. Soc. Chem. Commun.*, 1975, 772.
7. On palladium(II) catalized reaction of allylenaminones, some acridines have been obtained (see lit. 4).

(Received in Japan 20 May 1982)