## CYCLOAROMATIZATION OF & OXOKETENE DITHIOACETALS WITH 2-PICOLYLLITHIUM: A FACILE QUINOLIZINIUM CATION ANNELATION<sup>1</sup>

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Summary:  $\alpha$ -Oxoketene dithioacetals derived from various cyclic and acyclic ketones are shown to be useful intermediates for the synthesis of substituted and fused quinolizinium derivatives by reaction with 2-picolyllithium followed by cyclization in the presence of borontrifluoride etherate.

In the course of our studies on aromatic annelation involving the reactions of allyl and benzylmagnesium halides with  $\alpha$ -oxoketene dithioacetals<sup>2,3</sup>, we have recently developed a facile method for the synthesis of fused thioresorcinol dimethyl ethers<sup>4</sup> by reacting these intermediates with propargylmagnesium bromide followed by cyclization of the resulting carbinolacetals with borontrifluoride etherate and methanol. In continuation of these studies, we further contemplated to investigate the reactions of lithio-3-azaallyl systems (1) with  $\alpha$ -oxoketene dithioacetals with a view to enhancing the scope of our method, for the synthesis of heteroaromatic systems. As a part of this general synthetic strategy, we have studied the reaction of 2-picolyllithium with  $\alpha$ -oxoketene dithioacetals and we present our results in this communication.



When 2a was reacted with 2-picolyllithium (1.5 eqv), the corresponding carbinolacetal 3a was obtained in nearly quantitative yield (95%). The carbinol 3a was directly subjected to cyclization in the presence of borontrifluoride etherate in refluxing benzene, when the light coloured crystalline solid obtained was characterized as 6-methylthio-7,8,9,10-tetrahydrobenzo [b] quinolizinium tetrafluoroborate (<u>4a</u>) (82%); v max (KBr): 1640, 1610, 1568, 1030-1150(br) cm<sup>-1</sup>; <sup>1</sup>H n.m.r. (CDCl<sub>2</sub>) (250 MHz); § 1.94(m,4H,CH<sub>2</sub>); 2.48(s,3H,SCH<sub>3</sub>); 3.15(t,2H,CH<sub>2</sub>); 3.32(t,2H,CH<sub>2</sub>); 8.04(t,1H,J= 7Hz, H-3); 8.16(t,1H,J=7Hz, H-2); 8.26(s,1H,H-11); 8.36(d,1H,J=7Hz,H-1); 10.03(d,1H,J=7Hz,H-4); <sup>13</sup>C n.m.r.(CDCl<sub>2</sub>):  $\delta$  16.20(SCH<sub>3</sub>); 20.51, 21.67(CH<sub>2</sub>,C-8,C-9); 29.40,29.72(CH<sub>2</sub>,C-7,C-10); 123.90, 126.92, 128.00, 132.86, 135.46 (CH,C-1,C-2,C-3,C-4,C-11); 140.59, 142.49, 143.34, (C-6a, C-10a, C-11a); 150.09(C-6); MS(m/z): 230(8%,  $M^+$ -BF<sub> $\mu$ </sub>); 215(9%,  $M^+$ -BF<sub> $\mu$ </sub>-15); Found: C,52.87; H,5.01; N,4.44%; C110H116BF10NS requires: C,53.00; H,5.05; N,4.42%. The other cyclic ketene dithioacetals 2b-g similarly afforded the annelated quinolizinium derivatives 4b-g in good yields (Table). The generality of this reaction was further established by reacting the  $\alpha$ -oxoketene dithioacetals <u>2h-m</u> derived from open-chain active methylene ketones with 2-picolyllithium under similar conditions, when the corresponding 4-methylthio-2-substituted quinolizinium tetrafluoroborates 4h-m were obtained in 73-86% overall yields.

The overall transformation is depicted in the Scheme. The cyclodehydration step proceeds as expected by participation of the pyridine ring followed by elimination of methylmercapto group. Quinolizinium ring has been known to exist in certain complex alkaloids and several synthetic routes have been developed for the synthesis of these cations<sup>5</sup>. One of the common approaches consists of cyclocondensation of 2-picolyllithium with enolether or monoketal of a  $\beta$ -dicarbonylcompound<sup>6-9</sup>, followed by cyclodehydration of the intermediate adduct in the presence of acid. However, the choice of  $\beta$ -dicarbonyl compounds employed in these reactions is limited, in particular for cyclic derivatives. The present procedure, which utilizes easily accessible  $\alpha$ -oxoketene dithioacetals from a wide variety of cyclic and acyclic active methylene ketones provides a simple and high yield synthetic route for quinolizinium derivatives with diverse structural features. Further work to extend this reaction to other systems with  $\alpha$ -methylimino function is in progress.

In a typical procedure, a solution of  $\underline{2a}$  (2.02g, 0.01 mol) in dry tetrahydrofuran (25ml) was added to a solution of 2-picolyllithium<sup>10</sup>(0.015 mol) in 25 ml of THF at -20°C under N<sub>2</sub> atmosphere. The reaction mixture was further stirred at -15°C for 2 hrs and worked-up as described earlier<sup>3</sup> to give crude carbinol <u>3a</u> (2.80g, 95%), which was dissolved in dry benzene (50 ml) and BF<sub>3</sub>.Et<sub>2</sub>O(2 ml) and refluxed for 2 hrs. Work-up<sup>3</sup> of the reaction mixture gave a viscous residue, which was purified by passing through silica gel column (hexane-ethylacetate) to give <u>4a</u> (2.60,82%). In the case of carbinols <u>3c-m</u> colourless solids were separated on refluxing in benzene and BF<sub>3</sub>.EtO, which were filtered, dissolved in acetone (10 ml) and treated with saturated NaHCO<sub>3</sub> solution (100 ml) to give the corresponding 4c-m, which were crystallized from glacial acetic acid.

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5,6-Dihydro-7-methylthionaphtho [1,2-b] quinolizinium tetrafluoroborate (4c): v max (KBr): 1630, 1610, 1598, 980-1140(br) cm<sup>-1</sup>; <sup>1</sup>H n.m.r. (DMSO-d<sub>6</sub>) (250MHz):  $\delta$  2.53(s,3H,SCH<sub>3</sub>); 3.06(t,2H,CH<sub>2</sub>); 3.53(t,2H,CH<sub>2</sub>); 7.51(m,3H,H-2, H-3,H-4); 8.10(t,J=7Hz,1H,H-12); 8.20(d,J= 6.5Hz,1H,H-1); 8.41(t,J=7Hz,1H,H-11); 8.58(d,J=7Hz,1H,H-12); 9.12(sH,H-13); 10.10(d,J= 7Hz,1H,H-9); <sup>13</sup>C n.m.r.(DMSO-d<sub>6</sub>):  $\delta$ 16.71(SCH<sub>3</sub>); 26.69, 27.79(CH<sub>2</sub>, C-5,C-6); 120.97, 124.04, 126.11, 127.73, 128.46, 128.56, 131.70, 134.55, 136.33 (CH,C-1,C-2,C-3,C-4,C-9, C-10,C-11,C-12,C-13); 129.46, 138.48, 140.25, 140.60, 141.44, 143.64 (C-4a,C-6a,C-7, C-12a,C-13a,C-13b); MS(m/z); 278(11%,M<sup>+</sup>-BF<sub>4</sub>); 263(27%,M<sup>+</sup>-BF<sub>4</sub>-15); Found: C,59.01; H,4.50; N,3.86%, C<sub>18</sub>H<sub>16</sub>BF<sub>4</sub>NS requires: C,59.10; H,4.38, N,3.83%.

2-p-Methoxyphenyl-4-methylthioquinolizinium tetrafluoroborate( $\frac{4}{2}$ ): v max (KBr) 1638, 1610, 1600, 1578, 1010-1110(br) cm<sup>-1</sup>; <sup>1</sup>H n.m.r.(DMSO-d<sub>6</sub>)(250MHz); & 3.06(s, 3H, SCH<sub>3</sub>), 3.89(s, 3H, OCH<sub>3</sub>); 7.20(d, A<sub>2</sub>B<sub>2</sub>2H, arom); 8.02(t, J=7Hz, 1H, H-7); 8.14(d, A<sub>2</sub>B<sub>2</sub>, 2H, arom); 8.25 (s, 1H, H-3); 8.32(t, J=7Hz, 1H, H-8); 8.51(d, J=7Hz, 1H, H-9); 8.78(s, 1H, H-1); 9.29(d, J=7Hz, 1H, H-6); <sup>13</sup>C n.m.r. (DMSO-d<sub>6</sub>) (100MHz); & 16.29(SCH<sub>3</sub>); 55.48(CH<sub>3</sub>O); 114.83, 118.69, 119.55, 123.22, 128.19, 129.46, 131.75, 135.54(CH, C-1, C-3, C-6, C-7, C-8, C-9 and arom); 143.91, 145.00, 147.41(C-2, C-9a and C-4); 125.91, 161.85(C-1' and C-4' of phenyl); MS(m/z); 282(8%, M<sup>+</sup>-BF<sub>4</sub>); 267(35%, M<sup>+</sup>-BF<sub>4</sub>-15); Found C, 54.27; H, 4.47; N, 3.88%; C<sub>17</sub>H<sub>16</sub>BF<sub>4</sub>NS requires: C, 53.90; H, 4.15; N, 3.70%.

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