

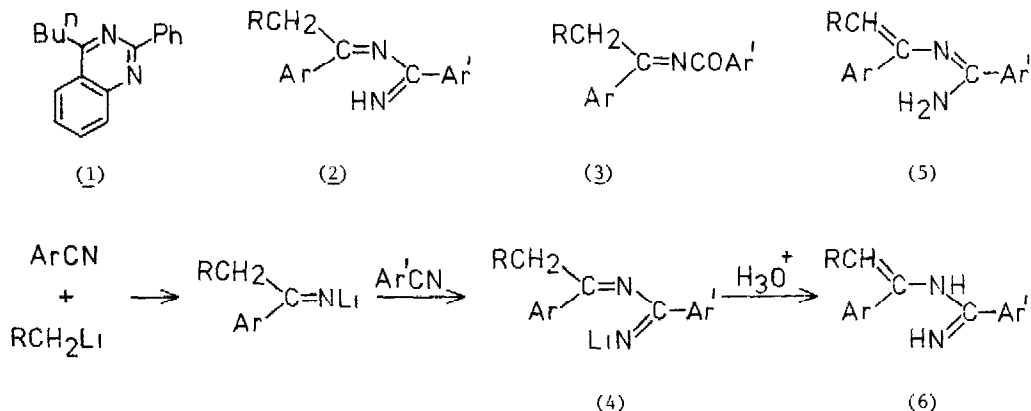
Synthesis of Enamides by the Reaction of Organolithium Compounds with Nitriles<sup>1</sup>

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The simple addition of an organomagnesium<sup>2</sup> or organolithium compound<sup>3</sup> to the triple bond of a nitrile may be complicated by removal of an  $\alpha$ -proton from the nitrile, or addition to the nitrile by the imine salt formed initially. The latter type of reaction usually leads to cyclic products, such as triazines and pyrimidines<sup>4-7</sup>, we now report the formation of acyclic products of a novel type.<sup>8</sup>



To n-butyl-lithium in ether-hexane was added an equimolar amount of o-chlorobenzonitrile in diethylether, followed by a second equimolar amount of o-chlorobenzonitrile and the mixture was stirred at room temperature overnight. After hydrolysis with ice-water, the main product isolated (61%) was not the quinazoline (1) (cf. ref. 7), nor a triazine or pyrazoline (cf. ref. 4), nor the compounds (2) or (3), derived from the intermediate (4), although the mass spectrum

(a) Dedicated to Professor H. Suschitzky on his 60th birthday.

and elemental analysis indicated the same molecular formula as (2). The  $^1\text{H}$  n.m.r. spectrum [ $\tau$  2.5-3.3 (8H, m, ArH), 4.5 br (2H, exch, NH), 4.9 (1H, t, CH=), 7.95 (2H, quintet,  $\text{CH}_2$ ), 3.6 (2H, sextet,  $\text{CH}_2$ ), 9.1 (3H, t,  $\text{CH}_3$ )] indicated the presence of a  $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}=\text{C}$  grouping, and the i.r. spectrum showed two NH stretching absorptions at  $\nu_{\text{max}}$  3312, 3450  $\text{cm}^{-1}$ . The i.r. frequencies were incompatible with the primary amino group present in structure (5) and we therefore assign the structure (6,  $\text{Ar}=\text{Ar}'=\text{o}-\text{ClC}_6\text{H}_4$ ,  $\text{R}=\text{Pr}$ ) to the product. Similar products were

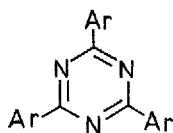
TABLE  
Enamidines (6)<sup>a</sup>

R	Ar	Ar <sup>1</sup>	Yield (%)	m p. (°C)
Pr	$\text{o}-\text{ClC}_6\text{H}_4$	$\text{o}-\text{ClC}_6\text{H}_4$	61	77 - 79
Pr	$\text{o}-\text{ClC}_6\text{H}_4$	$\text{C}_6\text{H}_5$	73	135 - 137
Pr	$\text{C}_6\text{H}_5$	$\text{C}_6\text{H}_5$	63	127 - 129
H	$\text{o}-\text{ClC}_6\text{H}_4$	$\text{C}_6\text{H}_5$	33 <sup>b</sup>	117 - 119

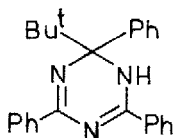
<sup>a</sup> Acceptable elemental analyses obtained.

<sup>b</sup> Impure. Crude product is a gum, and considerable losses are incurred on purification.

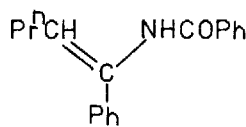
formed from other aromatic nitriles and from methyl-lithium, as shown in the Table. With aryl-lithium compounds, only the imines ( $\text{ArAr}'\text{C}=\text{NH}$ ), or the corresponding ketones, were obtained under mild conditions, and under more vigorous conditions increasing amounts of triaryltriazines (7) were formed (cf. ref. 5). With t-butyl-lithium and benzonitrile, the main product was the dihydrotriazine (8) (cf. ref. 4).



(7)



(8)



(9)

The equilibrium between the enamidines (6) and their tautomers (2, 5) evidently lies in the direction of the former, since the olefinic protons exchange only slowly in the presence of deuterium oxide. We note that an attempted preparation of the *N*-benzoylimine (3, R=Pr) gave the tautomeric enamide (9)<sup>9</sup>, we also suggest that a reported product from the reaction of diethylmagnesium with benzonitrile was not (2, Ar=Ar'=Ph, R = Me)<sup>10</sup> but the enamidine (6, Ar=Ar'=Ph, R=Me).

Our preliminary experiments suggest that the reactivity of the enamidines is intermediate between that of enamines<sup>11</sup> and that of enamides.<sup>12</sup> Hydrolysis of compound (6, Ar=Ar'=Ph, R=Pr) gave valerophenone and benzamide, and with benzoyl chloride the products included benzamide, valerophenone and *N*-(1-phenylpent-1-enyl)benzamide (9).

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#### REFERENCES

1. Dedicated to Professor H. Suschitzky on the occasion of his 60th birthday
2. M. S. Kharasch and O. Reinmuth, 'Grignard Reactions of Non-metallic Substances', Constable, London (1954)
3. B. J. Wakefield, 'The Chemistry of Organolithium Compounds', Pergamon, Oxford (1974).
4. R. M. Anker and A. H. Cook, *J. Chem. Soc.*, 323 (1941).
5. P. L. Compagnon and M. Miocque, *Ann. Chim. (France)*, 5, 23 (1970).

6. L O Moore, J. Org Chem , 31, 3910 (1966).
7. D J. Berry and B J. Wakefield, J Chem Soc (C), 642 (1971), D J Berry, J D Cook and B J Wakefield, J Chem Soc Perkin I, 2190 (1972)
8. A few enamidines fully substituted on nitrogen have been reported: A. Demoulin, H Gorissen, A. -M Hesbain-Frisque and L Ghosez, J. Amer. Chem Soc., 97, 4409 (1975).
9. A Padwa and W P Koehn, J. Org. Chem , 40, 1869 (1975)
10. A. A. Scala, N M. Bikales and E I. Becker, J. Org Chem , 30, 303 (1965).
11. Ed A G. Cook, 'Enamines Synthesis, Structure and Reactions', Marcel Dekker, New York and London, (1969)
12. R B Boar, J F McGhie, M Robinson, D H R Barton, D. C. Horwell and R V Stick, J Chem Soc Perkin I, 1237 (1975)