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FORMATION OF α-IMINOKETONES AND α-DIIMINES FROM ALIPHATIC α,α'-DIBROMOKETONES

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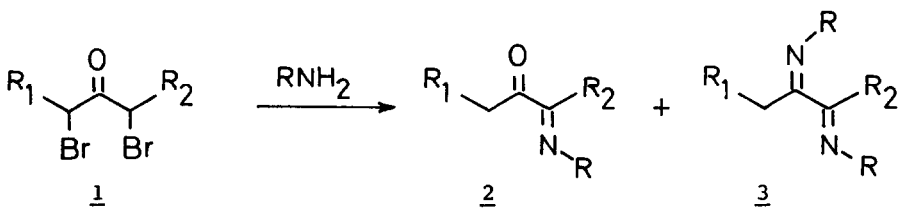
Summary : A novel reaction of aliphatic α,α'-dibromoketones with primary amines has been found to produce α-iminoketones and/or α-diimines, which can be selectively obtained under appropriate reaction conditions.

The base-induced skeletal rearrangement of α-haloketones to afford carboxylic acid derivatives is well known as the Favorskii rearrangement.[1] The reaction of alicyclic α,α'-dibromoketones, e.g. 3,5-dibromo-2,2,6,6-tetramethyl-4-piperidone, with primary amines was reported to afford the ring-contracted α,β-unsaturated carboxylic amides according to the latter rearrangement,[2] while a competition between Favorskii rearrangement and enaminoketone formation was observed when the same substrates were brought into reaction with secondary amines.[3] On the other hand, α,α'-dibromoketones and tertiary amines (or pyridines) have been shown to give rise to α,β-dehydrobromination[4] or α,α'-dehydrobromination,[5] yielding α,β-unsaturated ketones or cyclopropenones, respectively. The reaction of aliphatic α,α'-dibromoketones 1 with primary amines is, to our knowledge, not studied hitherto, albeit no reaction, other than the Favorskii rearrangement is



1 2 3

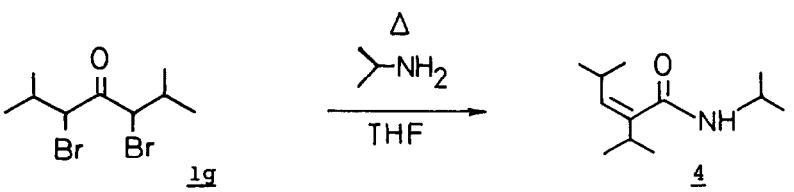
SCHEME I

expected. Therefore, we would like to disclose our preliminary results concerning a novel reaction of α,α'-dibromoketones 1 with primary amines. The reaction of α,α'-dibromoketones 1 with an excess of primary amines (5 equiv.) in dry ether at room temperature leads to an instantaneous formation of precipitated amine hydrochloride. Variable ratios of α-iminoketones 2 and α-diimines 3 were isolated from the remaining ethereal solution. Isopropylamine afforded α-imino-

ketones 2 ($R_2 \neq H$) as the major products but less sterically hindered primary amines, e.g. methylamine or ethylamine, produced increasing amounts of α-diimines 3 (Table I; entries 1-3).

α,α'-Dibromomethylketones 1 (R_2=H) reacted regiospecifically with primary amines to give rise to α-ketoaldimines 2 (R_2=H) and/or α-iminoaldimines 3 (R_2=H). No trace of the isomeric compound $R_1C(=NR)COCH_3$ or the corresponding α-diimine were detected in any cases. The amount of α-diimines 3 increased gradually when taking longer reaction times. As an example, 1,3-dibromo-2-butanone 1 (R_1=Me; R_2=H) gave with isopropylamine (5 equiv.) in ether during 20 minutes rise to α-iminoketone 2 (R_1=Me; R_2=H) as the major product (85 %) while α-diimine 2 (R_1=Me; R_2=H) was obtained exclusively after 17 h at room temperature (in ether, or preferably in pentane) (entries 5-7). The selective formation of α-iminoketone 2 (R_1=Me; R_2=H) is at best accomplished with 3 equiv. of the amine in ether (4 h RT).

The scope of the conversion of α,α'-dibromoketones 1 into α-iminoketones 2 or α-diimines 3 seemed to be limited by the steric hindrance in the starting ketone Indeed, 3,5-dibromo-2,6-dimethyl-4-heptanone 1g (R_1=R_2=i-Pr) resisted any reaction with isopropylamine under the normal reaction conditions (ether, 5 equiv. i-$PrNH_2$, RT). Even an overnight reflux period in ether with excess isopropylamine gave no consumption of starting material but in tetrahydrofuran under reflux the exclusive formation of the Favorskii rearrangement product 4 was observed (one isomer, presumably Z).



1g 4

SCHEME II

From the mechanistic point of view the unexpected formation of α-iminoketones 2 and α-diimines 3 presumably results from a more favorable nucleophilic action of primary amines (aminolysis) as compared to secondary amines, which are more basic but probably less nucleophilic due to steric hindrance. The latter features of secondary amines explain the ready formation of Favorskii rearrangement products Aminolysis of oxallylic bromides 6 via delocalized carbenium ions 8 yields intermediates 9 which are readily converted into α-iminoketones 2. The regioselective enolization from 1 to 6 (when R_2=H) originates from the fact that the most acidic α-hydrogen is located at the 1-position (bromomethyl group). The positive charge of the delocalized carbenium ion 8 is better stabilized at the brominated carbon

TABLE I Reaction of α,α'-Dibromoketones with Primary Amines[a]

Entry		R_1	R_2	R	Solvent	(Time)	α-Iminoketone 2	α-Diimine 3	Yield[b,c]	B.p. (°C/torr)
1	a	Me	Me	i-Pr	ether	(17 h)	98	2	72	61-62/15
2	b	Me	Me	Et	ether	(22 h)	18	82	68	73-82/15[c]
3	c	Me	Me	Me	ether	(17 h)	56	44	63	51-56/14[c]
4	d	Et	Et	Me	ether	(24 h)	55	45	60	-[e]
5	e	Me	H	i-Pr	ether	(20 min)	85[f]	0[f]	-[c]	-
6	e	Me	H	i-Pr	ether	(2 h)	77[f]	23[f]	-[c]	-
7	e	Me	H	i-Pr	pentane	(17 h)	1[f]	99[f]	-[c]	-
8	f	Et	H	i-Pr	ether	(22 h)	25	75	40	62-80/13[c]
9	f	Et	H	i-Pr	pentane	(22 h)	0	100	-[c]	-

[a] An excess of 5 equiv. primary amine in a 10% solution of 1 in an appropriate solvent was used (RT)

[b] Considerable loss of product was noticed during vacuum distillation (residual tars); compounds 2 and 3 have to be kept in the refrigerator under an inert atmosphere.

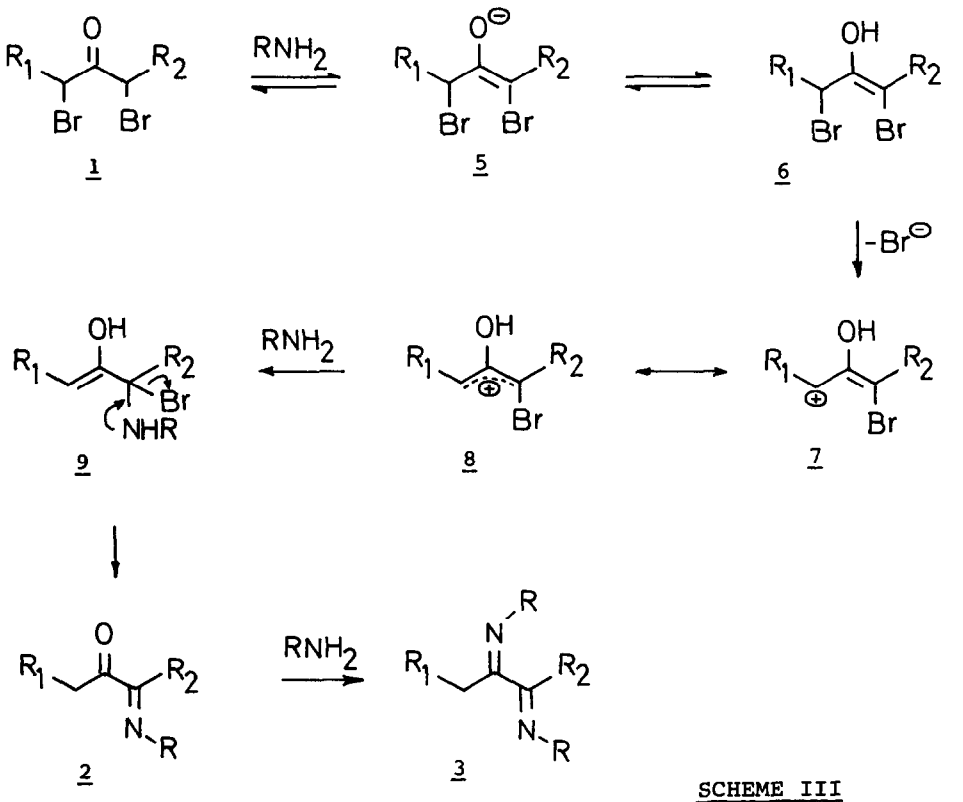
[c] Isolated yields obtained after distillation; yields of crude products are always nearly quantitative

[d] Mixture of 2 and 3

[e] Decomposition on distillation

[f] Ratio determined by NMR and GLC

which is attacked by the amine. α-Iminoketone 2 is then further converted into α-diimine 3 by the excess of amine, as evidenced by control experiments.
The reaction presented in this preliminary account is comparable with the aforementioned formation of enaminoketones from cyclic α,α'-dibromoketones and secondary amines,[3] and with the base-induced synthesis of α-diones from α,α'-dibromoketones.[6] A comprehensive research of the competition between Favorskii rearrangement and aminolysis is now in progress in our laboratory.



SCHEME III

References

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1. A.S. Kende, Org. Reactions, 1960, 11, 261; A.A. Akhrem, T.K. Ustynyuk and Y.A. Titov, Russ. Chem. Rev., 1970, 39, 732.
2. H. Pauly and I. Rossbach, Ber., 1899, 32, 2000; H. Pauly and C. Boehm, Ber., 1900, 33, 919.
3. a) K. Sato, Y. Kojima and H. Sato, J. Org. Chem., 1970, 35, 2374 b) K. Sato, Y. Inoue, S. Kuranami and M. Ōhashi, J. Chem. Soc. Perkin I, 1977 1666 c) K. Sato, M. Ōhashi, E. Aoki and Y. Murai, J. Org. Chem., 1977, 42, 3713 d) K. Sato, S. Inoue, M. Ōhashi and S. Kuranami, Chem. Lett., 1975, 405.
4. F.G. Bordwell and K.M. Wellman, J. Org. Chem., 1963, 28, 2544.
5. K.T. Potts and J.S. Baum, Chem. Rev., 1974, 74, 189.
6. M. Utaka, S. Matsushita and A. Takeda, Chem. Lett., 779 (1980).

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