Tetrahedron Letters No. 42, pp 3591 - 3592, 1975. Pergamon Press. Printed in Great Britain.

REACTION OF LITHIUM ORGANOCUPRATES WITH NITROSTYRENES

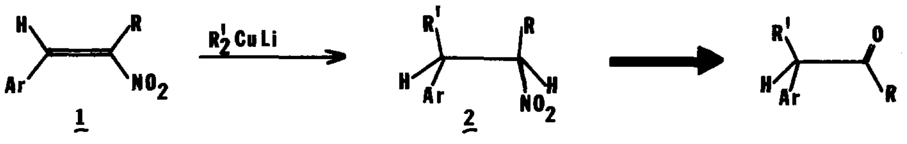
Stephen B. Bowlus

Pharmaco Inc., Interstate Research Park, Champaign, Illinois 61820

(Received in USA 23rd June 1975; received in UK for publication 9th September 1975)

The chemistry of the nitro moiety has been considerably advanced through investigations in which nitroalkane anions were used as acyl anion equivalents.[1] In connection with other studies, we wished to exploit the known nitro-carbonyl chemistry for the preparation of aryl and biaryl ketones. Inasmuch as nitroolefins have been shown to be good Michael acceptors with oxygen- or sulfur-stabilized carbanions[2] and with Grignard reagents,[3] our attention focussed upon reactions of these compounds.

Attempts to alkylate the nitrostyrene 1a by the procedure described[3] gave poor and poorly reproducible yields of the desired nitroalkane 2a; arylation of 1a failed completely with both phenyl Grignard and phenyllithium. Since lithium organocuprates are known to give 1,4-addition products with a number of unsaturated systems[4]--although by a distinctly different mechanism than the Michael reaction--we next investigated these reagents (eq. 1).



a Ar = 4-ClC$_6$H$_4$ R = CH$_3$
b Ar = C$_6$H$_5$ R = H
c Ar = 2-pyridyl R = CH$_3$

The reaction of 1a with lithium diphenylcuprate proceeded smoothly in ether solution at 0-5° when an excess of the reagent was added slowly to the substrate. Additional experiments gave the results summarized in the Table. The reactions involving lithium diphenylcuprate were in all cases attended by the formation of biphenyl, in keeping with observations of nitro-catalyzed coupling of organocuprates.[5]

Table

Conjugate Addition of Lithium Organocuprates to Nitrostyrenes[a]

Substrate	Cuprate, R'_2CuLi R' =	Nitroalkane Yield[b] %
1a	Ph	76
	CH_3	79
	n-C_4H_9	43
1b	Ph	c
	CH_3	54
1c	Ph	12
	CH_3	d

a Substitution per equation (1). Structures of all compounds were established by spectrometric measurements and combustion analysis. b Isolated yield after purification. c Substrate polymerized. d 78% of 1c recovered unchanged.

These extensions showed that the reaction was not as general as had been hoped; the examples shown, however, are believed to be extreme. For example, the pyridyl nitrogen of 1c could be expected to coordinate with the reagent, substantially altering the reactivity of the cuprate. It should be noted that in cases where successful reaction occurred, there was no evidence obtained for either competitive 1,2-addition to the substrates, or further reaction of the monoalkylated product with the reagent, as has been reported for the reaction of nitroolefins with Grignard reagents.[3]

Thus, while the scope of the reaction remains to be defined, the conjugate addition of lithium organocuprates to nitroolefins appears to be an attractive possibility for reactions synthetically equivalent to the α-alkylation, and particularly the α-arylation of ketones, this latter being a transformation for which few alternatives exist.[6]

REFERENCES

1. For example, see J. E. McMurry, Accts. Chem. Res., 7, 281 (1974).
2. D. Seebach and H. F. Leitz, Angew. Chem., Int. Ed. Engl., 8, 983 (1969); ibid., 10, 501 (1971); D. Seebach and V. Ehrig, ibid., 13, 400 (1974).
3. G. D. Buckley, J. Chem. Soc., 1947, 1494; G. D. Buckley and E. Ellery, ibid., 1947, 1497.
4. G. H. Posner, Org. Reactions, 19, 1 (1972).
5. G. M. Whitesides, J. San Filippo, Jr., C. P. Casey, and E. J. Panek, J. Amer. Chem. Soc., 89, 5302 (1967).
6. R. A. Rossi and J. F. Bunnett, J. Org. Chem., 38, 1407 (1973); H. C. Brown and M. M. Rogic, J. Amer. Chem. Soc., 91, 4304 (1969).