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DIANIONS OF *N*-MONOSUBSTITUTED-3-(PHENYLSULFONYL)PROPANAMIDES. CONVENIENT REAGENTS FOR THE SYNTHESIS OF 5-ALKYL-2(5*H*)-FURANONES

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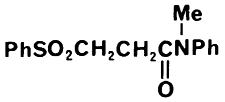
Treatment of *N*-phenyl-3-(phenylsulfonyl)propanamide with 2 equiv. of butyllithium at -78 °C afforded the dianion. Aldehydes and ketones upon treatment with the dianion provided stable γ-hydroxy amides, which were converted in good yields to 5-alkyl-2(5*H*)-furanones. Optically active (*R*)- and (*S*)-5-octyl-2(5*H*)-furanones, and (*R*)- and (*S*)-5-tridecyl-2(5*H*)-furanones were prepared from aldehydes and the dianions, derived from chiral *N*-monosubstituted-3-(phenylsulfonyl)propanamides.

The reaction of the enolate anions continues to play an important role in organic synthesis.[1)] A number of efficient techniques have been developed for the stereoselective formation of these reactive species and the enantioselective and diastereoselective construction of carbon-carbon bonds.[2)]

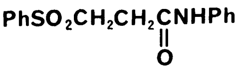
In contrast, relatively little attention has been given to the reaction of homoenolate anions or homoenolate anion equivalents.[3,4)] Uda *et al.* found that the dianion could be prepared from 3-(phenylsulfonyl)propionic acid and reacted with cyclopentanone to give a dihydro-2(3*H*)-furanone in 37% yield.[4g)]

The purpose of this communication is to report our observation on the utility of the dianions of *N*-monosubstituted-3-(phenylsulfonyl)propanamides as



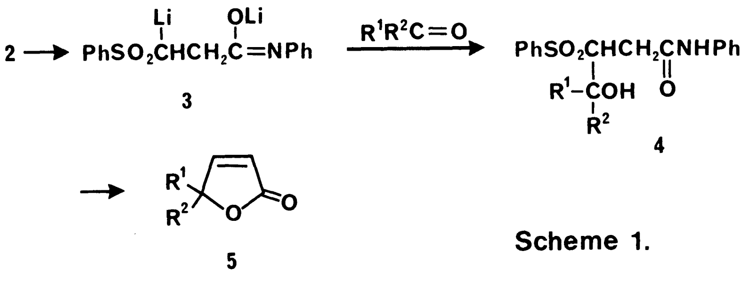
$PhSO_2CH_2CH_2C(=O)N(Me)Ph$

1



$PhSO_2CH_2CH_2C(=O)NHPh$

2



Scheme 1.

the homoenolate anion equivalent for the preparation of racemic and optically active 5-alkyl-2(5*H*)-furanones from carbonyl compounds (Scheme 1).

Although treatment of *N*-methyl-*N*-phenyl-3-(phenylsulfonyl)propanamide (1) with 1 equiv. of butyllithium at -78 °C gave intractable decomposition products, probably due to the elimination of lithium benezenesulfinate,5) the dianion 3 could be readily prepared from *N*-phenyl-3-(phenylsulfonyl)propanamide (2).

Thus, addition of 2 equiv. of butyllithium to a solution of 2 in THF at -78 °C gave a pale yellow solution of the dianion 3. Reaction of 3 with 1.1 equiv. of nonanal in THF at -78 °C for 2 h gave *N*-phenyl-4-hydroxy-3-(phenylsulfonyl)dodecanamide (4a) in 73% yield: mp 103-106 °C; ^{1}H NMR ($CDCl_3$) δ 9.35 (s, 1H, NH), 6.95-8.20 (m, 10H, aryl CH), 4.05-4.50 (m, 2H, OH and CH), 3.95 (m, 1H), 3.00 (d, J = 6.0 Hz, 2H, CH_2), 0.60-1.90 (m, 17H); IR (KBr) 3350 (OH), 1665 (C=O), 1320, 1160 (SO_2) cm^{-1}. Treatment of 4a with dilute hydrochloric acid in refluxing dioxane for 4 h gave 5-octyl-4-(phenylsulfonyl)-dihydro-2(3*H*)-furanone, which without purification was treated with triethylamine in chloroform at room temperature for 18 h to afford 5-octyl-2(5*H*)-furanone (5a)6) in 53% overall yield from 4a after purification by silica gel chromatography: bp 115 °C/0.8 mmHg (1 mmHg = 133.322 Pa); ^{1}H NMR ($CDCl_3$) δ 7.38-7.55 (m, 1H), 5.92-6.08 (m, 1H), 4.87-5.07 (m, 1H), 0.56-1.82 (m, 17H); IR (neat) 1760 (C=O), 1600 (C=C) cm^{-1}. Found: C, 73.50; H, 10.12%. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27%. Other examples are given in Table 1.

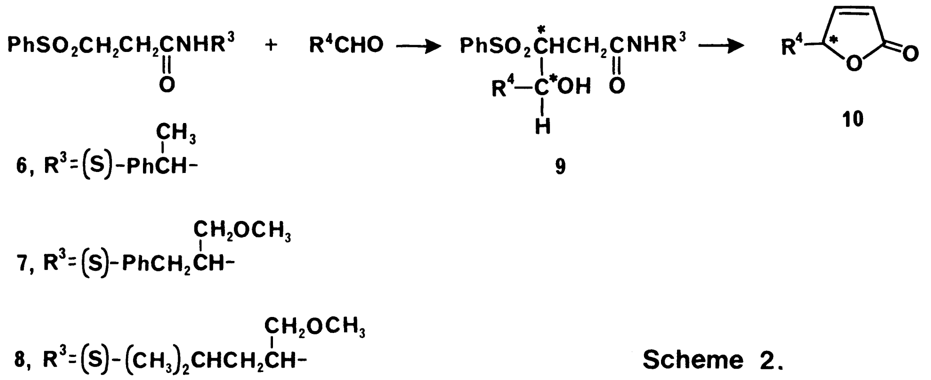
Table 1. Preparation of 5-alkyl-2(5*H*)-furanones from carbonyl compounds

$R^1R^2C=O$	Reaction conditions[a] temp/°C	time/h	Yield/%[b] of 4	Yield/% of[b] furanone (5)
Nonanal	-78	2	73 (4a)	53 (5a)
Cyclohexanecarbaldehyde	-78	2	80 (4b)	84 (5b)
Isovaleraldehyde	-78	2	71 (4c)	50 (5c)
Cyclohexanone	-78	2	57 (4d)	80 (5d)
Hexanal	-78 → -10	3.5	54 (4e)	71 (5e)
2-Pentanone	-78 → -10	3.5	60 (4f)	71 (5f)
Heptanal	-78 → -10	3.5	69 (4g)	83 (5g)

a) All reactions were carried out in an argon atmosphere.
b) Isolated yields.

To demonstrate the versatility of this method we have synthesized both enantiomers of 5-octyl-2(5*H*)-furanones (10, R^4 = n-C_8H_{17})7) and 5-tridecyl-2(5*H*)-furanones (10, R^4 = n-$C_{13}H_{27}$)7,8) which serve as intermediates in the synthesis of avenaciolide,9) cerulenin,10) sex pheromone of rove bettle,11) and protolichesterinic acid12) (Scheme 2).

Addition of nonanal to a solution of the dianion derived from *N*-(*S*)-α-methylbenzyl-3-(phenylsulfonyl)propanamide (6) ($[\alpha]_D^{25}$ -79.5° (c 1.0, dioxane)) gave a mixture of diastereomeric adducts 9 in 66% combined yield. The more mobile diastereomer (I) was isolated by column chromatography as an oil, $[\alpha]_D^{25}$ -91.5° (c 0.47, dioxane).$^{13)}$ Lactonization of the diastereomer as described above gave (*S*)-(+)-5-octyl-2(5*H*)-furanone (10, R^4 = *n*-C_8H_{17}) in 84% chemical yield and 98% optical purity.$^{8)}$ The less mobile diastereomer (II) was obtained as an oil, $[\alpha]_D^{25}$ -51.0° (c 1.1, dioxane), which was transformed into (*R*)-(-)-5-octyl-2(5*H*)-furanone (10, R^4 = *n*-C_8H_{17}) in 80% chemical yield and 100% optical purity.$^{8)}$ The results of the reaction of the dianions derived from optically active amides are listed in Table 2.



Scheme 2.

Table 2. Synthesis of optically active 5-alkyl-2(5*H*)-furanone (10) using chiral dianions

Amide	R^4CHO	Yield/% of 9	Composition/%$^{a)}$	R^4 in 10	Yield/% of 10	$[\alpha]_D^{25}$ $^{b)}$	Optical purity/%$^{c)}$
6	Nonanal	66	I 32	*n*-C_8H_{17}	84	+67.7°	98 (*S*)
			II 28	*n*-C_8H_{17}	80	-69.1°	100 (*R*)
6	Tetradecanal	65	I 29	*n*-$C_{13}H_{27}$	86	+43.0°	83 (*S*)
			II 26	*n*-$C_{13}H_{27}$	86	-49.7°	96 (*R*)
7	Nonanal	53	I 27	*n*-C_8H_{17}	60	-57.7°	83 (*R*)
			II 24	*n*-C_8H_{17}	80	+58.2°	84 (*S*)
8	Nonanal	46	I 28	*n*-C_8H_{17}	73	-59.6°	86 (*R*)
			II 16	*n*-C_8H_{17}	90	+68.8°	99 (*S*)

a) Numerals I and II indicate the order of elution of the diastereomers. The third component is a mixture of two diastereomers.$^{13)}$ b) Measured in dioxane (c 2.0). c) Optical purity based on $[\alpha]_D^{25}$ -69.2° (c 2, dioxane) for (*R*)-5-octyl-2(5*H*)-furanone and $[\alpha]_D^{25}$ -51.7° (c 2, dioxane) for (*R*)-5-tridecyl-2(5*H*)-furanone. See Ref. 8.

These data indicate that the use of the amide derived from (*S*)-(-)-α-methylbenzylamine as the chiral auxiliary provides 5-alkyl-2(5*H*)-furanones of high optical purity.

Since the chiral amide **6** is readily available and the method is operationally very simple, these procedures represent an efficient alternative to existing asymmetric syntheses of 5-substituted-2(5*H*)-furanones.[4j,7,8]

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