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# Amberlyst-15 mediated decomposition of α-diazo carbonyl compounds

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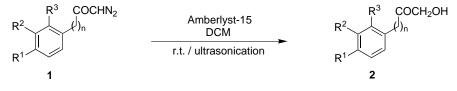
Abstract—An efficient heterogeneous catalytic method for the synthesis of  $\alpha$ -hydroxy ketones from  $\alpha$ -diazo carbonyl compounds 1, 3 and 6 in the presence of Amberlyst-15, a macro reticular ion exchange resin, is reported. The desired products were obtained at room temperature or by ultrasonication in good yield. Interestingly, novel fused 3-furanones and bicycloalkane-1,3-diones were obtained as unusual products in the case of alicyclic  $\alpha$ -diazo carbonyl compounds. © 2001 Elsevier Science Ltd. All rights reserved.

 $\alpha$ -Diazo carbonyl compounds are important intermediates and have been exploited in synthetic organic chemistry for the synthesis of a variety of complex molecules in recent years.<sup>1</sup> Reactions of  $\alpha$ -diazo carbonyl compounds have been extensively studied using various acids, bases and metal complexes including Lewis acids as catalysts.<sup>1</sup> The reaction of  $\alpha$ -diazo carbonyl compounds with several Lewis acids such as BF3 Et2O,<sup>2</sup>  $InCl_{3}^{3}$   $SnCl_{2}^{4}$   $TiCl_{4}^{5}$   $Sc(OTf)_{3}^{6}$  and  $Cu(OTf)_{2}^{7}$  has been applied as a general strategy for the synthesis of 1,3-dicarbonyl compounds and natural products. The reaction of  $\alpha$ -diazo carbonyl compounds with protic/ aprotic acids<sup>8</sup> such as aqueous or concentrated acetic acid, HCl, H<sub>2</sub>SO<sub>4</sub>, SiO<sub>2</sub>/acetic acid, perchloric acid, trifluoroacetic acid and trifluoromethanesulfonic acid has been studied. These acidic media are often employed even though they are corrosive, require careful handling, generate by-products and always require an aqueous work-up.

To the best of our knowledge, there is no report<sup>1</sup> dealing with the reaction of  $\alpha$ -diazo carbonyl compounds and a solid ionic matrix such as Amberlyst-15.<sup>9</sup>

Amberlyst-15 has customarily been applied to the deprotection of acetals,<sup>10</sup> protection of carbonyl compounds in the presence of 1,2-ethanedithiol,<sup>11</sup> Michael reaction,<sup>12</sup> preparation of enol ethers<sup>13</sup> and tetra-hydropyranyl ethers.<sup>14</sup> Herein, we wish to report our extensive studies on the reaction of  $\alpha$ -diazo carbonyl compounds with the macro reticular ion-exchange resin of the type Amberlyst-15 as applied to the synthesis of  $\alpha$ -hydroxy ketones and novel bicycloalkane-1,3-diones, as well as fused 3-furanone ring systems in a heterogeneous manner.

To a solution of  $\alpha$ -diazo ketone **1a** (125 mg) in 5 ml of commercial grade dichloromethane was added Amberlyst-15 (150 mg) and the reaction mixture was allowed to stir at room temperature for 8 h (Scheme 1). The reaction was followed by TLC until the disappearance of starting material; the reaction mixture was filtered and concentrated under reduced pressure. The crude reaction mixture was purified by silica gel column chromatography and formed the corresponding  $\alpha$ -hydroxy ketone **2a**<sup>15</sup> in 82% yield (Table 1). In order to



# Scheme 1.

*Keywords*: Amberlyst-15; diazo carbonyl compounds; heterogeneous catalyst; hydroxy ketones. \* Corresponding author. Tel.: +91 278 567760; fax: +91 278 567562; e-mail: salt@csir.res.in

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reduce the reaction time, the reaction was carried out under ultrasonication to afford the product 2a in 30 minutes (Table 1). The remarkable reactivity of Amberlyst-15 gave us impetus to study it further in reaction with other  $\alpha$ -diazo carbonyl compounds in a heterogeneous manner.

Initially we studied other aromatic compounds **1b–e** and aliphatic diazo compounds **1f**,**g** which afforded the respective  $\alpha$ -hydroxy ketones **2b–g** both room temperature and under ultrasonication. These reactions were also carried out in acetone as a solvent for all the diazo compounds **1**, which afforded **2** in comparable yield. The resulting intermediate undergoes an O–H insertion reaction<sup>16</sup> to give the  $\alpha$ -hydroxy ketone **2**. Moreover, the  $\alpha$ -hydroxy ketones are versatile intermediates in the synthesis of several natural products such as frontalin.<sup>17</sup>

Encouraged by these results with aromatic compounds; we subsequently investigated the reaction of various

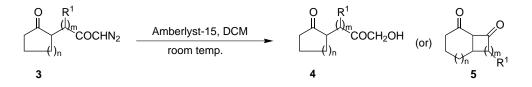
alicyclic  $\alpha$ -diazo carbonyl compounds (Scheme 2) with Amberlyst-15, which afforded unexpected results. The reaction of diazo compounds **3a–c** having a two/threecarbon chain length in the presence of Amberlyst-15 resulted in the corresponding  $\alpha$ -hydroxy ketones<sup>15</sup> (Table 2). In the case of diazo compound **3d**, having a three-carbon chain length tethered to a cyclohexanone ring system, reaction with Amberlyst-15 furnished the 1,3-dione **5d** instead of the corresponding  $\alpha$ -hydroxy ketone **4d**. We confirmed this curious cyclization by performing the reaction with diazo compound **3e**. It is interesting to note that these bicycloalkane-1,3-diones **5** have also been synthesized from diazo ketones **3d**,e using SnCl<sub>2</sub><sup>4b</sup>/TiCl<sub>4</sub><sup>5</sup> as a catalyst.

We were further interested in studying the effect of ring size with only one carbon in the chain in the  $\alpha$ -diazo carbonyl compounds. Diazo carbonyl compounds 1, 3 and 6 involved in this work were prepared based on literature precedents.<sup>1,18</sup> Then, we extended our investi-

Table 1. Reaction of aromatic α-diazo carbonyl compounds 1a-g with Amberlyst-15

Substrate	R <sup>1</sup>	R <sup>2</sup>	<b>R</b> <sup>3</sup>	п	Time		Yield <sup>a</sup> (%)
					Room temp. (h)	Ultrasonication (min)	
1a	OMe	Н	Н	0	8	30	82
1b	Н	Н	Н	0	7	20	77
1c	Me	Н	Н	0	5.5	20	92
1d	Н	Me	Н	0	6	25	80
1e	Н	-CH=CH-CH=CH-		0	7	35	79
1f	Н	Н	Н	1	7	30	75
1g	Н	Н	Н	2	6	25	76

<sup>a</sup> Yields (unoptimized) refer to isolated and chromatographically pure compounds 2.



#### Scheme 2.

Table 2. Reaction of alicylcic  $\alpha$ -diazo carbonyl compounds with Amberlyst-15

Substrate	$\mathbb{R}^1$	n	т	Time (h)	Yield <sup>b</sup> of 4%	Yield <sup>b</sup> of 5%
3a	Н	1	1	5	76	_
3b	Н	1	2	5	82	-
3c	Н	2	1	5	85	_
3d	Н	2	2	2.5	_	71 <sup>4b,5</sup>
3e	Me	2	2	6	_	69

<sup>b</sup> Yields (unoptimized) refer to isolated and chromatographically pure compounds 4 and 5.

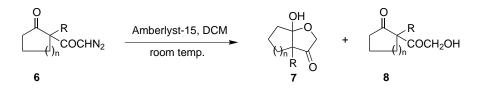


Table 3. Fused 3-furanones ring systems 7 produced via Scheme 3

Substrate	R	п	Time (h)	Yield <sup>c</sup> of 7%	Yield <sup>c</sup> of 8%
6a	Me	1	1	39	38
5b	CH <sub>2</sub> CH=CH <sub>2</sub>	1	1	34	35
be	Me	2	0.5	87	_
6d	CH <sub>2</sub> CH=CH <sub>2</sub>	2	0.5	74	_

<sup>c</sup> Yields (unoptimized) refer to isolated and chromatographically pure compounds 7 and 8.

gation on diazo compounds **6a–d** (Scheme 3). Treatment of diazo ketones **6a,b** with Amberlyst-15 resulted in the respective novel fused 3-furanone skeleton **7a,b** and  $\alpha$ -hydroxy ketones **8a,b**. However, in the reaction of an  $\alpha$ -diazo ketone tethered to a cyclohexanone ring **6c,d** the corresponding fused 3-furanones **7c,d**<sup>15</sup> were formed (Table 3). The reason may be the formation of a favorable 6,5-fused ring system **7c,d** rather than the strained 5,5-fused ring system **7a,b** under the experimental conditions. It is worth noting that the fused 3-furanone skeleton is present in many natural products such as avermectin B.<sup>19</sup> It may also be noted that the olefin moiety present in the diazo compounds **6b,d** stayed intact under the reaction conditions.

In summary, the reaction of various  $\alpha$ -diazo carbonyl compounds with a solid ionic matrix, Amberlyst-15 under mild heterogeneous conditions furnished  $\alpha$ -hydroxy ketones, novel fused 3-furanones and bicy-cloalkane-1,3-diones. The mild reaction conditions together with the heterogeneous manner makes the use of Amberlyst-15 an important alternative to classic acidic catalysis and other methods, since both by-products and aqueous work-up are avoided.

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- 15. All new compounds gave satisfactory spectral data consistent with their structures. Selected spectral data, (2b): colorless solid mp 103-105°C; IR (KBr) 3391, 2927, 2845, 1678, 1603, 1576, 1512, 1422, 1250, 1181, 1103, 1029, 977, 821 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>/CD<sub>3</sub>CN) δ 7.89 (d, 2H, J=8.9 Hz, Arom.-H), 6.99 (d, 2H, J=8.9 Hz, Arom.-H), 4.78 (s, 2H, OCH<sub>2</sub>), 3.86 (s, 3H, OCH<sub>3</sub>), 3.49 (br s, 1H, OH); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>/CD<sub>3</sub>CN)  $\delta$ 54.9 (OCH<sub>3</sub>), 64.6 (OCH<sub>2</sub>), 113.6 (=CH), 126.3 (quat.-C), 129.5 (=CH), 163.8 (quat.-C), 197.0 (C=O). Anal. calcd for C<sub>0</sub>H<sub>10</sub>O<sub>3</sub>: C, 65.05; H, 6.07. Found: C, 65.13; H, 6.12. (4b): colorless thick liquid; IR (neat) 3445, 2960, 2877, 1731, 1452, 1406, 1274, 1158, 1069, 732 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>) δ 4.19 (s, 2H, OCH<sub>2</sub>), 3.32 (br s, 1H, OH), 2.50 (t, 2H, J=7.0 Hz), 1.40–2.21 (m, 9H); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>) δ 21.1 (CH<sub>2</sub>), 23.9 (CH<sub>2</sub>), 30.1 (CH<sub>2</sub>), 36.4 (CH<sub>2</sub>), 38.5 (CH<sub>2</sub>), 48.4 (CH), 68.6 (OCH<sub>2</sub>), 210.0 (C=O), 221.2 (C=O). Anal. calcd for C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>: C, 63.51; H, 8.29. Found: C, 63.59; H, 8.37. (7c): colorless solid mp 120-122°C; IR (KBr) 3380, 2944, 2911, 1760, 1457, 1413, 1232, 1097, 1076, 1020, 938 cm<sup>-1</sup>; <sup>1</sup>H NMR (200 MHz, CDCl<sub>3</sub>)  $\delta$  4.16 (dd, 2H,  $J_1 = 13.5$  Hz,  $J_2 = 1.6$

- Hz, OCH<sub>2</sub>), 2.91 (s, 1H, OH), 1.90–2.00 (m, 1H), 1.35– 1.75 (m, 7H), 1.22 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C NMR (50 MHz, CDCl<sub>3</sub>)  $\delta$  13.7 (CH<sub>3</sub>), 21.0 (CH<sub>2</sub>), 23.5 (CH<sub>2</sub>), 33.1 (CH<sub>2</sub>), 34.0 (CH<sub>2</sub>), 51.3 (quat.-C), 67.9 (OCH<sub>2</sub>), 106.0 (quat.-C), 217.6 (C=O); mass m/z (%): 170 (M<sup>+</sup>, 24), 153 (20), 142 (6), 124 (8), 112 (63), 97 (48), 83 (48), 69 (69), 55 (96), 41 (100). Anal. calcd for C<sub>9</sub>H<sub>14</sub>O<sub>3</sub>: C, 63.51; H, 8.29. Found: C, 63.46; H, 8.28.
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