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AN EFFICIENT METHOD FOR CYCLOPROPANATION VIA APROTIC DIAZOTIZATION OF 3-(TRI-n-BUTYLSTANNYL)PROPYLAMINES

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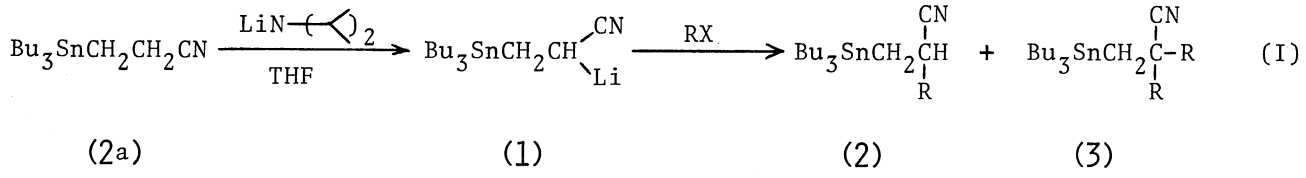
Reactions of 2-lithio-3-(tri-n-butylstannyl)propionitrile (1) with alkyl halides or carbonyl compounds gave the corresponding 2-substituted 3-(tri-n-butylstannyl)propionitriles (2), which were reduced to amines (4) and then diazotized to give alkyl cyclopropanes or cyclopropanemethanols, respectively, in moderate overall yields.

We have recently reported a method for generation of 2-lithio-3-(tri-n-butylstannyl)propionitrile (1)[1]. In the present paper, we wish to report an efficient synthetic method for cyclopropanes with incorporation of carbon atom of cyano group.

Initially, we have examined the alkylation reaction of (1). Treatment of (1) with a variety of alkyl halides in tetrahydrofuran (THF) at -40°C for 1 hr and at 25°C for 1 hr led to the desired 2-alkyl-3-(tri-n-butylstannyl)propionitriles (2)[2] and a small amount of dialkylated products (3) as eq. (I) (Table I).



(2a) (1) (2) (3) (I)

The nitriles (2a)-(2g) thus obtained were easily converted to 2-alkylated 3-(tri-n-butylstannyl)propylamines (4a)-(4g) by treating with lithium aluminum hydride ($LiAlH_4$) in ether at 10°C for 5 hr. Similarly, the reactions of (2h)-(2k)[1] with $LiAlH_4$ gave (4h)-(4k) in good yields.

Table I. The Alkylation of Lithiated Nitriles (1)

RX	Yield (%)[a] (2)[b]/(3)[b]
Methyl iodide	2b (65)/(21) 3b
Benzyl bromide	2c (63)/(17) 3c
1-(Chloromethyl)naphthalene	2d (69)/(13) 3d
3-Chloro-2-methyl-1-propene	2e (72)/(4) 3e
t-Cinnamyl bromide	2f (68)/(6) 3f
2-Bromoethyl phenyl ether	2g (70)/(16) 3g

a) The products were isolated by tlc. Yields were calculated on the basis of alkyl halides. *b)* Satisfactory infrared, proton magnetic resonance, and mass spectral data were obtained for all new substances reported herein.

Amines (4) were diazotized with a slight excess of isoamyl nitrite (AmONO) in the presence of appropriate carboxylic acid as proton donor at 60°C for 30 min.[3] Under these conditions it was expected that the thermal decomposition of 3-(tri-n-butylstannyl)propanediazonium(s) would occur to yield the corresponding cyclopropane derivatives. In fact, approximately quantitative volume of gas was evolved and cyclopropanes (5) (65-95% yield) were obtained, together with a small amount of olefins (6) (2-22% yield). These products were distilled and the residues were found to be corresponding tri-n-butylstannyl carboxylate (see eq. II). The structures of the cyclopropanes and cyclopropanemethanols were firmly established by ir, pmr and mass spectral data. These results are summarized in Table II.

The following is a typical experimental procedure.

Cyclopropyl-1-naphthylmethane (5d)

To lithium diisopropylamide (0.12 mol) in anhydrous THF (200 ml) was added (2a) (37.9 g, 0.11 mol) over 30 min at -78°C. After stirring for 1.5 hr at this temperature, the reaction mixture was warmed to -40°C during 5 min and then 1-(chloromethyl)naphthalene (17.7 g, 0.10 mol) in 10 ml of THF was added to this solution. Then it was stirred for 1 hr at -40°C and 1 hr at 25°C. Following an aqueous acidic workup, the reaction mixture was chromatographed on silica gel with n-hexane as eluent to provide 33.5 g (69%) of 2-(1-naphthylmethyl)-3-(tri-n-butylstannyl)propionitrile (2d) and 8.20 g (13%) of (3d). (2d): an oil; n_D^{23} 1.5498; ir(cm^{-1})(neat) 2245 1515, 800, 780; NMR δ (CCl_4) 0.10~2.15(m, 29H), 2.70~3.55(m, 3H), 7.10~8.05(m, 7H); Mass $C_{26}H_{39}N^{120}Sn$ M^+ 485(2), m/e 428(100). (3d): mp 68.5~69.5°C (n-pentane); ir(cm^{-1}) (KBr) 2230, 1512, 808, 787; NMR δ (CCl_4) 0.15~2.05(m, 29H), 3.35(s, 4H), 7.10~8.15(m, 14H); Mass $C_{37}H_{47}N^{120}Sn$ M^+ 625(1.5), m/e 568(100).

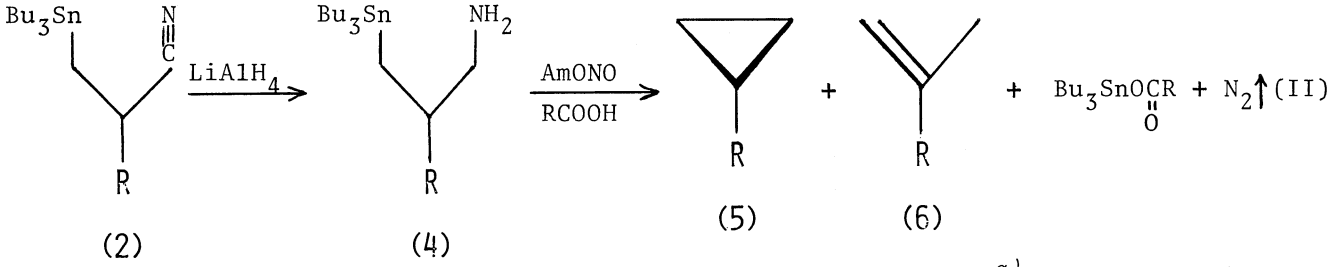


Table II. The Reduction of Nitriles (2) and Deamination[a] of Amines (4)

(2)	−R	Amine (4) Yield(%)[b]	RCOOH[c]	Isolated Yield(%)[d] (5)	(6)[e]	NMR (δ_{TMS}ppm, CCl_4) of (5)
2a	−H	79	┼COOH	95[f]	2[f]	[g]
2b	−Me	87	┼COOH	89[f]	6[f]	[h]
2c	$-CH_2Ph$		AcOH	(78)	(6)	[i]
2d	$-CH_2$-α-Nap	86	┼COOH	87	4	[j]
2e	$-CH_2CH{=}CH_2$ CH_3		┼COOH	(65)[f]	(17)[f]	−0.13~0.23(m, 2H), 0.23~1.13 (m, 3H), 1.76(s, 3H), 1.90(d, J=6.28 Hz, 2H), 5.50~5.90(m, 2H)
2f	$-CH_2CH{=}CHPh$	76	┼COOH	71	11	−0.10~1.12(m, 5H), 2.10(t, J= 5.44 Hz, 2H), 5.53~6.63(m, 2H), 6.93~7.50(m, 5H)
2g	$-CH_2CH_2OPh$	90	┼COOH	88[k]	4[k]	−0.08~1.30(m, 5H), 1.62(q, J= 6.60 Hz, 2H), 3.91(t, J=6.60 Hz, 2H), 6.55~7.40(m, 5H)
2h	$-\underset{OH}{\overset{H}{C}}-{}^{n}Pr$	81	AcOH	67[l]		0.12~0.63(m, 4H), 0.67~1.87(m, 8H), 4.32(q, J=7.00 Hz, 1H), 8.83~9.30(m, 3H)
2i	$-\underset{OH}{\overset{H}{C}}-Ph$	87	AcOH	73		[i*]
2j	$-\underset{OH}{\overset{CH_3}{C}}-Ph$	91	AcOH	70		0.15~0.73(m, 4H), 0.80~1.33(m, 1H), 1.50(s, 3H), 1.88(s, 1H), 7.24(s, 1H)
2k	$-\underset{OH}{\overset{}{C}}-(CH_2)_4-CH_2$		┼COOH	(65)	(22)	−0.10~0.50(m, 4H), 0.50~1.00 (m, 1H), 1.00~1.95(m, 11H)

a) Amine, 0.01 mol; isoamyl nitrite, 0.012 mol; acid, 0.010 0.015 mol; chloroform, 20 ml; 60°C; 30 min; unless otherwise indicated. *b)* Isolated yield by column chromatography: ethanol-benzene(1:6). *c)* ┼COOH: pivalic acid, AcOH: acetic acid. *d)* Values in parentheses were calculated from (2), without isolation of (4). *e)* These olefins did not isomerise under the reaction conditions. *f)* Determined by vpc and pmr. *g)* W. G. Dauben and W. T. Wipke, J. Org. Chem., 32, 2976 (1967). *h)* L. Friedman and J. H. Bayless, J. Amer. Chem. Soc., 91, 1790 (1969) and references cited therein. *i)* C. J. Pouchert and J. R. Campbell, "The Aldrich Library of NMR Spectra" Aldrich Chemical Company, Inc., Milwaukee, Wisconsin, (1974) Vol. 4, p. 5-D. *i*)* Ibid, Vol. 5, p. 1-D. *j)* See typical experimental procedure. *k)* Ref. 3). *l)* The yield was obtained as 3,5-dinitrobenzoate (mp 64~65°C).

To (2d) (9.68 g, 20 mmol) in 40 ml of ether was added $LiAlH_4$ (20 mmol) in ether (31 ml) at -40°C. After the solution was stirred for 30 min at 0°C and 5 hr at 10°C, the reaction mixture was quenched with 5 ml of 10% aq THF, and was filtered. After removal of the solvent, purification of the residue with silica gel column chromatography with ethanol-benzene (3:17) gave 8.40 g (86%) of 2-(1-naphthylmethyl)-3-(tri-n-butylstannyl)propylamine (4d): an oil; n_D^{23} 1.5582; ir(cm^{-1})(neat) 3400, 1620; NMR δ (CCl_4) 0.15~2.15(m, 31H), 2.15~3.45(m, 5H), 7.05~8.25(m, 7H); Mass $C_{26}H_{43}N^{120}Sn$ M^+ 489(1), m/e 432(100).

To a solution of (4d) (4.843 g, 10 mmol) and isoamyl nitrite (1.41 g, 12 mmol) in chloroform (15 ml) was added 5 ml of 2.00 M (10 mmol) pivalic acid in chloroform at room temperature, and the mixture was heated for 30 min at 60°C. Gas evolution was observed and slightly reddish solution resulted. The reaction mixture was washed with saturated sodium hydrogencarbonate, and the solvent was evaporated. The residue was chromatographed on Merck silica gel F254 (containing 1% silver nitrate) preparative layer plate with n-pentane to provide 1.586 g (87%) of cyclopropyl-1-naphthylmethane (5d) (Rf 0.80) and 0.073 g (4%) of (6d) (Rf 0.55). (5d): bp 124 126°C/3 mmHg; n_D^{23} 1.6038; ir(cm^{-1})(neat) 3083, 3010, 1603, 1516, 1023, 796, 783; NMR δ (CCl_4) -0.05~0.70(m, 4H), 0.70~1.45(m, 1H), 2.97(d, J=6.45 Hz, 2H), 6.98~8.15(m, 7H); Mass M^+ 182(48), m/e 141(100), 154(35).

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References and notes

1) S. Teratake, Chem. Lett., 1123 (1974).

2) All alkylated nitriles (2) and (3) were isolated by silica gel column chromatography or preparative layer chromatography.

3) The deamination of (4g) with isoamyl nitrite in chloroform using a variety of carboxylic acid showed the following acidity dependence [carboxylic acid, (5g)/(6g): trifluoroacetic acid, 48/52; benzoic acid, 71/29; acetic acid, 87/13; pivalic acid, 96/4; citraconic acid, 95/5.

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