NOTE ON THE CONVERSION OF SOME HYDRAZIDES INTO ALDEHYDES IN n-BUTYLAMINE SOLUTION

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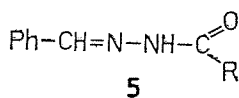
Recently Type **1** (R = OEt) N-(3-quinazolinio)amidates and their dimers (**2**, R = OEt), respectively, were found to undergo cleavage in n-butylamine solutions, both at ambient and elevated temperatures, into the corresponding 4(3H)-quinazolinones (**3**) and ethyl carbazate (**4a**). The amidates **1** (R = Ph) in contrast, when similarly treated, furnished only small amounts of the expected benzohydrazide (**4b**), N-benzylidenebenzohydrazide (**5b**) being the second main cleavage product in addition to the quinazolinones **3** [1, 2]. The formation of **5b** clearly shows that, under the applied conditions, part of the primary product benzohydrazide is reduced to benzaldehyde which subsequently condenses with the unchanged hydrazide.

$(R^2, R^4 = H, Me)$

$(R^2 = H, Me)$

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1*
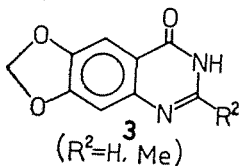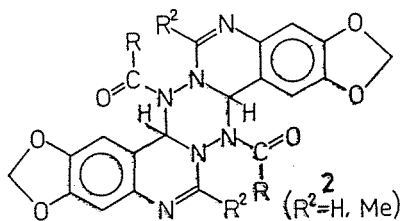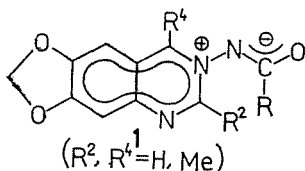
Benzohydrazide and some of its ring substituted derivatives have been known to be converted into *N*-benzylidenebenzohydrazides when allowed to stand for several weeks in alkaline solutions [3, 4]. This reaction was later shown to be an autoxidative process [5], and became the basis of the Kalb—Gross aldehyde synthesis [6] which consists in treatment of aroylhydrazines in the presence of various bases with various oxidizing agents, among which the combination ammonia — potassium hexacyanoferrate(III) proved the most
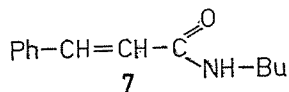
$$H_2N-NH-C\overset{\displaystyle O}{\underset{\displaystyle R}{\big<}}$$

4
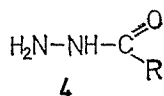
	R
a	OEt
b	Ph
c	$3-MeOC_6H_4$
d	$4-MeOC_6H_4-$
e	$3,4,5-(MeO)_3C_6H_2-$
f	$2-O_2NC_6H_4-$
g	$4-Cl-3-O_2NC_6H_3-$
h	Me
i	$Cl-(CH_2)_3-$
j	$Ph-CH=CH-$

$$Ph-CH=N-NH-C\overset{\displaystyle O}{\underset{\displaystyle R}{\big<}}$$

5

	R
a	OEt
b	Ph

$$R-C\overset{\displaystyle O}{\underset{\displaystyle R}{\big<}}$$

6

	R
a	Ph
b	$3-MeOC_6H_4-$
c	$4-MeOC_6H_4-$
d	$3,4,5-(MeO)_3C_6H_2-$

$$Ph-CH=CH-C\overset{\displaystyle O}{\underset{\displaystyle NH-Bu}{\big<}}$$

7

advantageous [5]. The limitations of the Kalb—Gross aldehyde synthesis are rather severe. It is not applicable to the synthesis of aliphatic aldehydes [5, 6], and three side reactions — *viz*. formation of carboxylic acids, N,N'--diaroylhydrazines and N-aroyl-N'-[(subst.)benzylidene]-hydrazines — often compete with or completely suppress the formation of aldehydes even in the aromatic series [5, 6].

In view of these limitations of the original Kalb—Gross synthesis it was thought worthwile to test whether the reaction of benzohydrazide (**4b**) with butylamine could be modified so as to furnish benzaldehyde rather than N--benzylidenebenzohydrazide (**5b**) and, if so, to explore the scope and limitations of this reaction.

Our results are summarized below, *cf*. Table I.

(1) When benzohydrazide (**4b**) was allowed to react with butylamine for a sufficiently long time, benzyldehyde was obtained in acceptable yields. The aldehyde is trapped in the reaction mixture by the reagent in form of N-benzylidenebutylamine, but this product is hydrolyzed during work-up by TLC, or else is converted into compounds **5a** and **5b** when treated with the hydrazides **4a** and **4b**, respectively.

Table I
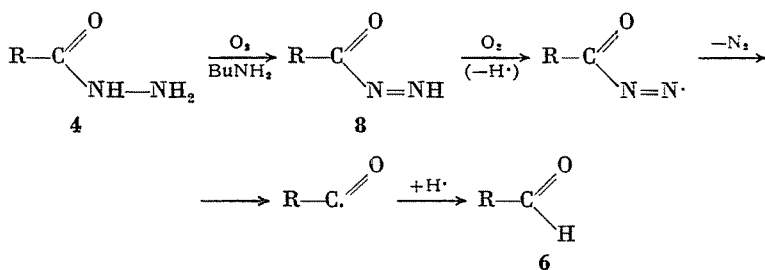
Reactions of some hydrazides with butylamine[a]

Run No.	Hydrazide	g	Butyl-amine, ml	Conditions	Reaction time, h	Method of isolation	Product	Yield, %
1.	**4b**	0.5	25	Reflux	30	*A*	**5a**	59
2.	**4b**	0.5	25	Room temperature	500	*A*	**5b**	60
3.	**4b**	0.5	25	Room temperature	200	*B*	**5b**	61
4.	**5b**	0.5	25	Room temperature	250	*A*	**5a**	67
5.	**4c**	0.5	25	Reflux	50	*C*	**6b**	34
6.	**4d**[b]	0.5	25	Reflux	15	*C*	**6c**	69
7.	**4d**	0.5	25	Reflux	30	*C*	**6c**	73
8.	**4d**[c]	0.3	15	Reflux	30	*C*	**4d**[d] / **6c**	83 / traces[e]
9.	**4e**	0.5	25	Reflux	50	*C*	**6d**	60
10.	**4e**	0.5	25	Room temperature	500	*C*	**6d**	50
11.	**4j**	0.5	25	Reflux	25	*C*	**7** [11]	45
12.	[f]	0.5	25	Reflux	100	*D*	**5b**	63

[a] All experiments, except those noted, were performed in air   [b] Under oxygen   [c] Under argon   [d] Unchanged starting substance   [e] Detected by TLC   [f] N,N'-Dibenzoylhydrazine

(2) When the reaction of benzohydrazide (**4b**) and butylamine is inter-rupted at a comparatively early stage (Table I, run No. 3) *N*-benzylidenebenzo-hydrazide (**5b**) may be isolated in good yields without adding an additional amount of benzohydrazide to the reaction mixture before work-up. When subjected to the action of butylamine, this product is also converted into benzaldehyde. Thus, *N*-benzylidenebenzohydrazide (**5b**) and, presumably, its congeners are intermediates of the reactions leading to aromatic aldehydes, rather than side products as originally thought [5].

(3) *N,N'*-Dibenzoylhydrazine, too, is converted into benzaldehyde when allowed to react with butylamine for a sufficiently long time, which shows that *N,N'*-diaroylhydrazines should not be regarded as useless side products of the Kalb—Gross aldehyde synthesis.

(4) Aldehydes **6** were obtained in good yields also from the methoxy substituted benzohydrazides **4b**—**4e** with butylamine. The presence of air was found to be indispensable for the formation of the aldehydes since the hydrazide **4d**, when treated with butylamine under argon, furnished only traces of *p*-methoxybenzaldehyde (as the result of traces of oxygen still being present in the reaction mixture) while most of the starting material was recov-ered unchanged. Based on this observation and on analogy with the oxidation of phenylhydrazine in aqueous solution to yield benzene and nitrogen [7] the probable course of the conversion of aroylhydrazines into the correspond-ing aldehydes appears to be that shown in Scheme 1. Thus, the key interme-

$$R-C\overset{O}{\underset{NH-NH_2}{\diagdown}} \quad \xrightarrow[\text{BuNH}_2]{O_2} \quad R-C\overset{O}{\underset{N=NH}{\diagdown}} \quad \xrightarrow[(-H\cdot)]{O_2} \quad R-C\overset{O}{\underset{N=N\cdot}{\diagdown}} \quad \xrightarrow{-N_2}$$

$$\textbf{4} \qquad\qquad\qquad\qquad\qquad \textbf{8}$$

$$\longrightarrow \quad R-C.\overset{O}{\diagup} \quad \xrightarrow{+H\cdot} \quad R-C\overset{O}{\underset{H}{\diagup}}$$

$$\textbf{6}$$

Scheme 1

diates **8** of the reaction sequence are thought to be identical with those of the well-known McFadyen — Stevens aldehyde synthesis [8]; in the latter case, however, their formation does not require the presence of oxygen or an oxidant.

(5) No aldehydes were obtained when the substituted benzohydrazides **4f** and **4g** were treated with butylamine, and no reaction at all took place when compound **4a** or the aliphatic hydrazides **4h** and **4i** were similarly treated. Thus, the limitations of the butylamine induced formation of aldehydes from hydrazides are similar to those of the Kalb—Gross synthesis.

(6) Cinnamohydrazide **4j** is converted by butylamine into the corresponding amide **7**. Formation of the latter product is obviously the result of a competing nucleophilic reaction at the carbonyl group of compound **4j** and shows that the formation of carboxylic acids in the Kalb—Gross synthesis is probably the result of a similar process rather than of subsequent oxidation of the aldehydes or of one of their non-specified precursors, as thought earlier [5]. It occurred to us that the unfavourable competing reaction might be suppressed by replacing the reagent butylamine by triethylamine. However, no reaction took place when either of the hydrazides **4b** and **4g** was treated with triethylamine.

Experimental

The hydrazides **4b**—**4e**, **4j** and **5b**, and N,N'-dibenzoylhydrazine, respectively, were dissolved in butylamine and allowed to react with the solvent as specified in Table I until, according to TLC (Kieselgel G, benzene—MeOH, 10 : 2), the starting compounds as well as, in the case of hydrazide **4b**, the intermediate **5b** completely disappeared from the reaction mixture. In run No. 3 the reaction was interrupted at the stage of formation of the intermediate **5b**. The solvent was removed by distillation in vacuum, and the resulting residues were worked up by methods (A)—(D) as indicated in Table I.

(A) The residue was dissolved in ethanol (20 ml) and again evaporated to dryness. This procedure was repeated several times, in order to remove the last traces of the amine. In the experiments starting with hydrazides **4b*** and **5b** the residues were finally dissolved in ethanol and converted either into compound **5a** [9] or **5b** [10] by adding ethyl carbazate (**4a**) and benzohydrazide (**4b**), respectively. For the yields, see Table I.

(B) The dry residue was worked up by preparative TLC (Kieselgel PF$_{254+366}$, benzene—acetone, 10 : 2).

(C) The amine was removed as described under (A), and the residues were worked up by preparative TLC (Kieselgel PF$_{254+366}$, benzene—MeOH, 10 : 2 in the case of **4c**—**4e**, and benzene—acetone, 2 : 1 in the case of **4j**). The resulting aldehydes **6b**—**6d** and N-butylcinnanamide (**7**) were identified by comparison (mp., IR, R$_f$) with authentic samples.

(D) The residue was worked up as described under (A) except that, after complete removal of the amine, the crude product was subjected to preparative (TLC Kieselgel PF$_{254+366}$, benzene—acetone, 2 : 1) and only the aldehyde containing fraction was treated with benzohydrazide.

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* The IR spectrum of the dry residue obtained starting with compound **4b** proved identical with that of an authentic sample of N-benzylidenebutylamine prepared from benzaldehyde and butylamine.

Summary

Benzohydrazide and some of its ring substituted derivatives, when treated with butyl-amine in the presence of air, furnish benzaldehydes *via* the corresponding *N*-benzylidene-benzaldehydes. Cinnamohydrazide yields *N*-butylcinnamamide under the same conditions.

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