Tetrahedron Letters,Vol.23,No.7,pp 699-702,1982 0040-4039/82/070699-04$03.00/0
Printed in Great Britain ©1982 Pergamon Press Ltd.

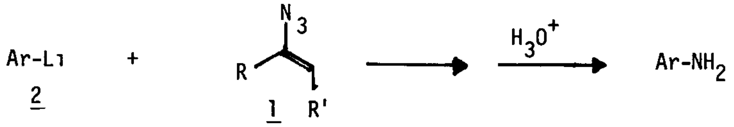
A NOVEL AMINATION OF AROMATIC AND HETEROAROMATIC COMPOUNDS[1]

Alfred Hassner*, Paul Munger and Benjamin A. Belinka, Jr , Department of Chemistry, State University of New York, Binghamton, New York 13901

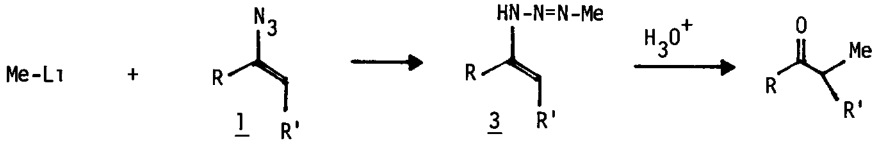
Abstract Vinyl azides act as NH_2^+ equivalents in reaction with aromatic or heteroaromatic lithium derivatives thus providing a direct method for amination of such compounds.

Aromatic and heteroaromatic primary amines have maintained a pivotal role in organic chemistry, largely due to their ease of conversion to a variety of functional groups. In spite of many known synthetic pathways leading to amines[2] (mostly by reduction of other functions), there is still lacking a good and facile method for direct introduction of the amino group into aromatic compounds A recent report by Trost and Pearson[3] on this subject, prompts us to disclose our preliminary results on amination of aromatic and heteroaromatic lithium compounds.

During our research on the reactivity of vinyl azides[4,5] with lithium compounds, we discovered that vinyl azides (1) can act as NH_2^+ equivalents upon reaction with aromatic lithium reagents Thus, reaction of 1 with 2, followed by dilute acid work-up produces aromatic primary amines in fair to good yields (see Table I), in what amounts to an overall NH_2-transfer process (Eq 1) This is remarkable since we had shown earlier[5] that simple alkyl lithium reagents (Me-Li, Bu-Li, t-Bu-Li) react with these vinyl azides by alkyl transfer to carbon with formation of alkylated ketones (Eq 2) These transformations were shown to occur via alkyl vinyltriazenes 3, that decompose to alkyl diazonium ions and primary enamines followed by C-alkylation of the latter The aromatic aminations (Eq. 1) are analogous to Trost's findings[3] using Grignard reagents and phenylthiomethyl azide 4 (Eq 3)



(1)



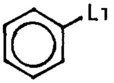
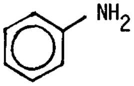
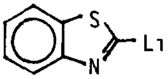
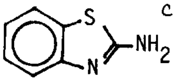
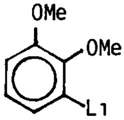
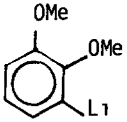
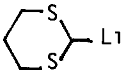
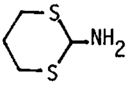
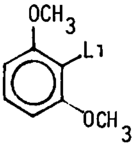
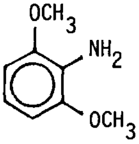
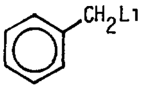
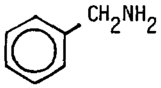
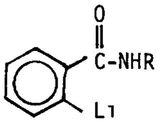
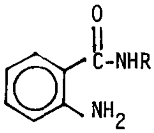
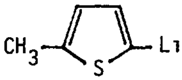
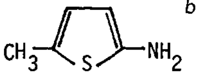
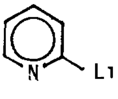
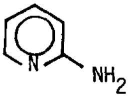
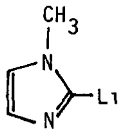
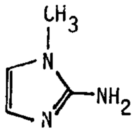
(2)

$$\text{Ar-Li} \xrightarrow{MgBr_2} \text{Ar-MgBr} + \underset{4}{\text{Ph-S-CH}_2\text{-N}_3} \longrightarrow \xrightarrow{KOH} \text{ArNH}_2 \qquad (3)$$

Unlike reagent 4,[3] our vinyl azides can be used in the preparation of heterocyclic amines as well (see Table I) and even benzyl lithium can be transformed in 80% yield into benzyl amine Furtherfore, whereas Grignard reagents are more effective than organolithium reagents in reaction with azide $PhSCH_2N_3$, the opposite is true for our vinyl azides.

Table I

Amination[a]

Li Reagent	Product	% Yield	Li Reagent	Product	% Yield
		68%		 [c]	53%
	 [c]	60%			64%
	 [c]	70% 61%[d]			60%
	 [c]	52%		 [b,c]	58%
	 [c]	45%		 [c]	45%

---

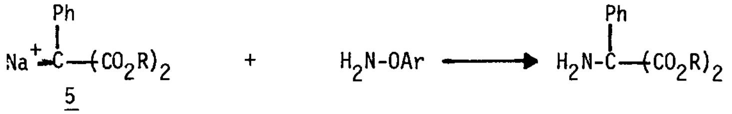
[a] Unless otherwise specified We have used mostly vinyl azides 1, R Ph, R:H or 1, R H, R'.tBu

[b] Isolated as the hydrochloride

[c] Intermediate triazene isolated en route

[d] Work up instead with KOH, THF, MeOH

For comparison with other aminating reagents, pyridine can be transformed into 2-aminopyridine while amination with O-sulfonylhydroxylamines leads to N-aminopyridinium salts.[6] Since many aromatic and heterocyclic halogen-lithium compounds are readily accessible either by direct lithiation or by halogen-lithium exchange, our method represents a useful synthesis of aromatic and heteroaromatic amines This method also supplements the amine transfer reaction of Sheradsky and others[7,8] in which stabilized carbanions (e g , 5) but not aromatic carbanions can be aminated with O-substituted hydroxylamine reagents (Eq 4)

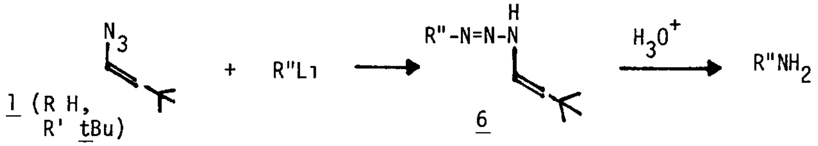


$$\mathrm{Na^{+}\,{}^{-}\overset{Ph}{C}{-}(CO_2R)_2} \quad + \quad \mathrm{H_2N\text{-}OAr} \longrightarrow \mathrm{H_2N\text{-}\overset{Ph}{C}{-}(CO_2R)_2} \qquad (4)$$

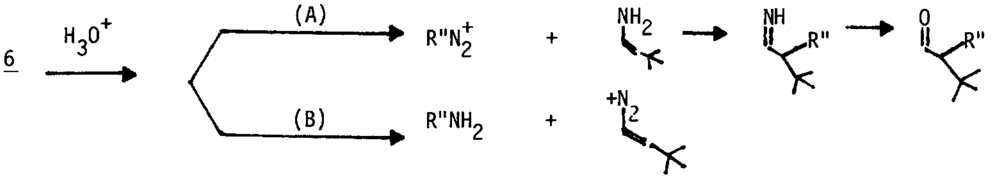
5

In a typical procedure 1 5 g (11 mmol) of di-O-methylresorcinol is transformed into its 2-lithio derivative by treatment with one equivalent of n-butyllithium in THF at 0° and standing at 25° for 18 hrs This is followed by addition of 1 45 g (10 mmol) of 1-azidostyrene (1, R Ph, R' H) at -78°C After allowing the reaction mixture to reach 25° (over 2 hr), the mixture is worked up either with 10% HCl or with KOH and the product is isolated in 52% yield as the free amine after basification Alternatively, the hydrochloride salt is obtained by concentration of the aqueous layer.

We have shown that attack of the organolithium reagents on vinyl azides (e g. 1) proceeds on nitrogen to form vinyl triazene intermediates 6, and in fact, several of these have been isolated in our reaction Treatment of 6 (R" aromatic) with dilute HCl leads to evolution of N_2, and formation of amine (Eq. 5) It is clear that the fate of 6 on protonation is highly dependent on the nature of the substituents on nitrogen When R" is aliphatic (i e , Me), R" transfer to carbon takes place via $R''N_2^+$ and primary enamines[5] (Eq 6, Path A)



(5)



(6)

However, when R" is aromatic or heteroaromatic, decomposition to the amine $R''NH_2$ is preferred (Path B). The other reaction product, a vinyldiazonium salt, is presumably transformed into an aldehyde or a ketone. Indeed, in at least one case using α-azidostyrene we were able to identify acetophenone as a product of the reaction.

Theoretically any organic azide should be usable in the NH_2 transfer reaction. There is, in fact, an example recorded in which phenyl azide was reacted with 2-lithio benzo-1,3-thiazole and related compounds to produce the 2-amino compound, but in this case aniline may be one of the products as well.[9] Tosyl azide has been extensively studied in reactions with carbanions,[10] but it usually leads to tosyl amine and diazo compounds (e.g., 6, Path B, R":Tos).[11] A major advantage of using vinyl azides or $PhSCH_2N_3$ as reagents for amination of R"-Li is that, regardless of which Pathway (A or B) is chosen in the decomposition of triazene 6, $R''NH_2$ should be the only basic amine product (because any enamine would be hydrolyzed). Further work on the scope and mechanism of these transformations is in progress.

Acknowledgment: This investigation was supported by NCI Grant CA-19203 from DHEW. A Meyerhoff Fellowship Award to AH is gratefully acknowledged.

References

1. Synthetic Methods 18. For the previous paper in this series see A. Hassner, B.A. Belinka, Jr., Mark Haber and Paul Munger, Tetrahedron Lett., 1863 (1981).
2. M.S. Gibson in "The Chemistry of the Amino Group," S. Patai Ed., Interscience Publishers (1968) p. 37.
3. B.M. Trost and W.H. Pearson, J. Amer. Chem. Soc., 103, 2483 (1981).
4. (a) G. L'abbe and A. Hassner, Angew. Chem. Inter. Ed., 10, 98 (1981); (b) A. Hassner and A.B. Levy, J. Amer. Chem. Soc., 93, 5469 (1971); ibid., 93, 2051 (1971); (c) A. Hassner, A.S. Miller and M.J. Haddadin, J. Org. Chem., 37, 2682 (1972).
5. B.A. Belinka, Jr. and A. Hassner, J. Amer. Chem. Soc., 102, 6185 (1980).
6. Y. Tamura, Y. Miki, Y. Sunida and M. Ikeda, J. Chem. Soc. Perkin Trans., 1, 258 (1973).
7. (a) T. Sheradsky and Z. Nir, Tetrahedron Lett., 77 (1969); (b) T. Sheradsky, G. Salemnick and Z. Nir, Tetrahedron, 28, 3833 (1972).
8. For a review see Y. Tamura, J. Minamikawa and M. Ikeda, Synthesis, 1 (1977).
9. B.A. Tertov, V.V. Burykin, and A.V. Koblik, Khimiya Geterotsiklicheskikh Soedinenni, 11, 1552 (1972).
10. M. Regitz, Angew. Chem. Int. Ed. (Eng.)., 6, 733 (1967).
11. In the case of 4 it is possible that base catalyzed decomposition of intermediate triazene takes a similar course leading to $Ph\text{-}S\text{-}CH{=}N_2$ rather than as suggested in Ref. 3.

(Received in USA 21 October 1981)