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A NEW ROUTE TO DISUBSTITUTED CYCLOPENTENONES USING 2,3-DIBROMO-1-(PHENYLSULFONYL)-1-PROPENE AS A PIVOTAL REAGENT

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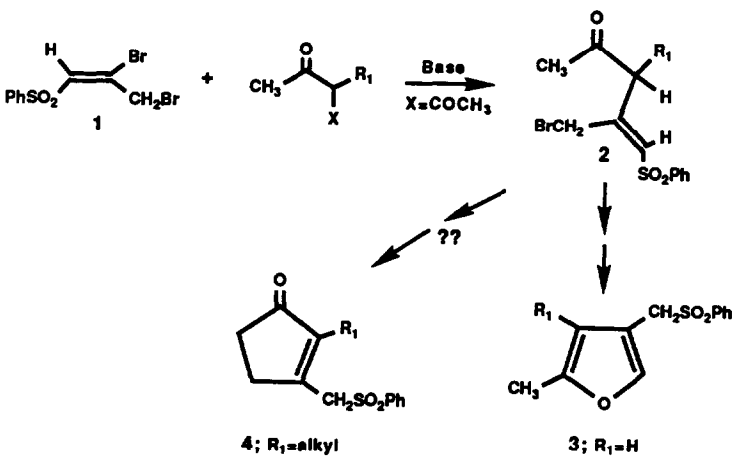
Abstract: 2,3-Dibromo-1-(phenylsulfonyl)-1-propene acts as a dielectrophile towards 1,3-diketones and β-ketoesters providing an entry into a variety of 2,3-disubstituted cyclopentenones including *cis*-jasmone.

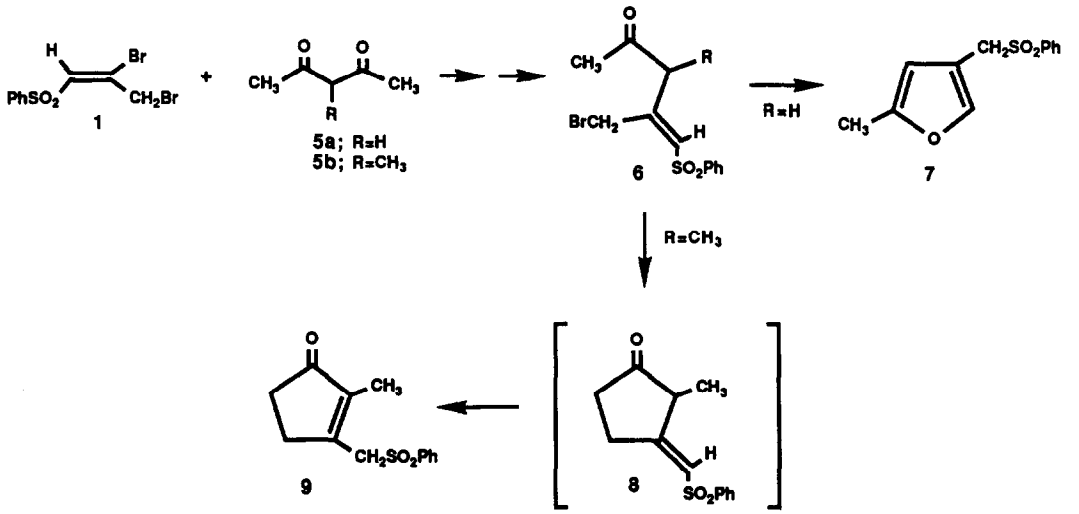
In connection with our continuing interest in developing synthetic methodology targeted towards the construction of polyoxygenated heterocycles[1], we have examined the behavior of 2,3-dibromo-1-(phenylsulfonyl)-1-propene (1) (DBP) as a versatile dielectrophile and have elaborated its use as a furan precursor.[2] By initial alkylation of various activated ketones with DBP, then ultimate ring closure on oxygen, we were able to access a variety of substituted and annulated furans (i.e. **2**→**3**).[2] If ring closure could be induced to occur on the methyl carbon rather than the



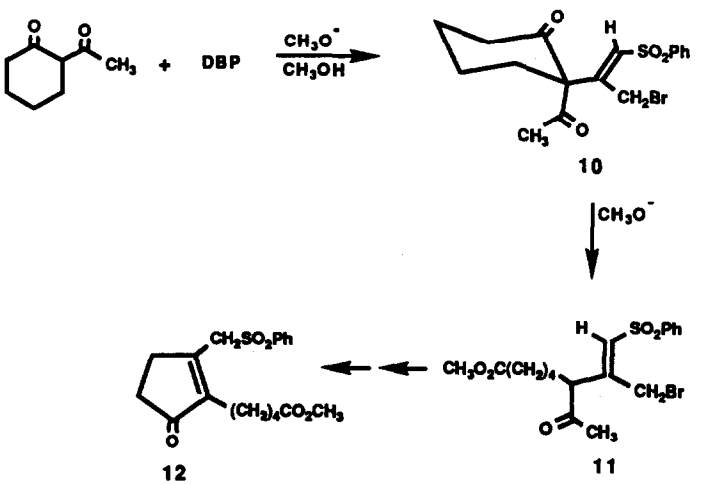
oxygen atom of the carbonyl group, the expansion of this methodology into the synthesis of carbocycles could be realized. This would provide a simple and direct route to the cyclopentenone moiety, a structural unit found in many natural products, such as the jasmonoids[3] and prostaglandins[4], and for which new routes continue to be developed.[5]

In this communication we report that the use of 1,3-dicarbonyls *substituted at the C-2 position induces a complete reversal in the mode of ring closure.* Previously, we had shown that treatment of DBP with 2,4-pentanedione (**5a**) in methanolic sodium methoxide results in the formation of furan **7** via a sequence of alkylation, deacetylation and ring closure.[2] Whereas the reaction of DBP with 3-methyl-2,4-pentanedione (**5b**) follows the same course of alkylation and deacetylation, the subsequent ring closure reaction of **6** afforded cyclopentanone **9** in 60% overall

yield.[6] This transformation proceeds by an initial cyclization producing **8** as a transient species which rapidly isomerizes to the observed cyclopentenone.[7]

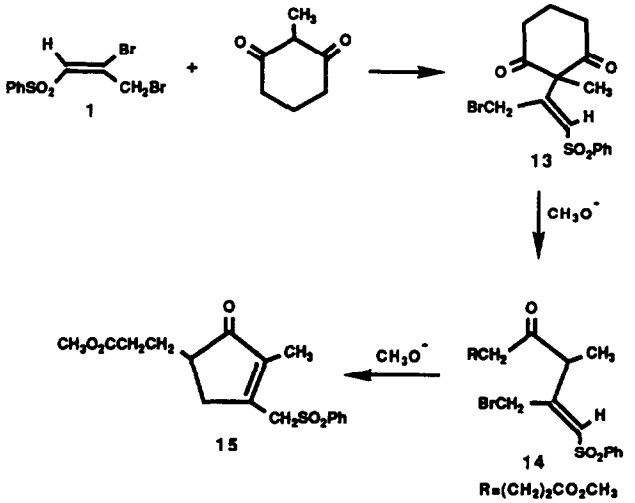


This methodology is tolerant of alkyl groups other than methyl. For example, treatment of DBP and 2-acetylcyclohexanone with an equivalent of methanolic sodium methoxide at 25°C results in the formation of dione **10**. Addition of a further equivalent of base induces a ring opening reaction, presumably as a consequence of the stability of the resultant anion[8], giving rise to ketoester **11**. An additional equivalent of base effects ring closure to the long-chain cyclopentenone **12** in 52% overall yield.

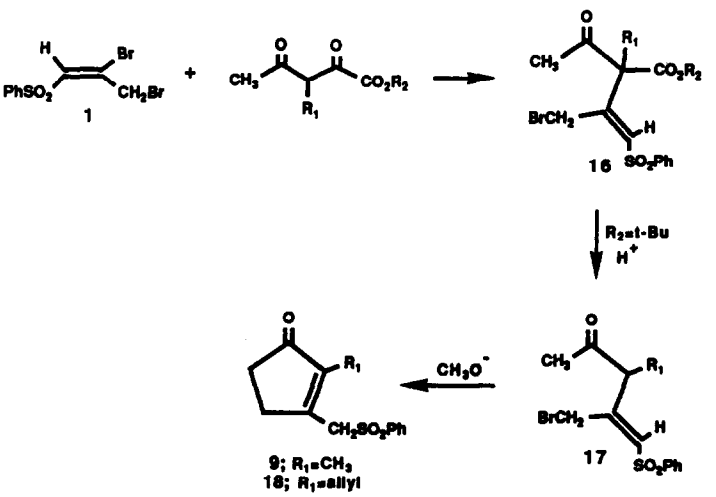


We were next interested in examining the possibility of introducing alkyl groups at the 5-position of the cyclopentenone ring. To that end, we treated an equimolar solution of DBP and 2-methyl-1,3-cyclohexanedione in DMF with an equivalent of sodium hydride at 0°C. This resulted in

the formation of dione adduct **13**, which underwent deacylative ring-opening under the methanolic sodium methoxide conditions to give the open-chain ketoester **14**. S_n2-Displacement using another equivalent of sodium methoxide afforded cyclopentenone **15** in 69% overall yield.

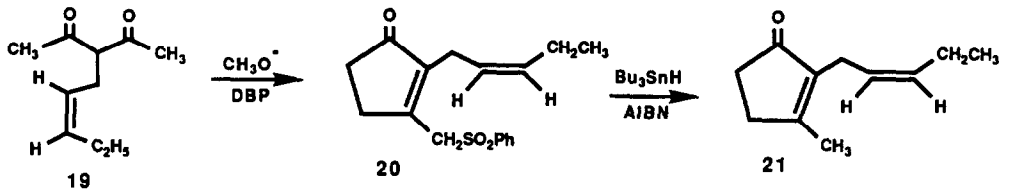


In addition to 1,3-diketones, substituted β-ketoesters may also be successfully employed in this reaction sequence, although under a different set of experimental conditions.[9] Alkylation of the ketoester with DBP using sodium hydride in THF produces the isolable intermediate **16**, which in the case of the t-butyl ester can be decarboxylated with acid to give **17**. Subjection of **17** to the basic experimental conditions described above affords cyclopentenones **9** (69%) and **18** (80%), respectively.



One of the particular strengths of the methodology lies in the convenience with which each of the substituents can be incorporated into the ring. For example, the C_2 substituent in the cyclopentenone may be introduced by C_2-alkylation of the initial 1,3-diketone. Furthermore, the pendant sulfone at the C_3 position offers a versatile site for further elaboration via alkylation[10] or

Julia coupling[11], among other methods.[12] To demonstrate the applicability of the method to natural product synthesis, we considered *cis*-jasmone to be a particularly amenable target.[13] Thus, treatment of DBP with diketone **19** in methanolic sodium methoxide provided cyclopentenone **20**, which was reductively desulfonylated using tributyltin hydride and AIBN in refluxing benzene[14] to provide *cis*-jasmone **21** in 72% overall yield.



19 **20** **21**

In conclusion, the reaction of substituted β-diketone and β-ketoester anions with DBP provides a simple and efficient route to functionalized cyclopentenones and should be a valuable reaction in the repertoire of synthetic organic chemists. We are currently investigating the scope and limitations of this method.

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References and Notes

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