

ANION OF 1-[(2-METHOXYETHOXY)METHOXY]-2-PHENYLSULFONYLCYCLOPROPANE

AS A NEW  $d^3$ -REAGENT:

PREPARATION OF  $\beta$ -SUBSTITUTED  $\alpha,\beta$ -UNSATURATED ALDEHYDES

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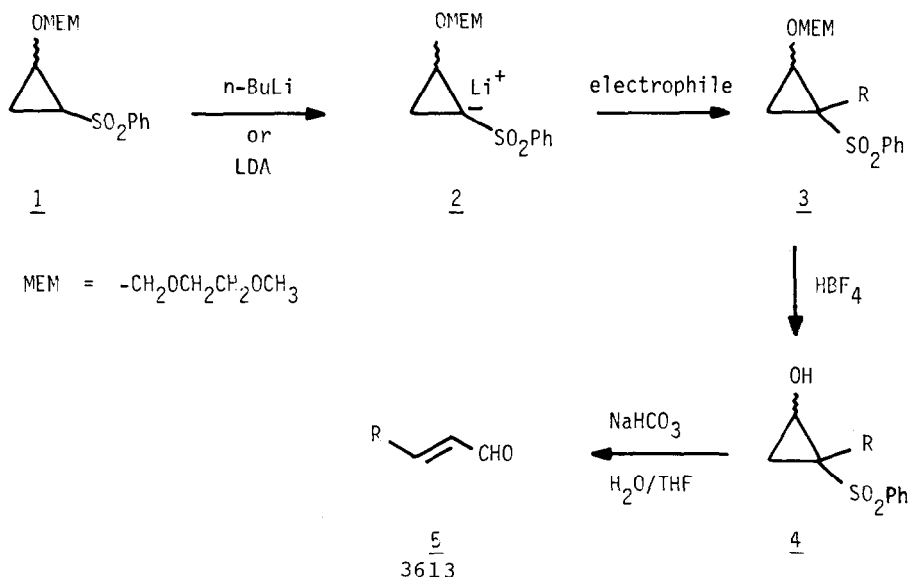
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**Abstract:** Preparation of  $\beta$ -alkylsubstituted  $\alpha,\beta$ -unsaturated aldehydes using a new  $d^3$ -reagent is described.

The formation of carbon-carbon bonds by mean of three-carbon homologating agents has long been a subject of intensive investigation.<sup>1</sup> The homoenolate anions and their equivalents ( $d^3$ -synthons)<sup>2</sup> have been widely used for such purposes for many years. Because of their synthetic utilities, development of homoenolate anions and equivalents is still to be attractive. We are interested in finding new  $d^3$ -reagents which can be used for the preparation of  $\alpha,\beta$ -unsaturated aldehydes,<sup>3</sup> an important class of organic compounds as useful synthetic intermediates. We now wish to report a new  $d^3$ -reagent, a carbanion of 1-[(2-methoxyethoxy)methoxy]-2-phenylsulfonyl-cyclopropane (1)<sup>4</sup>, and its synthetic application for the preparation of  $\alpha,\beta$ -unsaturated aldehydes.

Scheme I



The prerequisite sulfone 1 was prepared by oxidation of the corresponding sulfide<sup>5</sup> with *m*-chloroperbenzoic acid in dichloromethane or hydrogen peroxide-acetic acid (80% yield). Deprotonation of the sulfone 1 leading to the sulfone anion 2<sup>6</sup> was accomplished by treatment with lithium diisopropylamide (1.1-1.2 equiv.) in tetrahydrofuran in the presence of hexamethylphosphortriamide (1 equiv.) at -78°C for 1 hr (Method A) or with *n*-butyl lithium in tetrahydrofuran at -78°C for 1 hr (Method B). The sulfone anion 2 obtained by both methods reacted smoothly with various alkyl halides (-78°C to room temperature, overnight) to give the adduct 3 in good yields. The reaction of the sulfone anion 2 (Method B) with aldehydes and ketones occurred readily at -78°C (3 hr) to afford the hydroxyalkylated product 3: at higher temperature (0°C or room temperature), the retro-aldol type reaction took place giving the starting materials. The results are summarized in Table 1.

Having compounds 3 in hand, we next studied the synthetic transformation of these compounds to the desired  $\alpha,\beta$ -unsaturated aldehydes as depicted in Scheme I. Hydrolysis of the MEM-protecting group<sup>7</sup> of compound 3 was easily performed by treatment with excess 50% aqueous tetrafluoroboric acid<sup>8</sup> in refluxing dichloromethane for 5-7 hr to furnish the corresponding cyclopropanol sulfone 4 in quantitative yield, which was pure enough for using in the next step. It should be noted that the cyclopropanol derivatives 4 are stable upon standing at room temperature. Treatment of the crude cyclopropanol sulfones 4d-k with saturated aqueous NaHCO<sub>3</sub> solution in THF at reflux for 4 hr afforded *trans*- $\beta$ -substituted  $\alpha,\beta$ -unsaturated aldehydes 5a-h in good yields. When compounds 3l-n were subjected to the same hydrolytic conditions as above, the  $\beta$ -phenylsulfonyl  $\beta,\gamma$ -unsaturated aldehydes 6a-c were obtained instead of the desired cyclopropanol derivatives. The formation of 6a-c resulted from the acid-catalyzed ring opening of the initially formed cyclopropanol intermediates of type 4 [R = -C(OH)(CH<sub>3</sub>)<sub>2</sub> and R = -CH(OH)CH(CH<sub>3</sub>)<sub>2</sub>, respectively].

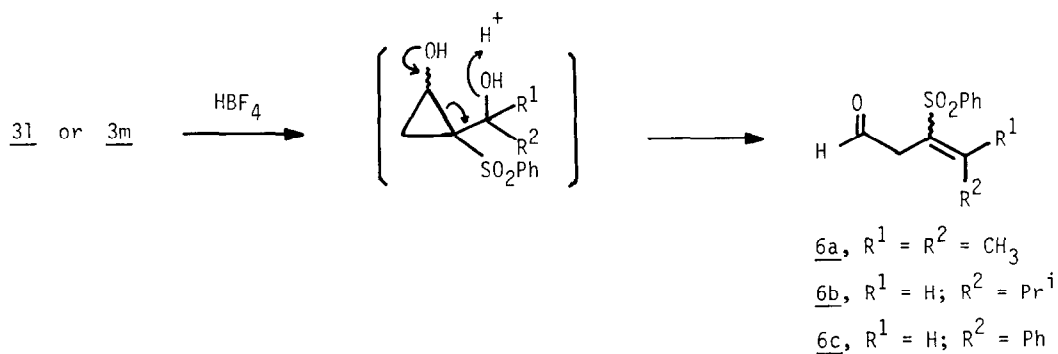


Table 1: Preparation of compound 3 and  $\beta$ -substituted  $\alpha,\beta$ -unsaturated aldehydes 5.

Electrophile	Compound <u>3</u> (%) <sup>a,c</sup>	Compound <u>5</u> , (%) <sup>b,c</sup>
CH <sub>3</sub> -I	<u>3a</u> ; R = CH <sub>3</sub> (80)	-
CH <sub>2</sub> =CHCH <sub>2</sub> Br	<u>3b</u> ; R = CH <sub>2</sub> =CHCH <sub>2</sub> (61)	-
n-C <sub>4</sub> H <sub>9</sub> Br	<u>3c</u> ; R = n-C <sub>4</sub> H <sub>9</sub> (81)	-
n-C <sub>7</sub> H <sub>15</sub> Br	<u>3d</u> ; R = n-C <sub>7</sub> H <sub>15</sub> (70)	<u>5a</u> , 80
n-C <sub>8</sub> H <sub>17</sub> Br	<u>3e</u> ; R = n-C <sub>8</sub> H <sub>17</sub> (68)	<u>5b</u> , 82
n-C <sub>9</sub> H <sub>19</sub> Br	<u>3f</u> ; R = n-C <sub>9</sub> H <sub>19</sub> (66)	<u>5c</u> , 65
n-C <sub>11</sub> H <sub>23</sub> Br	<u>3g</u> ; R = n-C <sub>11</sub> H <sub>23</sub> (67)	<u>5d</u> , 70
n-C <sub>12</sub> H <sub>25</sub> Br	<u>3h</u> ; R = n-C <sub>12</sub> H <sub>25</sub> (74)	<u>5e</u> , 87
n-C <sub>13</sub> H <sub>27</sub> Br	<u>3i</u> ; R = n-C <sub>13</sub> H <sub>27</sub> (65)	<u>5f</u> , 77
n-C <sub>15</sub> H <sub>31</sub> Br	<u>3j</u> ; R = n-C <sub>15</sub> H <sub>31</sub> (73)	<u>5g</u> , 90
n-C <sub>16</sub> H <sub>33</sub> Br	<u>3k</u> ; R = n-C <sub>16</sub> H <sub>33</sub> (73)	<u>5h</u> , 89
Acetone	<u>3l</u> ; R = -C(OH)(CH <sub>3</sub> ) <sub>2</sub> (91)	<u>6a</u> , 77
Isobutyraldehyde	<u>3m</u> ; R = -CH(OH)CH(CH <sub>3</sub> ) <sub>2</sub> (92)	<u>6b</u> , 40
Benzaldehyde	<u>3n</u> ; R = -CH(OH)Ph (81)	<u>6c</u> , 28 43 <sup>d</sup>

a) Isolated yields after thin-layer chromatography (SiO<sub>2</sub>).

b) Isolated yields based on 3.

c) All new compounds gave satisfactory <sup>1</sup>H-NMR, IR and mass spectral data.

d) Hydrolysis was performed by employing conc.HCl/CH<sub>2</sub>Cl<sub>2</sub> at room temperature (24 hr).

Our above results clearly demonstrate that the sulfone anion 2 serves as the synthetic equivalent of 3-lithio acrolein (d<sup>3</sup>-reagent), and the present method is of general use for the preparation of  $\beta$ -alkyl-substituted  $\alpha,\beta$ -unsaturated aldehydes.

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(Received in UK 3 June 1985)