A NOVEL RING CONTRACTION OF LUMAZINES TO THEOPHYLLINES

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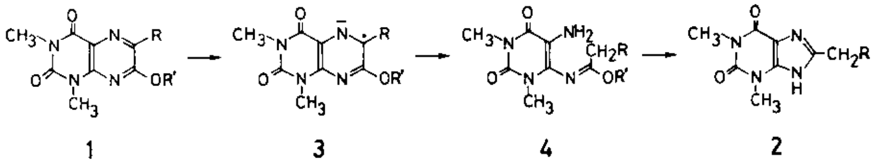
Abstract ——— An unusual ring contraction of 7-methoxy-1,3-dimethyllumazines proceeded by an activated aluminum in methanolic ammonia to give 8-alkyltheophyllines.

Reduction of heterocyclic compounds by cathodic electrons[1,2] has often caused a ring cleavage or contraction. Here is described an unusual ring contraction of 1,3-dimethyllumazines (**1**) into theophyllines (**2**) by an activated aluminum.

Reduction of 7-methoxy-1,3-dimethyllumazine (**1a**) by aluminum treated with mercuric chloride in methanolic ammonia afforded 8-methyltheophylline (**2a**). The 8-methyl carbon atom of **2a** is originated from the C-6 atom of **1a**, since the reduction of the 7-ethoxy and 6-alkyl analogues (**1b-e**) gave the respective theophyllines (**2a-d**). However, 8-hydroxy-1,3-dimethyllumazine (1f) gave no theophylline but decomposition products.

It is likely that the ring contraction proceeded via a radical anion 3 and a ring cleaved iminoether **4** by successive electron addition, because a deep violet color developed at an early stage of the reaction and **1c** remained unchanged on attempted



	R	R'
a :	H	CH_3
b :	H	CH_2CH_3
c :	CH_3	CH_3
d :	CH_2CH_3	CH_3

	R	R'
e :	$CH(OH)CH_3$	CH_3
f :	CH_3	H
g :	$CO_2CH_2CH_3$	CH_3
h :	$COCH_3$	CH_3

	R
a :	H
b :	CH_3
c :	CH_2CH_3
d :	$CH(OH)CH_3$

hydrogenation over PtO_2. The iminoethers **4a-e** will readily cyclize into **2**, whereas the carboxamide **4f** would hardly cyclize into **2** under the reaction conditions. Presence of a carbonyl group at the 6-position also altered the reaction path; the 6-ethoxycarbonyl derivative **1g** gave 6-ethoxycarbonyl-1,3-dimethyllumazine[3] as the only isolable product (17%), and the 7-acetyl analogue **1h** formed a complex mixture of decomposition products.

Following is the general procedure for the conversion of **1** into **2**: small pieces of Al foil (3 g) were immersed in $HgCl_2$ 100 mg/150 ml H_2O for 15 min. The washed solid was added to **1** (2-3 mmol) in 28% aqueous NH_3 (5 ml) and CH_3OH (150 ml). After stirring at 25 °C for 2 h, the mixture was filtered and evaporated. Extraction of the product with $CHCl_3$ and crystallization from C_2H_5OH gave **2**, as shown in Table 1.

Table 1. Conversion of 1 into 2 and The UV and ^1H NMR Spectra of 2.

Substrate	Product	Yield	UV[a)]	^1H NMR[b)]
1a	**2a**	54%	272(1.11)	3.38(3H, s), 3.20(3H, s), 2.35(3H, s)
1b	**2a**	81%		
1c	**2b**	75%	273(1.08)	3.40(3H, s), 3.20(3H, s), 2.70(2H, q, J=7), 1.23(3H, t, J=7)
1d	**2c**	75%	273(1.15)	3.40(sH, s), 3.20(3H, s), 2.67(2H, t, J=7), 1.80(2H, m), 0.88(3H, t, J=7)
1e	2d[c)]	41%	273(1.14)	4.08(1H, m), 3.41(3H, s), 3.21(3H, s), 2.73(2H, d, J=7), 1.10(3H, d, J=7)

a) λ_{max}/nm($\varepsilon/10^4$) in CH_3OH; b) /ppm in CD_3SOCD_3 and J/Hz; c) mp 287-289 °C, dec.

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3) mp 133-135 °C; m/z at 264(M^+); λ_{max}($\varepsilon/10^4$) in CH_3OH: 250(1.37), 267(sh., 1.13), and 333(0.88); ^1H NMR($CDCl_3$): 9.12(1H, s), 4.45(2H, q, J=7), 3.70(3H, s), 3.50(3H, s), and 1.40(3H, t, J=7).

4) **1h** was obtained from **1a** by the method of Baur et al.[5] in 56%; mp 223-224 °C; λ_{max}($\varepsilon/10^4$) in CH_3OH: 220(1.66), 250(0.83), 283(0.91), and 355(1.80); ^1H NMR(CD_3SOCD_3): 4.01(3H, s), 3.50(3H, s), 3.23(3H, s), and 3.30(3H, s). Reduction of **1h** by KBH_4 in CH_3OH gave **1e** (98%): mp 152-154 °C; λ_{max}($\varepsilon/10^4$) in CH_3OH: 214(1.30), 239(1.12), 266(0.84), and 326(1.26); ^1H NMR(CD_3SOCD_3): 4.95(1H, q, J=7), 4.07(3H, s), 3.50(3H, s), 3.30(3H, s), and 1.45(3H, d, J=7).

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