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THE GENERATION OF LITHIO-TRI-n-BUTYL-(2-CYANOETHYL)TIN. A NEW REAGENT FOR THE PREPARATION OF 2-SUBSTITUTED CYCLOPROPANE-1-CARBONITRILES AND SPIRO[2.n]ALKANE-1-CARBONITRILES

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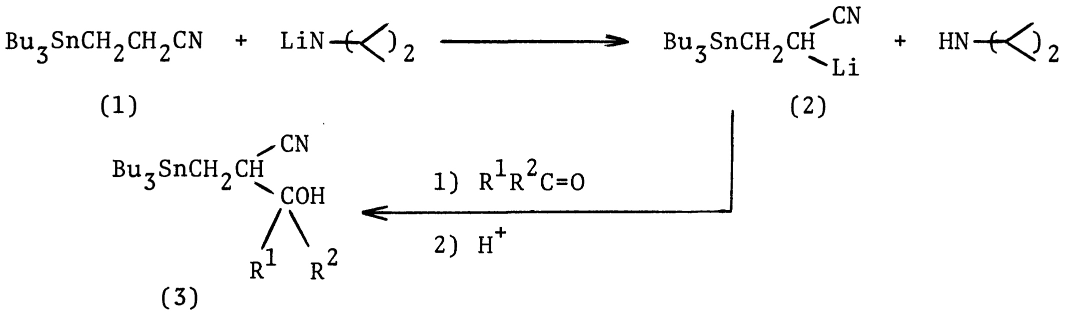
Tri-n-butyl-(2-cyanoethyl)tin is lithiated effectively and the resultant salt reacts with various carbonyl compounds to give corresponding addition products. Cyanocyclopropane derivatives can be prepared from the addition products through the 1,3-dehalostannylation reaction.

Simple cyclopropane derivatives have been prepared by the 1,3-elimination reaction of organotin compounds having suitable leaving groups at γ-position.[1,2] In this method, the necessary precursors, trialkyl-(3-hydroxypropyl)tin derivatives, were synthesized by the hydrostannation of allyl alcohols but this method can not be applied to prepare cyclopropane derivatives having functional groups. Thus, one of the major problems is how to prepare organotin compounds with a hydroxyl group at the γ-position in order to extend the cyclization reaction to the preparation of cyclopropanes having reactive functional groups.

We now wish to report the first example of the generation of carbanion of type (2) and a new synthetic method for the preparation of cyanocyclopropanes and 1-cyanospiro[2.n]alkanes by the use of tri-n-butyl-(2-cyanoethyl)tin.

Tri-n-butyl-(2-cyanoethyl)tin (1)[3] was treated with lithium diisopropylamide in tetrahydrofuran (THF) at -78°C for 1.5 hr. To the resulting colorless or faintly yellow solution was added equimolar amount of aldehydes or ketones at -78°C and then brought to room temperature. After the solution was quenched with aq THF at -20°C, neutralized by dilute hydrochloric acid, corresponding 3-substituted tri-n-butyl-(2-cyano-3-hydroxypropyl)tins (3) were isolated by silica gel column chromatograpy in good yields.[4]

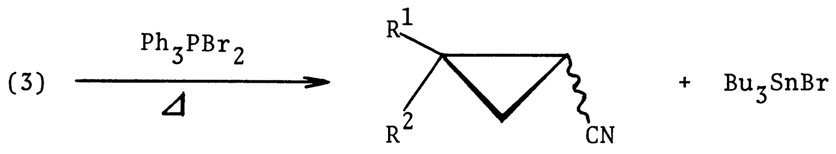


Not only acyclic aldehydes and ketones but cyclic ketones such as cyclopentanone also gave corresponding addition products in good yields. It is noteworthy that the reaction of (2) with α,β-unsaturated carbonyl compounds took place smoothly giving the corresponding 1,2-addition products while no 1,4-addition product was formed. The results are summarized in Table I.

Table I. Reaction of Lithio-tri-n-butyl-(2-cyanoethyl)tin with Carbonyl Compounds.

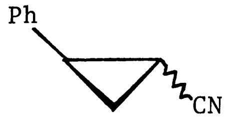
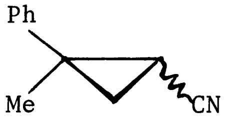
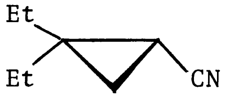
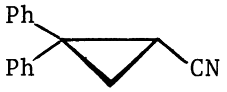
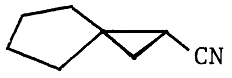
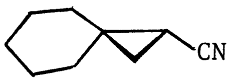
Carbonyl Compound	Product (3)			
	No.	R^1	R^2	Yield(%)
Benzaldehyde	3a	-H	-Ph	96
Acetophenone	3b	$-CH_3$	-Ph	93
Diethyl ketone	3c	-Et	-Et	94
Benzophenone	3d	-Ph	-Ph	83
Cyclopentanone	3e	$-CH_2(CH_2)_2CH_2-$		88
Cyclohexanone	3f	$-CH_2(CH_2)_3CH_2-$		92
Acrolein	3g	-H	$-CH=CH_2$	83
3-Buten-2-one	3h	$-CH_3$	$-CH=CH_2$	71
2-Cyclohexenone	3i	$-CH=CH-(CH_2)_2CH_2-$		77

The products (3a)-(3f) were readily converted into corresponding cyanocyclopropanes. Thus, (3a) was added to a suspension of triphenylphosphine dibromide in acetonitrile at -20°C and the resulting mixture was refluxed for 30 min, yielding a mixture of *trans*-2-phenylcyclopropanecarbonitrile (4a) and *cis*-2-phenylcyclopropanecarbonitrile (5a).5) The *trans*-(4a), mp 51-52°C,6) in 46% yield, *cis*-(5a), mp 36-37 °C, in 33% yield, were easily separated by preparative tlc. The reaction mentioned above proved to be also effective for the formation of spiro[2.n]alkanes from cyclic ketones. For example, treatment of (3e) or (3f) under similar reaction conditions led to the formation of spiro[2.4]heptane-1-carbonitrile (4e) or spiro-[2.5]octane-1-carbonitrile (4f) in 60% and 54% yields, respectively.7)



(4) or (5)

Table II. Synthesis of 2-Substituted Cyclopropane-1-carbonitriles.

Starting Material	Product		Yield(%)	mp, or bp(°C/mmHg)	Amide a) mp,°C (Lit.)
3a		trans(4a)	46	51-52	86-87 (85.5-86.5) b)
		cis(5a)	33	36-37	188-189 (189) b)
3b		trans(4b)	49	107-108/1	137-138 (137-138) c)
		cis(5b)	16	126-128/3	121-122 (121-122) c)
3c		(4c)	78	80-82/10	136-137 (136-137) d)
3d		(4d)	63	107-108	177-178 (178-179) e)
3e		(4e)	60	103-105/20	189-190 (190-191) f)
3f		(4f)	54	72-74/1.5	192-193 (192-193) f)

a) The cyano compounds were converted into the corresponding amides to determine the structures. b) C. Dipin and R. F-Jullien, Bull. Soc. Chim. France, 1993 (1964). c) C. Gibert and J. S-Penne, Bull. Soc. Chim. France, 2410 (1970). d) E. R. Nelson, M. Maienthal, L. A. Lane, and A. A. Benderly, J. Amer. Chem. Soc., **79**, 3467 (1957). e) H. M. Walborsky and F. M. Hornyak, J. Amer. Chem. Soc., **77**, 6026 (1955). f) L. M. Konzelman and R. T. Conley, J. Org. Chem., **33**, 3828 (1968).

The work described in this paper demonstrates that the carbanion from tri-n-butyl-(2-cyanoethyl)tin is a useful intermediate for the preparation of 2-substituted cyclopropane-1-carbonitriles and spiro[2.n]alkane-1-carbonitriles.

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References and notes

1) H. G. Kuivila and N. M. Scarpa, J. Amer. Chem. Soc., 92, 6990 (1970).

2) D. D. Davis, R. L. Chambers, and H. T. Johnson, J. Organometal. Chem., 25, C-13 (1970).

3) G. J. M. van der Kerk, J. G. Noltes, and J. G. A. Luijten, J. Appl. Chem., 7, 356 (1957).

4) All new products gave satisfactory elemental analysis and exhibited spectral properties in accordance with assigned structures.

5) *p*-Toluenesulfonyl chloride or thionyl chloride gives similar results; however, the yields are usually lower.

6) R. S. Givens and W. F. Oettle, J. Org. Chem., 37, 4325 (1972).

7) The structure of the cyanocyclopropanes and cyanospirane derivatives were firmly established by spectroscopy. Further they were convereted into the corresponding amides, carboxylic acids, and ethyl carboxylates and were identified by comparison with the respective authentic samples prepared by known methods (see TableII ref.).

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