Journal of Fluorine Chemistry, 36 (1987) 307–312

Received: November 24, 1986; accepted: February 10, 1987

STEREOCHEMICAL COURSE OF REDUCTIVE DEAMINATION INDUCED BY DIFLUOROAMINE

CARL L. BUMGARDNER* and VINOD R. DESAI

Department of Chemistry, North Carolina State University,
Raleigh, NC, 27695-8204 (U.S.A.)

SUMMARY

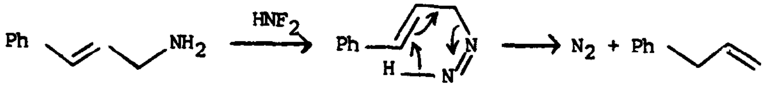
Optically active 2-phenyl-2-butylamine reacts with HNF_2 to give 2-phenylbutane with 56% net retention of configuation.

INTRODUCTION

Treatment of primary amines with HNF_2 is known to replace the amino group with a hydrogen atom, reductive deamination [1].

$$R\text{-}NH_2 \xrightarrow{HNF_2} R\text{-}H$$

When allylic amines are substrates, reductive deamination occurs with migration of the double bond, even when this leads to deconjugation. Thus, cinnamylamine gives rise to 3-phenylpropene [2]. This transformation is believed to involve cyclic concerted decomposition of a alkyldiimide intermediate, eqn. 1.

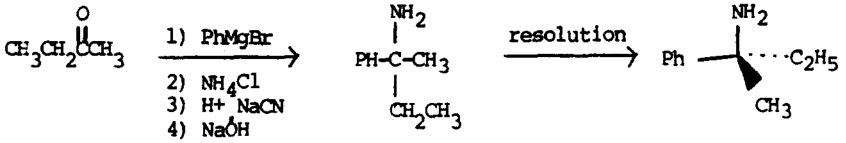


(1)

Although alkyldiimides are also implicated as intermediates in the HNF_2 induced deamination of saturated primary amines, the stereochemical course in these cases has not been determined. To shed light on this aspect of HNF_2 chemistry we examined the fate of optically active 2-phenyl-2-butylamine with HNF_2.

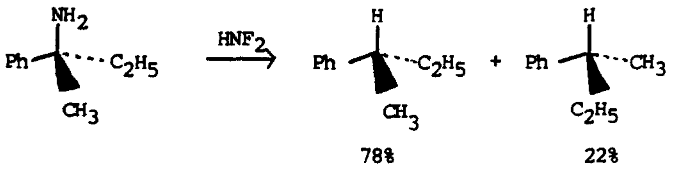
RESULTS

2-Phenyl-2-butylamine was synthesized as shown in eqn. 2 following the method described for preparation of 3-amino-3-methylhexane[3]. Partial resolution of the amine was achieved through the tartrate diastereomers following the procedure of Iffland and Buu [3]. From configurations and maximum rotations established previously [4] for 2-phenyl-2-butylamine we could characterize our starting material as R-(+)-2-phenyl-2-butylamine with ee of 42% (α^{25}_{546} = +7.6°, 1 dm., neat).



(2)

The deaminations were conducted in a glass vacuum system by condensing HNF_2 into the degassed amine in the manner previously described [1]. The hydrocarbon isolated (45%) was identified as 2-phenylbutane by its nmr and ir spectra. Comparison of its rotation (α^{25}_{546} = +5.7°, 1 dm., neat) with the established configurations and maximum rotations for 2-phenylbutane [4] showed that deamination proceeded with 56% net retention, eqn. 3.

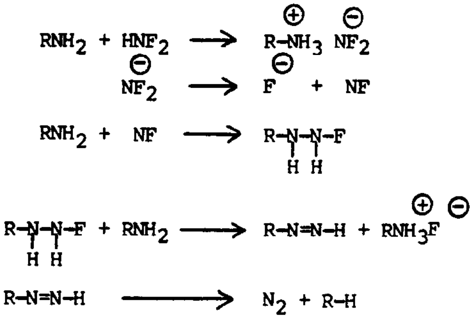


(3)

Examination of recovered 2-phenyl-2-butylamine indicated that it underwent no loss of optical purity during the course of the reaction.

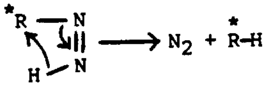
DISCUSSION

To account for reductive deamination using HNF_2 the series shown in scheme 1 was originally proposed [1].



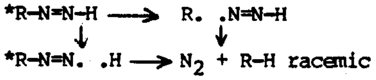
Scheme 1

These reactions capitalize on the special nature of HNF_2, its acidic character and its two fluorines which can function as leaving groups. The present findings allow us to comment on the course of the last step, the decomposition of alkyldiimide to molecular nitrogen and alkane. This collapse is obviously not concerted since complete retention would be expected, eqn. 4.



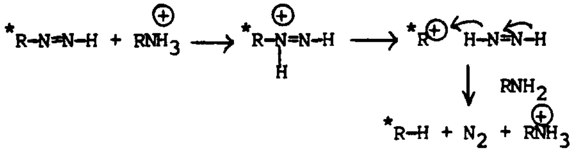
(4)

Furthermore, such a process would be thermally symmetry-forbidden [5]. A homolytic cleavage does not appear likely since Cram and Bradshaw [4] observed complete racemization in the homolytic decomposition of optically active diimides generated from hydrazine and tosylhydrazide derivates, eqn. 5.



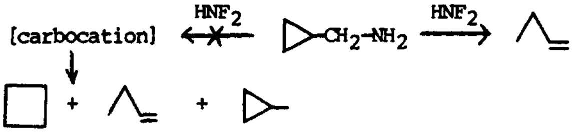
(5)

Acid-catalyzed decomposition of the alkyldiimide constitutes another possible route, eqn. 6.



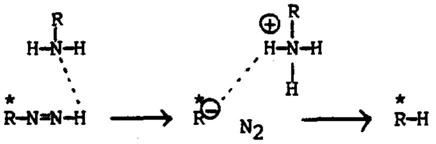
(6)

This pathway is not appealing since in earlier work [1,2] cyclopropylcarbinylamine was observed to undergo reductive deamination with HNF_2 cleanly to 1-butene, eqn. 7.



(7)

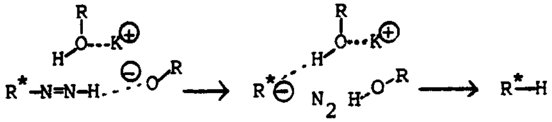
If a carbocation were involved, the characteristic trio of products [6], cyclobutane, 1-butene, and methylcyclopropane, should have been observed from the reaction shown in eqn. 7. A mode of decomposition consistent with the present observations is indicated in eqn. 8, where Wolff-Kishner type cleavage occurs with the amine acting as base and its conjugate acid as proton donor.



(8)

Since the proton is delivered to the 2-phenylbutyl group from the frontside, retention of configurations results. Competing symmetric solvation would of course give rise to racemic product, so the overall reaction leads to net retention. A similar scheme, eqn. 9, was suggested by

Cram and Bradshaw [4] to account for net retention when optically active alkyldiimides generated from several sources were decomposed with potassium alkoxides in solvents promoting ion-pairing.



(9)

In any event, reductive deamination induced by HNF_2 proceeds with net retention of configuration.

EXPERIMENTAL

Caution: HNF_2 should be handled with care. Experiments involving HNF_2 were conducted in a Plexiglas-shielded vacuum line.

R-(+)-2-Phenyl-2-butylamine

2-Phenyl-2-butylamine was prepared and resolved using the procedure of Iffland and Buu [3]. The optically active amine used for reaction with HNF_2 had b.p. 87° (10 mm), n^{25} 1.5150, $\alpha^{25}_{546} = +7.6°$ (1 dm., neat); reported [4] for R-(+)-2-phenyl-2-butylamine, b.p. 50-52° (2 mm), n^{25} 1.5148, max $\alpha^{25}_{546} = +18.2°$ (1 dm., neat).

Reaction of R-(+)-2-Phenyl-2-butylamine with HNF_2

The degassed amine described above (20 mmoles, 42% ee) was treated with HNF_2[7] (6.7 mmoles) in the manner previously described for primary amines [1]. After evolution of N_2 ceased, volatiles (N_2, trace of HNF_2) were removed by pumping and water was added to the residue. The resulting mixture was acidified with 10% aqueous HCl solution and extracted with ether. Distillation of the combined dried ether extracts from five similar runs* yielded 1.7g (43%) [9] of 2-phenylbutane, b.p. 50-52% (13 mm), identified by its n m r and ir spectra, $\alpha^{25} = +5.7°$ (1 dm. neat); reported [4] for S-(+)-2-phenylbutane max $\alpha^{25} = +24.3°$ (1 dm., neat).

---

*Only small scale runs were conducted because of safety considerations.

The combined aqueous acid solutions from the five runs were made alkaline with aqueous NaOH and the amine generated was extracted with ether. Distillation of the dried ether extracts gave 8.2 g of recovered R-(+)-2-phenyl-2-butylamine with the same ee as the starting material. This amount of amine accounts for 98% of that expected from the 2-phenyl-2-butylammonium fluoride produced in the reaction.*

ACKNOWLEDGEMENT

We are grateful to the National Science Foundation for financial support.

REFERENCES

1 C.L. Bumgardner, K.J. Martin and J.P. Freeman, J. Am. Chem. Soc., **85** (1963) 97.

2 C.L. Bumgardner and J.P. Freeman, J. Am. Chem. Soc., **86** (1964) 2233.

3 D.C. Iffland and N.T. Buu, J. Org. Chem., **32** (1967) 1230.

4 D.J. Cram and J.S. Bradshaw, J. Am. Chem. Soc., **85** (1963) 1108.

5 T.L. Gilchrist and R.C. Storr, 'Organic Reactions and Orbital Symmetry', second ed., Cambridge Univ. Press, Cambridge (1979).

6 T.H. Lowry and K.S. Richardson, 'Mechanism and Theory in Organic Chemistry', second ed., Harper and Row, N.Y. (1981) p 404.

7 W.H. Graham and C.O. Parkers, J. Org. Chem., **28** (1963) 850.

---

*Yield based on equation $3RNH_2 + HNF_2 = RH + N_2 + 2RNH_3\ F$ and the fact that a total of 12.7g of 2-phenyl-2-butylamine was used in the five runs.