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# Promotion of the Chromium Carbene Dötz Annulation Reaction Under Dry State Adsorption Conditions

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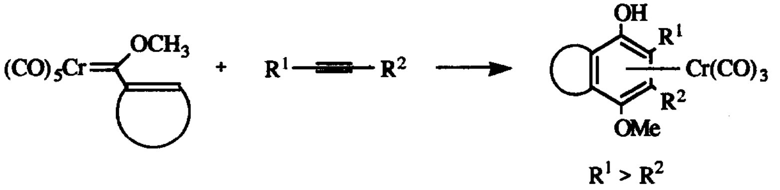
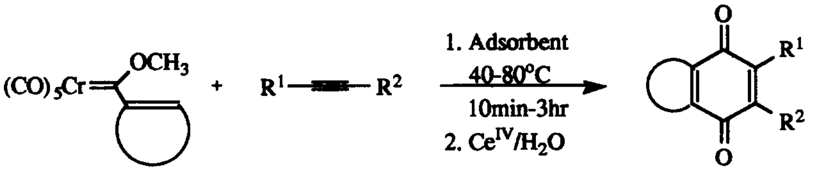
**Abstract:** The chromium carbene annulation reaction has been carried out in the solid-state by adsorption of the reagents onto silica, neutral alumina and anhydrous magnesium sulphate. The reaction rate and product yield are examined.

The reaction of vinylchromium carbene complexes with alkynes to produce highly substituted benzenoid compounds (Dötz reaction) was first reported 18 years ago[1] and has since been the subject of many synthetic applications.[2] The reaction is typically carried out at 40-75°C in ether solvents producing the air sensitive phenolic complexes with a high degree of regioselectivity with respect to the alkyne (Eq. 1). Despite its versatility and tolerance for a number of reactive functional groups, the Dötz annulation reaction often requires prolonged reaction times (2-72hr.) and in some cases proceeds to give only moderate yields of products. Furthermore, recent studies by Wulff,[3] concentrating on optimisation of reaction conditions (*i.e.* solvent, reagent concentrations and temperature), have led to enhanced yields of six-membered ring annulated products but at the expense of longer reaction times. In this Letter we now report a procedure which improves both the yield and rate of the Dötz annulation reaction by the application of Dry State Adsorption Conditions (DSAC).[4] The technique developed has resulted in promotion of the cyclisation reaction in times of 10min-3hr and the air-stable quinone products are isolated following oxidative work-up (Eq. 2).



(Eq. 1)



(Eq. 2)

The generality of this method was examined on a variety of simple substrates[6] with three solid supports being applied ($SiO_2$, $MgSO_4$, and $Al_2O_3$). As illustrated in Table 1, silica proved to be the superior solid support giving the highest yields of annulated products when compared to the other agents. With the exception of one case, that of pentacarbonyl(methoxybenzylidene)chromium with 1-pentyne (entry 4),[7] all reactions with silica proceeded in a significantly higher yield than obtained by using the more traditional "thermal" conditions (see yields in parentheses in Table 1). The silica promoted annulations are completed in the, generally, faster reaction times of 1.5-3hr. Again it can be noted from Table 1 that magnesium sulphate also promoted the reaction with good yields in two of the three cases tried (entries 1 and 2). On the other hand, neutral alumina gave a much lower yield, albeit in a very rapid reaction, in the one reported example (entry 1).

It is likely that the increased yields obtained when the DSAC technique is employed are due to the promotion of ligand exchange. Interaction with donor centres on the solid support should facilitate CO cleavage and, in turn, alkyne complexation.[5e] This primary decarbonylation process is considered to be the rate determining step during these cyclisation reactions.[8] Recently, similar dry state conditions have been reported in the area of chromium carbene chemistry. Reactions of pentacarbonyl(methoxyethylidene)chromium complexes with alkynes are facilitated to afford bicyclo[3.1.0]hexanes.[9]

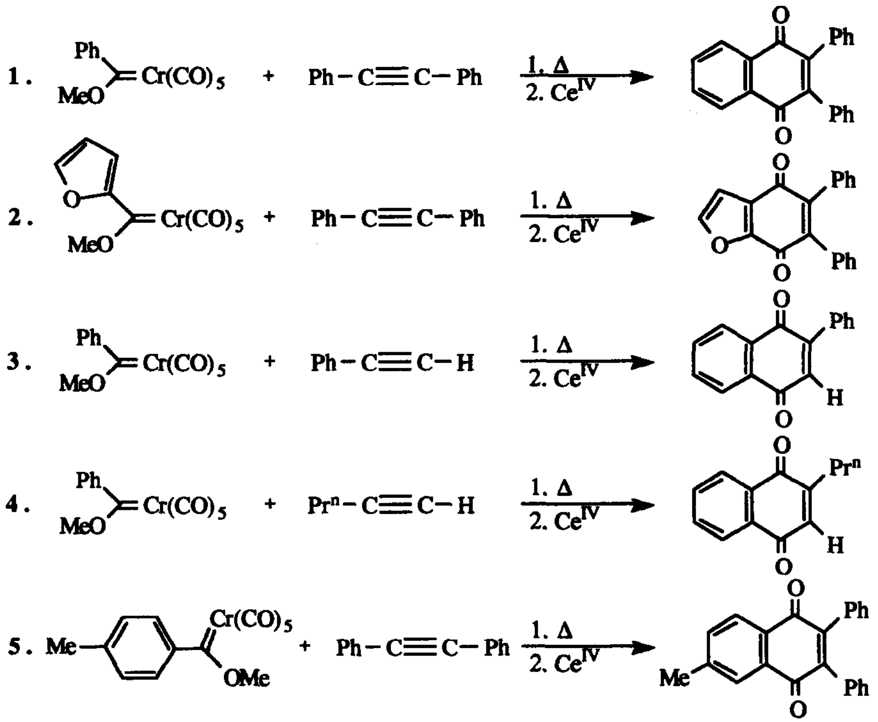
Additionally, in further studies we have found that sonication also readily promotes the Dötz annulation reaction at room temperature. More specifically, ultrasonication[10] of a solution of a metal carbene complex and an alkyne in di-*n*-butyl ether resulted in a rapid cycloaddition reaction (5-25min) furnishing the six-membered ring products in yields which were comparable to those previously obtained in the corresponding thermal reactions. The results obtained using sonochemical conditions will be reported in detail elsewhere.[11]

In conclusion, the dry state adsorption technique reported here provides a mild and rapid method for performing the Dötz annulation reaction. In particular, when silica is employed as the solid support, the yields of cyclised products are generally higher than previously obtained. Further applications of this technique to carbocyclic α,β-unsaturated carbene complexes, both aryl- and non-arylaminocarbene complexes and more volatile alkynes are currently under investigation.

## General Experimental Procedure.

A suspension of carbene complex (0.067-0.532mmol), adsorbent (10g/mmol of alkyne) and alkyne (1-1.5eq.) in hexane or ether was magnetically stirred for 5 minutes at room temperature and the solvent removed *in vacuo*. The round-bottom flask containing the resulting orange powder was purged with nitrogen and immersed in a heated oil bath and stirred. On completion of reaction, the solid was extracted with ether and filtered through a pad of Kieselguhr. The resulting crude product was taken up in 10ml of ether and treated with 8eq. of a 0.5M solution of ceric ammonium nitrate in 0.1M aqueous nitric acid at room temperature for 30 minutes. Following standard work-up procedures the product was purified by silica column chromatography.

Table 1. DSAC Promoted Annulation Reactions.



| Entry | Adsorbant[a] | Temp.(°C) | Time[b] | Yield[c] |
|---|---|---|---|---|
| 1 | $SiO_2$ | 40-50 | 180min | 86% (62%, ref. 12) |
| | $MgSO_4$ | 50 | 90min | 77% |
| | $Al_2O_3$ | 60-65 | 10min | 15% |
| 2 | $SiO_2$ | 50-60 | 120min | 74% (19%, ref. 13) |
| | $MgSO_4$ | 70-80 | 180min | 43% |
| 3 | $SiO_2$ | 60-65 | 90min. | 81% (67%, ref. 14) |
| | $MgSO_4$ | 60-70 | 90min | 18% |
| 4 | $SiO_2$ | 60 | 10min | 51% (80%, ref. 14) |
| 5 | $SiO_2$ | 50 | 180min | 70% (40%, ref. 13) |

[a] Silica gel (230-400 mesh), alumina and anhydrous magnesium sulphate were obtained from commercial suppliers. Alumina was neutralised with ethyl acetate prior to use. [b] The reaction was monitored by TLC analysis of extracts of small aliquots of solid mixture. [c] Isolated yields on chromatographic purification. Literature yields in parentheses. See ref. 15 for literature reaction conditions and times. Literature data on products: Entry 1; ref. 14. Entry 2; new compound. Entry 3; ref. 14. Entry 4; ref 14. Entry 5; new compound. Both new compounds were fully characterised by NMR, IR, microanalysis and mass spectroscopy.

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4. Smit and co-workers have found that adsorption of hexacarbonyldicobalt alkyne complexes onto silica dramatically improved the yields in both intramolecular and intermolecular Pauson-Khand reactions[6] with lower reaction temperatures and shorter reaction times.
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12. This yield refers to the parent tricarbonylchromium phenol complex. See ref. 1.
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15. Literature conditions and times for the reactions listed in **Table 1** are as follows: **Entry 1**; 45°C, $n$-Bu$_2$O, 3hr, ref. 1. **Entry 2**; 80°C, $n$-Bu$_2$O, 2.5hr, ref. 13. **Entry 3**; 45°C, THF, 23hr, ref.14 **Entry 4**; 45°C, hexanes, 72hr, ref. 14. **Entry 5**; 45°C, $n$-Bu$_2$O, 2hr, ref. 13.

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