A Carbonyl Ylide Approach to Substituted Furans

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Abstract: The diazosulphone **1** undergoes intermolecular reaction with aldehydes to form carbonyl ylides **2**. This reactive intermediate can then be trapped, in an inter- or intramolecular reaction, by alkynes or alkenes to yield substituted furans or tetrahydrofurans respectively.

Key words: diazo compounds, carbonyl ylide, ring closure, furans

The formation of carbonyl ylides from the reaction of metallocarbenoids with carbonyl compounds continues to be an important tool in the synthesis of oxygen containing heterocyclic systems.¹ Carbonyl ylides are usually generated by an intramolecular reaction; however, the intermolecular generation of carbonyl ylides has also been employed in heterocycle synthesis.² An example of intermolecular generation of nitrile ylides from nitriles and the ethyl ester of the diazosulphone 1 has been demonstrated by Moody et al.³ We envisaged that **1** would react with aldehydes, under rhodium(II) catalysis, in an analogous manner to yield carbonyl ylides 2. These could then undergo inter- or intramolecular trapping with dipolarophiles such as alkynes or alkenes. If 2 were trapped intermolecularly by an alkyne we expected the intermediate dihydrofuran 3 to readily aromatise by elimination of phenylsulphinic acid to yield substituted furans. Similar chemistry would be anticipated to occur for aldehydes bearing a tethered alkyne, giving rise to annulated furans (Scheme 1).

Initially we decided to explore the intermolecular trapping of **2**. We found that heating **1** with 3 equiv. of crotonaldehyde **4a**, 3 equiv. of dimethylacetylenedicarboxylate (DMAD) and 5 mol% rhodium octanoate dimer in 1,2dichloroethane gave the dihydrofuran **5a** as an inseperable mixture of isomers in 27% isolated yield. Heating 5a with 3 equiv. of triethylamine effected the elimination of phenylsulphinic acid to give the furan 6a in a low yield (Scheme 2). Subsequently, it was found that **5a** could be formed at room temperature from equimolar amounts of 1, 4a, and DMAD in the presence of rhodium octanoate dimer. Conversion to **6a** was then carried out in situ. This procedure was then applied to other aldehyde components (Table 1).⁴ The reaction was restricted to non-enolisable aldehydes, possibly due to the intervention of intramolecular α -proton abstraction from the carbonyl ylide.⁵ Although a number of alkyne components were tried in the reaction, it was found that only DMAD gave any furan product. The yields obtained could not be improved even by using DMAD in excess. It was also observed that, when propionitrile replaced the aldehyde component, the intermediate nitrile ylide could not be trapped with DMAD but was trapped intramolecularly by the ester functionality to form the oxazole 7 (52%) (Scheme 3), consistent with the findings of Moody et al.³

Aldehyde 4	R	Furan 6	Yield (%) ^a
4a	E-CH ₃ CH:CH 6a		35
4b	Ph	6b	42
4 c	4-MeOPh	6c	17
4d	4-MeO ₂ CPh	6d	15

^aIsolated.



Scheme 1

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Scheme 2



6a-d

Changing the dipolarophile from DMAD to *N*-phenylmaleimide increased the efficiency of trapping to furnish the tetrahydrofuran derivative **8** in good yield (77%), albeit as an inseperable mixture of isomers (Scheme 3).

Clearly the intermolecular trapping of 2 by alkynes was inefficient and limited in scope.

We next turned our attention to the intramolecular trapping of 2. The required aldehydes 9a-f, bearing a tethered alkyne, were readily prepared by known methods (Table 2). Heating equimolar amounts of 1 and the aldehyde 9af in the presence of 5 mol% rhodium octanoate dimer generated the annulated furans **10a-f** (Scheme 4, Table 2).¹² No separate step for the elimination of phenylsulphinic acid was required as elimination was found to occur under the reaction conditions. Interestingly, in a competition reaction between the acetylenic aldehydes 9d and 9e only 9d was found to react with 1 to give exclusively 10d as determined by GC/MS analysis of the crude reaction mixture. This tends to suggest that the cyclisation event and not the formation of the presumed carbonyl ylide intermediate is rate limiting. Also gratifying was the tolerance of alkyne substituents giving rise to potentially useful functionality at the 3-position in furans 10a-c.

Although attempted formation of the furan annulated cycloheptane 10f failed, the formation of an annulated seven-membered ring was achieved by reaction of 1 with the ester 11 (Scheme 5), which was prepared from the



Scheme 4

Table 2	Synthesis of Annulated Furans 9a-f
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Aldehyde 9 ^a	R	n	Furan 10	Yield (%) ^b
9a	MeO ₂ C	1	10a	42
9b	Me ₃ Si	1	10b	34
9c	Ph	1	10c ^c	36
9d	Н	1	10d	46
9e	Н	2	10e	65
9f	Н	3	10f	0

^aSee Refs. 6 to 11 respectively. ^bIsolated. ^cRef. 15.

available carboxylic acid by standard methods.¹² The lactone product was obtained as a single diastereomer of unknown relative stereochemistry. In this case in situ elimination of phenylsulphinic acid did not occur.

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Scheme 5

By the same procedure we found that we could react **1** with aldehydes **12a** and **12b** bearing a tethered alkene thereby generating the tetrahydrofurans **13a** and **13b** (Scheme 6, Table 3).¹³ In these cases elimination of phenylsulphinic acid did not occur under the reaction conditions. As with the tethered alkynes, a substituent on the alkene was tolerated, **13b**.



Table 3 Synthesis of Tetrahydrofurans 13a,b

Aldehyde 12	R	n	Furan 13	Yield (%)
12a	Н	1	13a	44
12b	Et	2	13b	28

^aRef. 14. ^bIsolated

The tetrahydrofuran **13a** was obtained as a 9:1 mixture of diastereoisomers. However, NOE studies did not allow us to determine the relative stereochemistry of the major diastereoisomer. The product **13b** arising from *cis*-6-nonen-1-al, was also obtained as a single diastereoisomer. In this case NOE studies indicated that **13b** was *cis*-ring fused and that the *cis*-stereochemistry in the alkene starting material was retained in the product (Figure 1).





Further studies on the reaction of **1** with carbonyl compounds are underway.

References and Notes

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 (4) General experimental procedure for the synthesis of
 - **furans 6**. A mixture of aldehyde **4** (0.5 mmol), dimethylacetylene dicarboxylate (0.5 mmol), methyldiazo(benzenesulphonyl) acetate **1** (0.5 mmol), rhodium octanoate dimer (0.025 mmol) and 1,2-dichloroethane (0.5 mL) was stirred at room

temperature for 1 hour. Triethylamine (0.5 mmol) and 1,2dichloroethane (0.5 mL) were added and the solution was heated at 65 °C for 2 hours. Column chromatography (silica, eluent iso-hexane/ether 95:5) was used to obtain pure products **6**.

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- (13) General experimental procedure for the synthesis of annulated furans 10 and tetrahydrofurans 12. To a mixture of aldehyde 9 or 11 (0.5 mmol), methyldiazo(benzenesulphonyl) acetate 1 (0.5 mmol) and 1,2-dichloroethane (0.1 mL) at 65 °C was added a slurry of rhodium octanoate dimer (0.025 mmol) in 1,2-dichloroethane (0.3 mL). The reaction mixture was heated at 65 °C for a further 0.75 hour. Column chromatography (silica, eluent isohexane/ether 95:5) was used to obtain pure products 10 or 12.
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