CHEMISTRY LETTERS, pp. 1065-1068, 1983. © The Chemical Society of Japan 1983

GENERATION AND REACTIONS OF THE ALLYLIC CARBANION SPECIES FROM 2-METHYL-3-(PHENYLTHIO)PROPENOIC ACID DERIVATIVES

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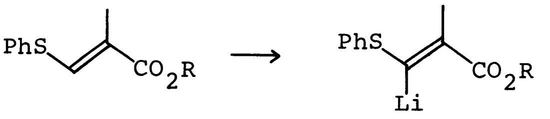
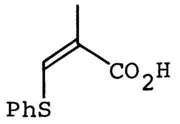
(*Z*)-2-Methyl-3-(phenylthio)propenoic acid and (*E*)-*N*-*t*-butyl-2-methyl-3-(phenylthio)propenamide produce selectively the corresponding allylic carbanion species, which react with aldehydes and ketones. The same carbanion species are also generated from 2-(phenylthiomethyl)propenoic acid and its *N*-*t*-butyl amide.

In the previous papers, we reported that (*E*)-2-methyl-3-(phenylthio)propenoic acid (**1**)[1)] and the methyl ester (**2**)[2)] produced selectively, upon treatment with lithium diisopropylamide (LDA) at -80 °C, the vinyl carbanion species (**3**) and (**4**), which reacted with carbonyl compounds to afford synthetically useful functionalized butenolides and cyclopentenones.[1-3)] If the allylic carbanion species could be generated selectively from the appropriate derivatives of **1**, **1** would be used more widely as a versatile intermediate in construction of complex organic molecules. We report here the results of the lithiation of the isomeric (*Z*)-acid (**5**) and the (*E*)-amide derivative (**6**), in contrast to the cases of **1** and **2**, leading selectively to the allylic carbanion species.



1 R= H
2 R= CH_3
3 R= Li
4 R= CH_3



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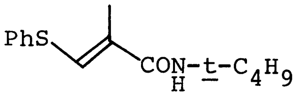

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Upon treatment with 2.4 mol equiv. of lithium 2,2,6,6-tetramethylpiperidide (LTMP) in tetrahydrofuran (THF) at -97 °C for 0.5 h the (*Z*)-acid (**5**)[4,5)] produced the allylic carbanion species (**7**), not the vinylic one, as indicated by a quenching experiment with deuterium oxide[6)] and by the reaction with aldehydes and ketones as described below.[7)] The allylic carbanion species (**7**) thus generated was treated with a slight excess of aldehydes or ketones at -97∿-80 °C for 1∿2 h to give the hydroxy carboxylic acid (**8**). In all of the reactions the separation of **8** was so difficult that the total crude product was subjected to lactonization by treating with *p*-toluenesulfonic acid in refluxing benzene to afford the α-phenylthio-methylene lactone (**9**) as the sole isolable product. The results are summarized in Table 1. The (*E*)-configuration of the phenylthiomethylene group in each **9** was established on the basis of the following evidence: appearance of the olefinic

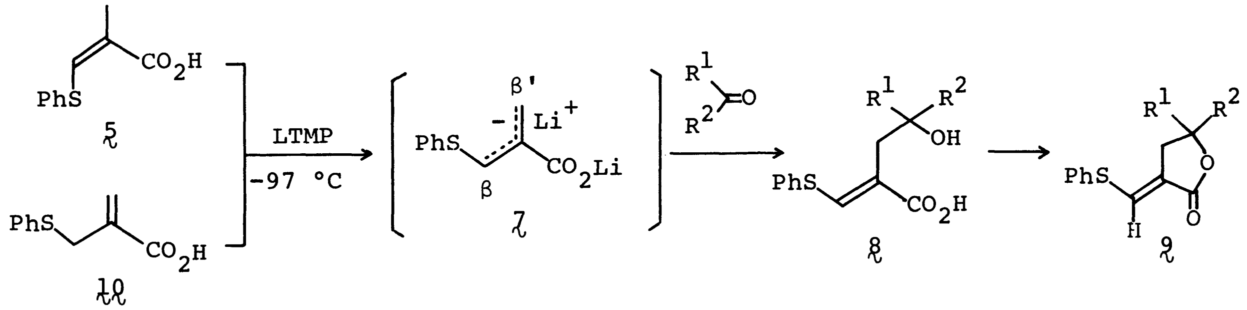

Table 1. Reaction of the allylic carbanion species (7) with aldehydes and ketones

Starting acid	Aldehyde or ketone	Product (9) R^1	R^2	Yield, %[a]
5	$CH_3CH_2CH_2CHO$	H	$CH_3CH_2CH_2$	43
"	$(CH_3)_2CHCHO$	H	$(CH_3)_2CH$	46
"	$CH_3CO(CH_2)_4CH_3$	CH_3	$CH_3(CH_2)_4$	34
"	cyclohexanone	$-(CH_2)_5-$		49
10	$(CH_3)_2CHCHO$	H	$(CH_3)_2CH$	40
"	cyclohexanone	$-(CH_2)_5-$		40

[a] Yields are for the isolated pure products. The remaining in each reaction was mostly polymeric acid material.

proton signal at δ 7.20–7.60 overlapped with the aromatic proton signals. Such a down field chemical shift is acceptable for the (*E*)-geometry in referring the values of the (*E*)-acid (1) and -ester (2), δ 7.70 and 7.51, respectively.[8)] Furthermore, it was found that, in attempts to separate compound (8) as the methyl ester, sometimes the starting material was recovered as the (*E*)-ester (2), not the (*Z*)-ester. Thus, these results clearly indicate that the (*Z*)-configuration in the starting acid (5) was no longer retained in the allylic carbanion species and that the adduct arising from the reaction at the β' site in 7 and having sterically more favorable (*E*)-configuration was the only isolable product.

From the result on the deuteration experiment of 7[6)] the isomeric acrylic acid derivative (10)[9)] would be expected to generate the same dianion species (7). Actually, under the identical conditions compound (10) produced 7 and reacted with isobutyraldehyde or cyclohexanone to yield, after lactonization, the same product (9) (Table 1).

For generation of an allylic carbanion species and for synthetic utility, we found that the (*E*)-amide derivative (6) as well as the isomer (11) was much more superior to the (*Z*)-acid (5). Thus, treatment of 6 or 11[10)] with 2.2 mol equiv. of LDA in THF at -80∿-70 °C for 1.5 h produced selectively the relatively stable allylic carbanion species (12).[11)] The reaction of the dianion (12) with aldehydes and ketones proceeded cleanly at -45∿-25 °C for 1.5 h to give the single adduct (**13**) in high yield.[12] The results are summarized in Table 2. It was found that, although an example, the reaction with an α,β-unsaturated ketone, cyclohexenone, gave only the 1,2-addition product (Table 2) and that the double bond in all **13** has (*E*)-configuration. Compound (**13**) could be transformed into the α-phenylthiomethylene lactone (**9**) in good yield by a simple operation, heating in refluxing xylene.

The dianion species (**12**), in contrast to the dianion (**7**), also reacted with other electrophiles. Thus, addition of methyl acrylate (-55∿-30 °C, 1 h), allyl bromide (-40∿-25 °C, 40 min), or propylene oxide (-40 °C∿room temp., 1 day) to (**12**) led to the corresponding adducts (**14**), (**15**), and (**16**) in 48, 59, and 42% yields, respectively.

From the above results, the selective generation of the allylic carbanion species (**7**) and (**12**) from **5** and **6** would be accounted for by decrease of the acidity

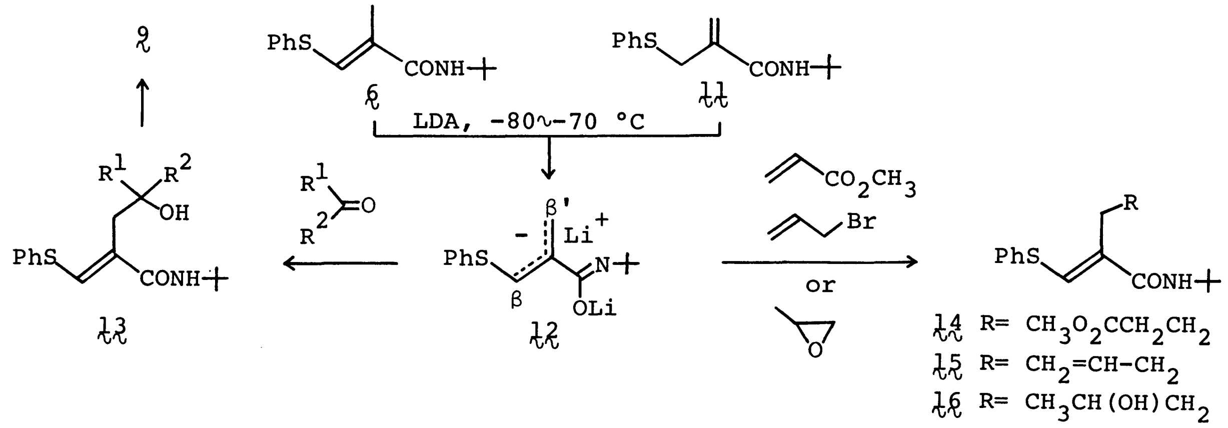

Table 2. Reaction of the allylic dianion species (**12**) with aldehydes and ketones

Aldehyde or ketone	Product (**13**)		Yield, %^{a}
	R^1	R^2	
$CH_3(CH_2)_2CHO$	H	$CH_3(CH_2)_2$	97
$(CH_3)_2CHCHO$	H	$(CH_3)_2CH$	95
p-$CH_3OC_6H_4CHO$	H	*p*-$CH_3OC_6H_4$	86
CH_3COCH_3	CH_3	CH_3	80
$CH_3(CH_2)_4COCH_3$	CH_3	$CH_3(CH_2)_4$	87
cyclohexanone	$-(CH_2)_5-$		73
cyclohex-2-en-1-one	$-(CH_2)_3CH=CH-$		83

[a] Yields are for the isolated pure products, on the basis of recovered **6** (*ca*. 10%).

of the olefinic hydrogen atom due to the (*Z*)-geometry in **5** and the amide functionality13) in **6**.

We thank the Ministry of Education, Science, and Culture of Japan for financial support (a Grant-in-Aid for Scientific Research, No. 56540318).

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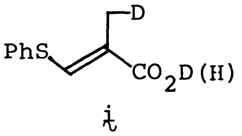
4) The pure (*Z*)-acid (**5**), mp 88∿89 °C (from ether–petroleum ether) was prepared from the (*E*)-ester (**2**) by sequential reactions [photoisomerization, lithiation of the resulting isomeric mixture and reaction with *n*-butyraldehyde (twice), saponification of the (*Z*)-ester recovered unchanged (*cf*. Ref. 7)].
5) All new compounds were characterized by combustion analysis as well as by IR and ^{1}H NMR spectroscopy.
6) The ^{1}H NMR spectrum of the recovered material revealed clearly the signals due to the deuterated species (**i**) and (**ii**). However, the yield and the proportion of **i** and **ii** could not be determined.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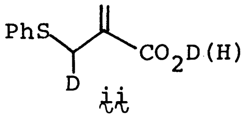
ii

7) Lithiation with LDA at -90∿-70 °C could not be detected. Also, no lithiation was observed upon treatment of the (*Z*)-ester with either LDA or LTMP at -90∿-70 °C. After quenching with deuterium oxide, the starting materials were completely recovered undeuterated.
8) The (*Z*)-isomer of **9** (R^1= H, R^2= *n*-C_4H_9), prepared by photoisomerization, revealed the olefinic proton signal at δ 6.88, being in good agreement with those of the (*Z*)-acid (**5**) and the ester, δ 7.10 and 6.83, respectively.
9) G. K. Pajagopalan and S. Swaminathan, Synthesis, **1976**, 409.
10) The amides (**6**) and (**11**) were easily prepared by the reaction of the corresponding acid chloride with *t*-butylamine.
11) Deuteration of **12** resulted in the 90% recovery of the *ca*. 80% β'-deuterated **6**.
12) We also found that the *N*,*N*-diisopropyl amide derivative produced the allylic monoanion species. In this case, however, the monoanion species was considerablely unstable, decomposed above -50 °C and the reaction with acetone gave two adducts (29 and 44%) arising from the addition of acetone on both β and β' reactive sites.
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(Received May 2, 1983)