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A SIMPLE SYNTHESIS OF SOME CYCLIC AND ACYCLIC CYCLOBUTENEDIONES

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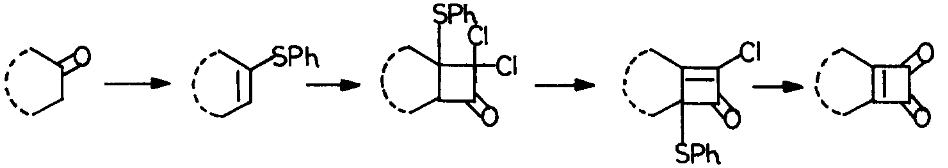
Summary Cyclobutenediones can be prepared from cyclic and acyclic ketones by a simple four step procedure.

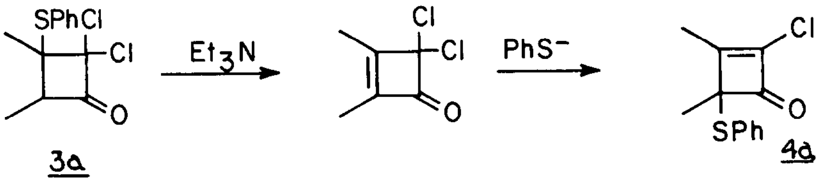
Having previously demonstrated that benzocyclobutenediones and alkynes could be converted to naphthoquinones through the intermediacy of phthaloylmetal complexes,[2-5] we sought to establish the same reaction sequence using cyclobutenediones and alkynes as a means of synthesizing benzoquinones. A search of the literature[6-14] showed that only certain types of cyclobutenediones were readily prepared (aryl substituted cyclobutenediones and derivatives of squaric acid and semisquaric acid). If cyclobutenediones could serve as precursors to benzoquinones, then a valid synthetic method would require a convenient source of cyclobutenediones with a variety of substitution patterns. To that end we have developed a new route to cyclobutenediones which takes cyclic or acyclic ketones to the desired products in four steps (eq 1).



(1)

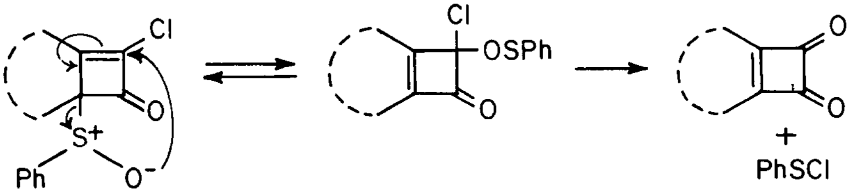
Our results are listed in Table 1. Phenylthioenol ethers 2a-d, easily prepared in large quantity and good yield from ketones 1a-d,[15] underwent a regiospecific [2 + 2] cycloaddition with dichloroketene (generated from Cl_3CCOCl and Zn-Cu according to Krepski and Hassner[16]) to provide the dichlorocyclobutanones 3a-d in good yield.[17] The regiochemistry shown for the cycloaddition is that expected on polarization arguments. To confirm this expectation, the cyclohexanone system 3b was dechlorinated (Zn, NH_4Cl, MeOH-THF, 0°) to the cyclobutanone (97% yield) which showed the expected decouplings in the 270 MHz 'H NMR at -40°C.

Treatment of the dichlorocyclobutanones 3a-d with Et_3N/CH_3CN was expected to eliminate thiophenol and produce the corresponding dichlorocyclobutenones which we had planned to hydrolyze to the cyclobutenediones.[18] Unexpectedly a facile, high-yield elimination of HCl occurred to give the "rearranged" products 4a-d in excellent yields.[19] While literature precedent would suggest the reaction might occur via an oxyallyl cation intermediate,[20] we have shown that dichlorocyclobutanone 3a undergoes a rapid elimination of thiophenol to the dichlorobutenone which is followed by readdition of PhS$^{\ominus}$ in an S$_N$2' fashion to give the observed product, 4a (eq 2).[21]



(2)

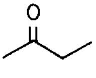
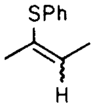
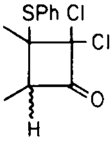
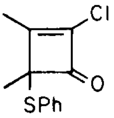
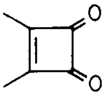
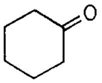
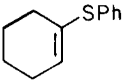
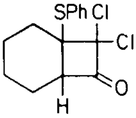
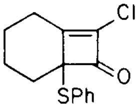
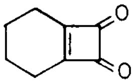
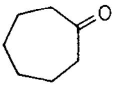
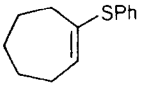
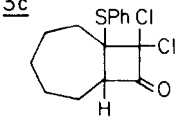
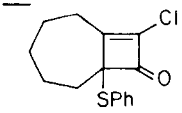
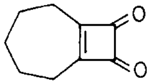
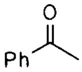
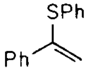
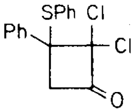
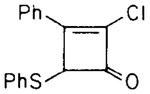
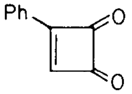
The "rearranged" products 4a-d turned out to be excellent precursors to the desired cyclobutenediones. Treatment of 4a-d with m-chloroperbenzoic acid led directly to cyclobutenediones 5a-d in yields ranging from 93%-99%.[22] We presume that peracid converts the sulfides to γ-chloroallyl sulfoxides which have previously been shown by Lansbury[23] to spontaneously fragment to carbonyl compounds and PhSCl via a [2,3] sigmatropic rearrangement (eq 3).



(3)

The simple reaction conditions and good overall yields from cyclic and acyclic ketones should make this route to cyclobutenediones a practical addition to the previously known methods of synthesis.[24] Also, as anticipated at the outset of this project, cyclobutenediones have proven to be valuable precursors to benzoquinones using our previously described organotransition metal method.[25,26]

Table I. Synthesis of Cyclobutenediones from Ketones[a]

ketones	thioenol ethers	[2+2] products	rearranged products	cyclobutenediones
1a 	2a  75 %	3a  not purified	4a  56 % from 2a	5a  93 %
1b 	2b  75 %	3b  63 % mp 70 - 72° (pentane)	4b  94 % mp 44 - 45° (pentane)	5b  94 % mp 45 - 47° (after dist.)
1c 	2c  93 %	3c  63 % mp 61 - 62° (pentane)	4c  87 % mp 59 - 61° (pentane)	5c  99 % mp 39 - 41° (after dist.)
1d 	2d  56 %	3d  62 % mp 111 - 112° (Et_2O)	4d  95 % mp 59 - 60° (ether-pentane)	5d  97 % mp 152 - 153° (CH_2Cl_2 - Et_2O)

a) All new compounds were characterized by IR, 270MHz ^1H NMR and low resolution mass spectra and gave satisfactory elemental analyses.

References and Notes

1. Fellow of the Alfred P. Sloan Foundation, 1983-1985.
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4. S. L. Baysdon and L. S. Liebeskind, Organometallics, 1982, 1, 771.
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13. W. T. Brady and R. D. Watts, J. Org. Chem., 1980, 45, 3525.
14. W. T. Brady and K. Saidi, ibid., 1980, 45, 727.
15. Thioenol ethers 2a and 2b were prepared by conversion of the ketone to the thiophenylketal (B. S. Ong and T. H. Chan, Syn. Comm., 1977, 7, 783) followed by thermal cracking-distillation at atmospheric pressure, 2c was directly prepared from the ketone according to F. Akiyama, Bull. Chem. Soc., Jpn., 1977, 50, 936; 2d was prepared from the thiophenylketal by Hg(II) induced elimination according to B. M. Trost and A. C. Lavoie, J. Am. Chem. Soc., 1983, 105, 5075.
16. L. R. Krepski and A. Hassner, J. Org. Chem., 1978, 43, 2879.
17. The procedure of reference 16 was generally followed with the exception that $POCl_3$ was not used: 3a from 1.1 eq Cl_3CCOCl in Et_2O at rt for 16h - unstable to purification; 3b from 1.1 eq Cl_3CCOCl in Et_2O at reflux for 16h; 3c from 2 eq Cl_3CCOCl in Et_2O at reflux for 12h; 3d from 1.2 eq Cl_3CCOCl in Et_2O at rt for 8h.
18. Our choice of thioenol ethers rather than enol ethers for this sequence was prompted by reports that a number of dichlorocyclobutanones derived from silylenol ethers were thermally unstable and underwent ring opening reactions: L. R. Krepski and A. Hassner, J. Org. Chem., 1978, 43, 3173-3179 and W. T. Brady and R. M. Lloyd, J. Org. Chem., 1979, 44, 2560-2564.
19. 4a: 1 eq Et_3N then 1 eq PhSH added to crude 3a in CH_3CN at 0° then warmed to rt, 2h; 4b: 1 eq Et_3N added to 3b in CH_3CN at 0° then warmed to rt, 12h; 4c: 1 eq Et_3N then 1 eq pHSH added to 3c in CH_3CN at 0° then warmed to rt, 2h; 4d: 1 eq Et_3N added to 3d in CH_3CN at 0°C then warmed to rt, 1.5h.
20. A. Hassner, J. L. Dillon, Jr., L. R. Krepski and K. D. Onan, Tetrahedron Lett., 1983, 1135-1138.
21. Treatment of 3a with K_2CO_3 in acetone led cleanly to the dichlorocyclobutenone, identical with an authentic sample prepared by a literature procedure (A. Hassner and J. L. Dillon, Jr., J. Org. Chem., 1983, 48, 3382-3386). The dichlorocyclobutanone on treatment with Et_3N and PhSH (1.1 eq each) gave a 98% yield of the "rearranged" product, 4a.
22. 5a: 1.1 eq MCPBA added to 4a in CH_2CL_2 at -78°C then warmed to rt, 12h. After addition of cyclohexene (to trap PhSCl), work-up and chromatography gave pure 5a (previously prepared: A. Trebs, K. Jacob and R. Tribollet, Justus Liebigs. Ann. Chem., 1970, 741, 101; 5b: 1.1 eq MCPBA added to 4b in CH_2Cl_2 at -78°C then warmed to rt, 8h. Addition of cyclohexene, workup, and distillation (Kuglrohr) gave 5b; 5c: 1.1 eq MCPBA added to 4c in CH_2Cl_2 at -78°C then warmed to rt, 12h. Addition of cyclohexene, workup, and chromatography gave 5c; 5d: 1.1 eq MCPBA added to 4d in $CHCl_3$ at 0°C. After 30 min cyclohexene was added and the mixture was refluxed for 3h. Workup and titration (2:1 pentane-ether) gave 5d (previously prepared: E. J. Smutny, M. C. Caserio and J. D. Roberts, J. Am. Chem. Soc., 1960, 82, 1973).
23. P. T. Lansbury and R. W. Britt, J. Am. Chem. Soc., 1976, 98, 4577-4581.
24. The reaction sequence is not completely general. Cyclopentanone could be carried through to the dichlorocyclobutanone stage but treatment with Et_3N led to ring opened products.
25. L. S. Liebeskind, J. P. Leeds, S. L. Baysdon and S. Iyer, submitted to J. Am. Chem. Soc.
26. This investigation was supported by PHS grant number CA 26374 awarded by the National Cancer Institute, DHHS.

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