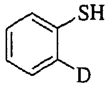
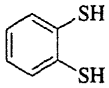
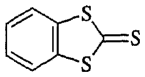
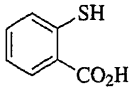
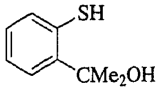
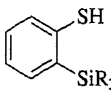
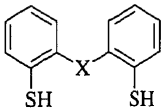
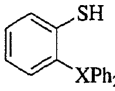
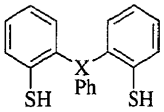
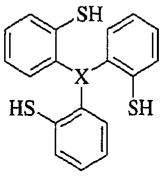
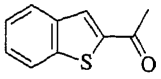
Table 1 Thiophenols formed by Reaction of Lithium 2-Lithiobenzenethiolate with Electrophiles

Electrophile	Product		Yield (%)	Ref.
D_2O			97	1a
S_8			96	1b
$[i\text{-}Pr_2NC(S)S]_2$			67	1c
CO_2			61	1a
Me_2CO			61	1a
R_3SiCl		R = Me R = Et R = Ph R = *t*-$BuMe_2$	92 79 43 28	1b, c
Me_2SiCl_2		X = $SiMe_2$ X = $[SiMe_2]_2$ X = $[SiMe_2\text{-}CH_2]_2$	44 40 33	1b
Ph_2XCl		X = P X = P=O	65 67	6
$PhXCl_2$		X = P X = P=O	76 63	6
XCl_3		X = P X = P=O X = SiH	56 67 11	6, 4
DMF, $MeCOCH_2Cl$			75	9

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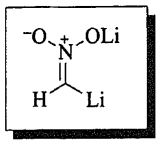
Lithium α-Lithiomethanenitronate[1]



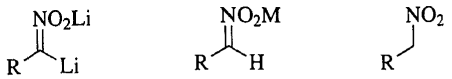
[–] $CHLi_2NO_2$ (MW 72.91)

(highly nucleophilic derivatives of nitromethane and of other primary nitroalkanes[2] for alkylation,[2–6] hydroxyalkylation,[2,5,7–12] and acylation[2,5,8,13])

Preparative Methods: the reagent may be generated in THF solution.[4,10,12] A solution of the nitroalkane in THF is treated with ~2 equiv ***n-Butyllithium*** or ***Lithium Diisopropylamide*** at temperatures between –75 and –95 °C; the yields of the subsequent reactions are higher when the double lithiation is carried out in the presence of the cosolvent HMPA or, preferably, of the nonmutagenic ***N,N'-Dimethylpropyleneurea*** (DMPU).[14] The solutions are usually bright yellow and are stable for a few hours at temperatures below about –50 °C; evaporation of the solvents at low temperature leads to residues which decompose spontaneously.

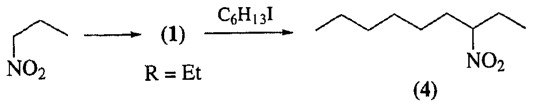
Reactivity of Doubly Lithiated Nitroalkanes (1). While nitronates (**2**) are readily generated from nitroalkanes (**3**) ($pK_a \approx 10$), their C-nucleophilicity is generally poor.[1,15,16] Alkylations of (**2**) with alkyl halides occur preferentially on oxygen, but the addition to aldehydes and ketones is highly reversible; the acylation is only possible with acylimidazolines or other special reagents.[1,17] The most useful reaction of (**2**) is their Michael addition to α,β-unsaturated carbonyl compounds. There have been several preparative improvements in recent decades: the use of silyl nitronates (see ***Trimethylsilyl Methanenitronate***), employment of new catalyst systems such as Al_2O_3 and ***Potassium Fluoride***,[15] application of high pressure,[18] and the use of dilithio derivatives (**1**). They are highly nucleophilic and react at carbon irreversibly with all electrophiles tested, including alkyl halides,[2–6] aldehydes and ketones,[2,5,7–12] acid chlorides,[2,5,8,13] and halogens such as bromine:[19] with α,β-enals[5] and α,β-enones[8] they add in a 1,2- not in a 1,4-fashion. The structure of reagents (**1**) is unknown; thus

in the formulae used here they are shown with the lithium at carbon, since this is where reactions with electrophiles occur.

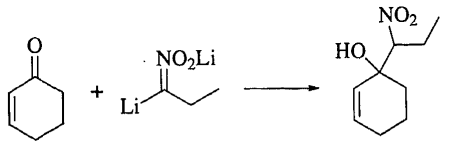


(1) (2) (3)

Applications of Simple Dilithionitronates (1) in Synthesis. Some products from reactions of the lithiated lithionitronates with electrophiles are shown in the accompaning equations. Thus nitropropane can be hexylated to give 3-nitrononane (**4**) in 50% yield (eq 1).[3,4] Nitropropane was also added to cyclohexenone to yield (52%) the unsaturated nitro alcohol (**5**), a type of compound not available by any other nitroaldol-forming method (eq 2).[8]

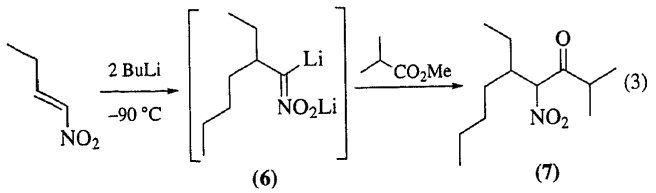


(1)

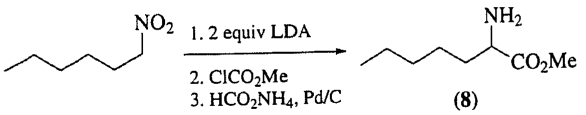


(2)

The 1,4-adduct of BuLi to 1-nitro-1-butene can be further lithiated in situ to form a doubly lithiated reagent (**6**) which is acylated by methyl 2-methylpropanoate, with formation after aqueous workup of the nitro ketone (**7**) in an overall yield of 30% (eq 3).[8] An application of nitroalkane *C*-acylation[2,5,8,13] to the synthesis of *rac*-amino acids is exemplified with the aminoheptanoic ester (**8**), prepared in two steps (50% yield)[13] from nitrohexane and methyl chlorocarbonate (eq 4).

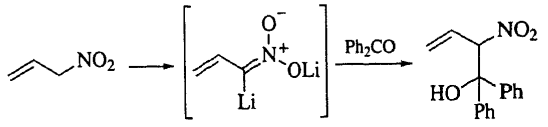


(3)

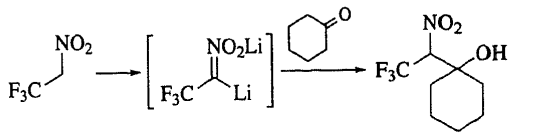


(4)

Dilithionitronates Bearing Additional Functional Groups. The doubly lithiated nitroalkanes can also be generated from precursors containing additional functional groups. For instance, 1-nitro-2-propene gives a reagent (**9**), which was added to benzophenone to give the otherwise not accessible nitroaldol adduct (**10**) in 53% yield (eq 5).[8] More surprising is the fact that nitroalkanes with β-leaving groups, such as trifluoronitroethane,[11,12] can also be doubly lithiated to give rather stable reagents of type (**11**). These may be used for the reactions with various electrophiles mentioned above. Thus the trifluoromethyl-substituted nitroaldol (**12**) with a tertiary hydroxy group could be prepared in 60% yield (eq 6).[12] *Retro*-nitroaldol cleavage occurs readily during bulb-to-bulb distillation (90 °C/10 mmHg).

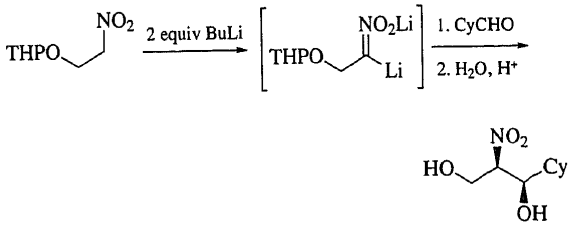


(5)



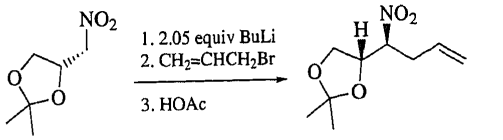
(6)

Nitroaldol additions of doubly lithiated alkoxyl-substituted nitroalkanes can be highly diastereoselective, as demonstrated by the addition of THP-protected 2-nitroethanol to cyclohexanecarbaldehyde to form (**13**) (64%) (eq 7).[5] Another example is the preferential formation of the (*S,S*)-diastereoisomer (**14**) in the allylation of a glyceraldehyde-derived nitro compound (68% yield; dr = 82:18) (eq 8).[6]



(7)

(13) >95% *syn*



(8)

(14) (*S,S*)

Related Reagents. *O,O*-Dilithio-1-nitropropene; Nitroethane; Nitromethane.

1. (a) Seebach, D.; Colvin, E. W.; Lehr, F.; Weller, T. *C* **1979**, *33*, 1. (b) Döpp, D.; Döpp, H. *MOC* **1990**, *E14b*, 780.
2. Seebach, D.; Lehr, F. *AG(E)* **1976**, *15*, 505.
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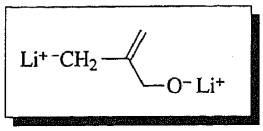
Lithium 2-Lithiomethyl-2-propenolate[1]



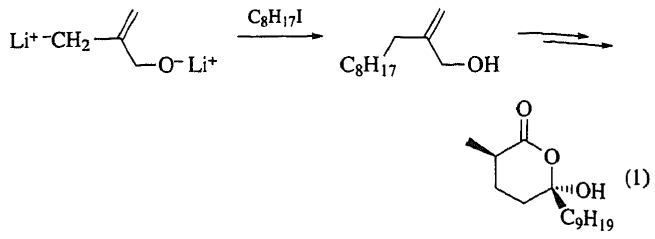
[–] $C_4H_6Li_2O$ (MW 83.98)

(nucleophilic reagent for the generation of functionalized isoprenoid compounds through alkylation or addition reactions)

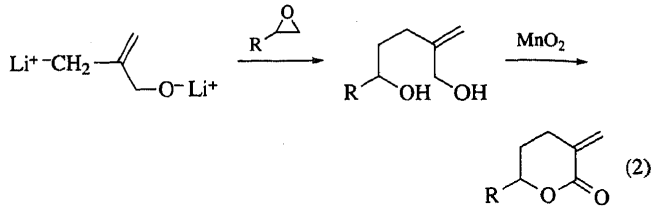
Physical Data: gold colored solid.
Solubility: insol hexane.
Preparative Methods: metalation of methallyl alcohol with ***n*-Butyllithium–Potassium *t*-Butoxide.**
Handling, Storage, and Precautions: air, water, and temperature (greater than 0 °C) sensitive.

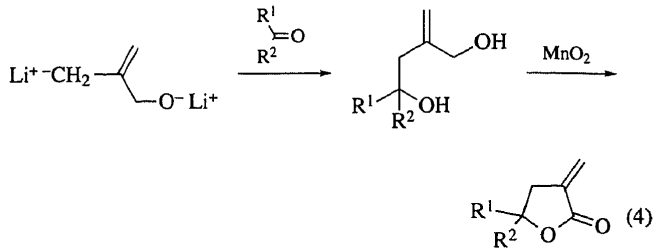
The allylic dianion is prepared by the action of *t*-BuOK/*n*-BuLi (i.e. Schlosser's base) in hexane on methallyl alcohol.[1] The active reagent is formed immediately upon the completion of the alcohol addition (0 °C). The yield of allylic anion formed appears to be extremely sensitive to reaction conditions (e.g. fresh *n*-BuLi,[1] solvent[2]).

The methallyl alcohol dianion can be alkylated with alkyl halides (eq 1)[3] or epoxides (eq 2),[4] silylated (eq 3),[2,5] or undergo addition reactions with aldehydes or ketones (eq 4).[1] This carbon–carbon bond-forming process introduces a functionalized isoprenoid unit.

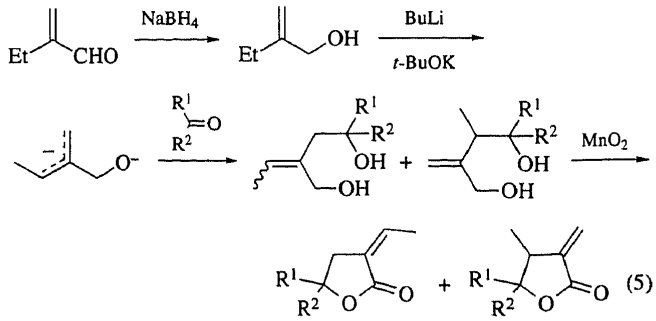


Malynolide





Related Reagents. A similar transformation is observed with 2-ethylallyl alcohol derived from commercially available 2-ethylacrolein (eq 5). The observed addition products are mixtures of 1,4-diols derived from attack on both the primary and secondary carbons. Oxidation with activated ***Manganese Dioxide*** gives the α-methylene- and (*Z*)-α-ethylidenebutyrolactones (eq 5).[6] See also ***Methallyllithium***.



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2. Trost, B. M.; Chan, D. M. T. *JACS* **1983**, *105*, 2315.
3. Kozikowski, A. P.; Nieduzak, T. R.; Scripko, J. *OM* **1982**, *1*, 675.
4. Carlson, R. M.; White, L. L. *SC* **1983**, *13*, 237.
5. Trost, B. M.; Chan, D. M. T.; Nanninga, T. N. *OS* **1984**, *62*, 58.
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