ethereal solution was washed with aqueous HCl and with water, dried, and evaporated. The residue was starting cyclobutene **18** (0.037 g; 95% recovery).

(2) A mixture of cyclobutene **18** (0.025 g), NaI (0.200 g), and acetic acid (10 mL) was heated on a steam bath (30 min). The resulting mixture was poured into water and extracted with ether. The ethereal solution was washed with aqueous $NaHCO_3$ and with water, dried, and evaporated. The residue was starting cyclobutene **18** (0.024 g; 96% recovery).

(3) A mixture of cyclobutene **18** (0.020 g) and powdered Cu (0.20 g) was heated (200 °C; 15 min) under argon, and the resulting mass was extracted with ether. The organic extract was purified through alumina (hexane) to give butadiene **19** (0.016 g; 80%).

Thermal Treatments of Acetylene 6. (1) At 210 °C in Perchlorobutadiene. A solution of acetylene **6** (0.300 g) in perchlorobutadiene (50 mL) was heated (210 °C; 1 h) under argon. Elimination of the solvent (0.5 mmHg; 90 °C) yielded a residue which by digestion with boiling hexane and TLC (silica gel; hexane) afforded: (a) starting acetylene **6** (0.038 g; 13% recovery), (b) *cis*-perchloro-1,4-diphenylbutenine (**30**) (0.060 g; 20%) [mp 231–4 °C: UV (C_6H_{12}) 216 nm, 225 (sh), 240 (sh), 253 (sh), 293 (sh), 305, 310 (sh), 325 (ε 74 000, 62 000, 41 000, 25 000, 19 500, 22 800, 21 000, 23 300); IR (KBr) 1565 (w), 1525 (w), 1405 (m), 1365 (m), 1345 (s), 1335 (s), 1308 (m), 1240 (m), 975 (s), 930 (s), 870 (m), 760 (m), 720 (s), 710 (s), 655 (m), 642 (m), 628 (m), 592 (s), 492 (m) cm^{-1}; MS (all ^{35}Cl) 612 ($C_{16}Cl_{12}^+$). Anal. Calcd for $C_{16}Cl_{12}$: C, 31.1; Cl, 68.9. Found: C, 31.3; Cl, 68.9], (c) perchloro-1-phenylnaphthalene (**27**) (0.040 g; 13%), mp 274–8 °C (lit.[7] 276–8 °C), (d) perchloro-1,2,4-triphenylbenzene (**29**) (0.030 g; 10%), mp 305–9 °C (lit.[6] 306–8 °C), and (e) perchloro-1,2,3-triphenylbenzene (**28**) (0.040 g; 13%), mp 293–6 °C (lit.[6] 293–6 °C). The structure of compounds **27**, **28** and **29** has been confirmed by IR and UV spectroscopy.[6,7]

(2) **At 190–5 °C.** Acetylene **6** (1.544 g) was heated (190–5 °C; 30 min) under argon. The resulting mass, by column chromatography (alumina; hexane), yielded: (a) a yellowish product that by recrystallizations from hexane–ether gave perchloro-1-phenylnaphthalene (**27**) (0.379 g; 25%), mp 274–8 °C and (b) a brown resin that by sublimation (250 °C; 0.5 mmHg) and TLC (silica gel; hexane) gave perchloro-1,2,4-triphenylbenzene (**29**) (0.116 g; 7.5%), mp 305–9 °C and perchloro-1,2,3-triphenylbenzene (**28**) (0.287 g; 19%), mp 293–6 °C.

(3) **At 140–5 °C.** Acetylene **6** (0.100 g) was heated (140–5 °C; 7 h) under argon. The resulting mass was treated as in (2) giving naphthalene **27** (0.010 g; 10%), 1,2,4-triphenylbenzene **29** (0.019 g; 19%) and 1,2,3-triphenylbenzene **28** (0.023 g; 23%).

(4) **At 110–20 °C in Perchlorostyrene.** A mixture of acetylene **6** (0.265 g) and perchlorostyrene (**1**) (0.285 g) as the solvent was heated (110–20 °C; 24 h) under argon. The resulting mass was treated as in (2) giving styrene **1** (0.271 g; 95% recovery), 1,2,4-triphenylbenzene **29** (0.067 g; 25%), 1,2,3-triphenylbenzene **28** (0.167 g; 63%), and an isomeric $C_{24}Cl_{18}$ (0.021 g; 8%), mp 319–21 °C: UV (C_6H_{12}) 212 nm, 224 (sh), 294 (ε 128 000, 91 800, 3470); IR (KBr) 1535 (w), 1380 (w), 1362 (s), 1340 (s), 1320 (s), 1142 (m), 1117 (m), 1070 (m), 910 (m), 882 (m), 870 (m), 780 (m), 775 (m), 762 (m), 730 (s), 717 (s), 695 (s), 680 (m), 660 (s), 650 (m), 640 (m), 620 (m), 580 (m), 565 (m), 555 (m) cm^{-1}; MS (all ^{35}Cl) 918 ($C_{24}Cl_{18}^+$).

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Registry No. **1**, 29082-74-4; **2**, 37123-28-7; **5**, 100571-02-6; **6**, 52598-45-5; **7**, 65350-47-2; **10**, 100571-03-7; **11a**, 29086-39-3; **11b**, 29086-38-2; **12**, 22551-88-8; **13**, 100571-04-8; **14**, 1012-84-6; **15**, 19635-52-0; **16**, 100571-05-9; **17**, 100571-06-0; **18**, 100571-07-1; **19**, 100571-08-2; **20**, 100571-09-3; **21**, 100571-10-6; **22**, 100571-11-7; **23**, 100571-12-8; **24**, 100571-13-9; **25**, 100571-15-1; **27**, 77302-45-5; **28**, 70994-48-8; **29**, 71140-77-7; **30**, 100571-14-0; $Cl_2C{=}CCl_2$, 127-18-4; $Cl_2C{=}CHCl$, 79-01-6; $SnCl_2$, 7772-99-8; Cu, 7440-50-8; NaI, 7681-82-5; cyclohexane, 110-82-7; perchlorobutadiene, 87-68-3.

Arynic Condensation of Ketone Enolates. 17.[1] New General Access to Benzocyclobutene Derivatives

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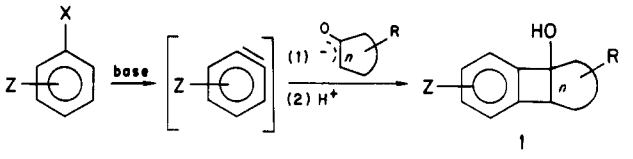
Arynic condensation of 1,2-diketone monoketal enolates appeared to be a very simple way to synthesize benzocyclobutene derivatives. X-ray diffraction and ^1H NMR spectra allowed us to determine the structure of the new compounds and to propose a mechanism concerning these condensations. Finally, during this work we devised a new and easily performed two-step synthesis of 1,2-diketones.

The abundant literature dealing with benzocyclobutene derivatives shows how attractive these compounds are.[2] They constitute an important family of starting materials for the obtention of a large variety of polycyclic compounds. Moreover their syntheses very often constitute an interesting challenge, and a convenient access to these structures is always desirable.[3]

Scheme I



For some years, our laboratory has been studying the synthesis and the chemical transformation of benzocyclobutene derivatives.

Our interest increased when we discovered that benzocyclobutenols **1** (Scheme I) had anticonvulsant properties[4]

(1) For part 16, see: Carre, M. C.; Gregoire, B.; Caubere, P. *J. Org. Chem.* **1984**, *49*, 2050.

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and could be transformed into new selective β_2 adrenergic blocking agents.[5]

Some years ago we showed that benzocyclobutenols could be obtained through arynic condensations of ketone enolates in an aprotic solvent (Scheme I).

Among the methods described for generating benzyne, elimination of hydrohalide acid from aryl halides is the best suited for large-scale preparations. Indeed, aryl halides are far from being the most easily obtained starting materials. Moreover the bases to be used are commercial sodium amide or the very easily obtained complex bases ($NaNH_2$–RONa)[6] where RONa is an in situ prepared alkoxide.

However, the reactions we previously described suffer from limitations. Indeed, in spite of considerable efforts, alcohols **1** were obtained only from cyclic ketone enolates for which $5 \leq n \leq 7$;[7] with a few exceptions[8] linear ketone enolates did not lead to the desired alcohols under the established conditions.

Potential applications in medicinal chemistry necessitate the preparation of benzocyclobutenols functionalized on the saturated ring. The above consideration led us to start a program aimed at improving the results previously obtained and at preparing for the first time, benzocyclobutenols bearing a function on the saturated ring and on the α position relative to the hydroxyl group.

Among the possible functions, a carbonyl group appeared as particularly well suited. In other words, considering the nature of the arynic condensations, we thought that condensation of monoprotected 1,2-diketones should lead to the desired products.

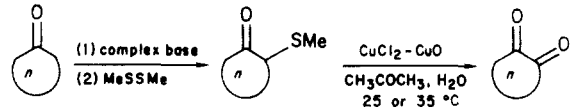
However, another problem arose when we decided to synthesize the necessary starting diketone monoketals. Indeed while the linear derivatives could be obtained from the method developed by Conia and co-workers,[9] on the contrary none of the described syntheses[10] were found general enough to prepare the cyclic compounds. Moreover in this series, these methods are somewhat limited by the expensiveness and/or the toxicity of the reagents used. So we decided to turn toward a two-step synthesis including the preparation of 1,2-diketones followed by monoketalization. The main difficulty with this strategy was the preparation of cyclic 1,2-diketones.

For a number of reasons we devised a new general preparation of 1,2-cycloalkanediones and succeeded in their monoprotection by modification of a literature method.

A portion of the studies has been published as a communication.[11] Details on the synthesis of 1,2-diketone monoketals and their arynic condensations are given in this paper.

Synthesis of 1,2-Diketones and Their Monoketals. There are a number of reports dealing with the preparation of 1,2-diketones.[10c,f,12] Among them, the simplest consists of the oxidation of the corresponding monoketone. Indeed cycloalkanones are either commercial products (n = 6–8, 10, 12) or easily prepared from commercial starting materials: cycloundecanone was prepared from cyclododecanone by ring contraction via a Favorskii-type rearrangement,[13a] and cyclononanone was obtained from 1,2-cyclononadiene[13b] by monohydroboration, followed by oxidation.[13c]

Table I



starting ketone 2, n	step 1, α-methylthio ketone 3, yield, %	step 2, 1,2-cycloalkanedione 4 reacn T, °C	t, h	yield, %	overall yield,[a] %
5	70[b]	35	0.5	60	42
6	90	35	0.5	80	72
7	70	35	1	70	49
8	86	35	0.5	87	75
9	77	25	0.5	70	54
10	90	25	0.25	45[c]	40
11	87	25	2	80	70
12	95	35	4	80	76

[a] From the starting cycloalkanone **2**. [b] Enolate was prepared at 0 °C. [c] Formation of corresponding monomethylthio enol ether in 50% yield characterized by IR and ^1H NMR spectra.

After having tested some of the more attractive methods given in order to transform cycloalkanones into cyclic 1,2-diketones we concluded that SeO_2 oxidation was the simplest to carry out, and a number of the diketones used in the present work were prepared in this way.[12a,31]

However, for some currently undetermined reason, SeO_2 oxidation sometimes led to low yields or to a mixture of products from which the wanted diketone was difficult to obtain pure. Moreover on a large scale, this preparation requires handling large amounts of toxic reagents. Finally traces of selenium derivatives accompanied the diketones even after careful purification.

In order to avoid the use of this oxidizing agent we tried to develop a new synthesis of cyclic 1,2-diketones.

Our attention was attracted by an interesting report of Gassmann and co-workers,[14] showing that oxidation of the methine carbon in the 3-position of the 3-(methylthio)-oxindoles with *N*-chlorosuccinimide followed by hydrolysis of the chlorinated intermediate, provides a simple route to isatin. Indeed, we previously showed that methylthio ketones can be easily obtained by α-methylthiolation of ketones using the very inexpensive complex bases and

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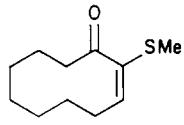
MeSSMe.[15] Furthermore, it is known[16] that α-chloro ketones can be obtained from simple ketones by using $CuCl_2$ as chlorinating agent. Finally copper salts are very efficient reagents in the hydrolysis of thio derivatives of carbonyl compounds.[17] These observations led us to think that under appropriate conditions 1,2-diketones could be obtained in *one pot* starting from α-methylthio ketones. The hypothesis was verified and 1,2-diketones were obtained by the two-step reaction; the results are grouped in Table I.

It is noteworthy that the oxidation of methylthio ketones was very fast even at room temperature. With one exception, diketones were obtained in good yields. Curiously, in spite of numerous efforts we were unable to improve the oxidation of cyclodecanone. Indeed, besides the expected diketone (formed in 45% yield) we always observed the formation of the corresponding monomethylthio enol ether **5** in 50% yield.



5

We have no explanation for this anomalous reaction. Still more curious was the behavior of **5**. We did not succeed in transforming it into the diketone using a number of classical methods such as hydrolysis with mercuric chloride in aqueous acetonitrile, with mercuric chloride and hydrochloric acid in aqueous ethanol, with titanium tetrachloride in acetic acid, or with silver nitrate in aqueous ethanol![18]

On the other hand, a number of interesting observations were made during this study. Control experiments carried out on α-(methylthio)cycloheptanone (25 mM) showed that reactions performed in the presence of CuO alone (100 mM) led to no oxidation after 1.5 h at room temperature or at 45 °C. Addition at room temperature of 2.5 mM of $CuCl_2$ to the above mixture of α-(methylthio)cycloheptanone and cupric oxide led to the rapid but incomplete formation of the expected diketone. Successive additions of 10 and 12.5 mM of $CuCl_2$ led to the formation of increasing amounts of diketone, but there was some starting ketone left after 3 h of contact. It was thus concluded that $CuCl_2$ could not be used in a catalytic or semicatalytic quantity.

Experiments performed at room temperature or at 45 °C with a number of α-(methylthio)cycloalkanones showed that $CuCl_2$ alone taken in a stoichiometric amount or in excess led to a mixture of products from which the starting α-methylthio ketone and the expected diketone were isolated: with the α-(methylthio)cyclodecanone we obtained the corresponding diketone and the methylthio enol ether **5** in 36% and 40% yields, respectively.

Trying to replace CuO by another noncupric base such as $CaCO_3$ led to the formation of the desired diketone but in lower yields. Using mercuric salts instead of cupric ones also led to the formation of diketone. With these salts and under the same conditions, we obtained cyclodecanedione (38%) and **5** (15%); a disadvantage of this method was the contamination of the compounds by mercuric derivatives.

Finally the efficiency of this new synthesis on a large scale was tested. Cyclododecanone (500 mM) was transformed into the corresponding α-methylthio ketone in 91% yield. The oxidation was performed on 450 mM and the corresponding diketone obtained in 80% yield.

Having obtained the cyclic 1,2-diketones, we were faced with the problem of their monoprotection as ketals.

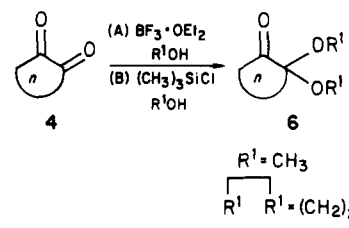
With ketones other than the cyclopentanedione we tried to obtain the dimethyl or ethylene ketal using one of the numerous methods of ketal synthesis given in the literature.[19] Thus methods such as PTSA in refluxing benzene, $HC(OMe)_3$/MeOH/HCl gas, and $HC(OMe)_3$/MeOH/catalytic H_2SO_4 were tried.

None of these reactions led to good results. Either a large amount of starting material was left unreacted or, on the contrary, a large amount of diketal was formed.

Moreover the reaction between the diketal and the corresponding diketone in order to prepare the required monoketal by transketalization[20] was not efficient enough to be used in the present work.

Finally, open as well as cyclic monoketals were obtained from two methods: the first with BF_3·OEt_2 as reagent and the second utilizing Me_3SiCl which was based on that developed by Chan and co-workers.[21a] We noted the following two exceptions: 1,2-cyclodecanedione monoketal was obtained in good conditions only by using PTSA in refluxing benzene. With 1,2-cyclopentanedione we were conducted to adopt the method developed by Fujita and co-workers[10c,d] though it does not allow the formation of ethylene ketals. Thus oxidation of α-(methylthio)cyclopentanone by $Tl(NO_3)_3$ in MeOH led to α,α-dimethoxycyclopentanone in reasonable yields. We have summarized in Table II the monoketals thus prepared.

Table II



4 **6**

$R^1 = CH_3$ $R^1 = (CH_2)_2$

compd 6					
n	R^1	method	T, °C	t, h	yield, %
6	CH_3	B	20	3	63
	$(CH_2)_2$	A	20	5	53
7	CH_3	B	20	0.5	81
	$(CH_2)_2$	B	20	7	70
8	$(CH_2)_2$	A	0–5	2	79
9	$(CH_2)_2$	A	20	1.5	60
10	$(CH_2)_2$[a]	A	20	5	16
		PTSA, benzene, Δ	78	5	28
11	$(CH_2)_2$	B	20	72	56
12	$(CH_2)_2$	B	20	36	55

[a] With the conditions B, the diketone was recovered unchanged.

Arynic Condensation of 1,2-Diketone Monoketal Enolates. Previous work[22] showed that in aprotic solvents,

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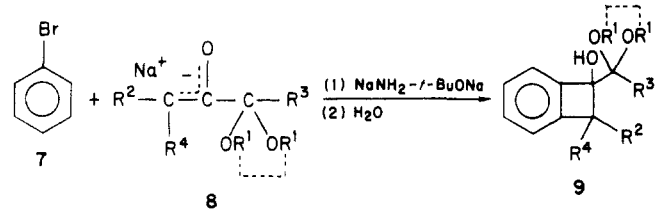
Table III



7 8 9

8	R^1	R^2	R^3	R^4	ratio 7/8	solv	T, °C	t, h	yield[a,f] 9, %
a	$(CH_2)_2$	H	CH_3	Et	0.5/1	THF	20	24	85
b	$(CH_2)_2$	CH_3	CH_3	CH_3	0.5/1	THF	20	17	40[b]
c	$(CH_2)_2$	H	CH_3	Pr	0.5/1	THF	20	1.5	80
d	CH_3	$(CH_2)_2$		H	0.5/1	THF	20	2.25	75
e	CH_3	$(CH_2)_3$		H	0.5/1	THF	20	1	76
f	$(CH_2)_2$	$(CH_2)_3$		H	0.5/1	THF	20	1	65
g	CH_3	$(CH_2)_4$		H	0.5/1	THF	20	2	92
					1.1/1	THF	20	3	80[c]
h	$(CH_2)_2$	$(CH_2)_4$		H	0.5/1	THF	20	0.75	92
i	$(CH_2)_2$	$(CH_2)_5$		H	0.5/1	THF	20	1.75	93
j	$(CH_2)_2$	$(CH_2)_6$		H	0.5/1	THF	20	2	42
k	$(CH_2)_2$	$(CH_2)_7$		H	1.1/1	DME	0	2	45[c]
l	$(CH_2)_2$	$(CH_2)_8$		H	0.5/1	THF	20	2	42
					1.1/1	THF	20	2	37[c]
					1.1/1	DME	0	5	66[c]
m	$(CH_2)_2$	$(CH_2)_9$		H	0.5/1	THF	20	15	49[d]
					0.5/1	THF	0	5	33[e]
					1.1/1	DME	0	2.8	70

[a] Yield of isolated alcohol 9 with respect to 7. [b] 10% of unreacted 7 recovered and formation of an ethylenic alcohol 10 in 14% yield. [c] Yield of isolated alcohol 9 with respect to 8. [d] Formation of the corresponding benzocyclenone in 8% yield. [e] Formation of the corresponding benzocyclenone in 33% yield. [f] Satisfactory combustion analytical data were reported for all compounds 9, except as noted in the following. Compound 9d was too unstable to analyze. The compounds 9b, 9e, 9g, and 9h did not analyze for C, H within ± 0.4%; however, they had the expected spectral properties including ^{13}C NMR; furthermore the alcohols 9e, 9g, and 9h were opened into the corresponding benzocyclenones 11e, 11g, and 11h, respectively, for which analytical data were correct.

this kind of condensation may be performed in the presence of $NaNH_2$ alone or in the presence of a complex base[23] such as $NaNH_2$–t-BuONa. In fact when the ketone enolate is a good activating agent of $NaNH_2$, no alkoxide is needed and the benzyne is smoothly generated by the nucleophilic complex base $NaNH_2$–ketone enolate.

On the contrary, when the ketone enolate is not an activating agent, a nonnucleophilic complex base must be used in order to generate the benzyne. Preliminary experiments rapidly showed that the 1,2-diketone monoketal enolates were not activating enough and the complex base $NaNH_2$–t-BuONa was used. With this reagent, arynic condensations were generally performed at room temperature in a few hours. The results thus obtained are reported in Table III.

Ketones 6 for which n = 11 or 12 necessitated to replace THF by DME in order to improve yields. Moreover when n = 7 or 10–12 the ratio 7/8 was made 1.1/1 in order to facilitate the separation of alcohols 9 from the remaining starting ketone.

Structure Determination and Discussion. The main characteristic of these condensations is that, with a few exceptions, the only products formed are benzocyclobutenols. The difference with what was observed with monoketones is particularly striking. For example, starting from aliphatic ketones, we were never able to prepare benzocyclobutenols. With cycloalkanones benzocyclobutenols were never formed when the ring size was larger than seven, and the yield with cyclopentanone was never higher than 20%.[7]

We have also showed that these results are due to a lack of stability of the sodium benzocyclobutenoxide.

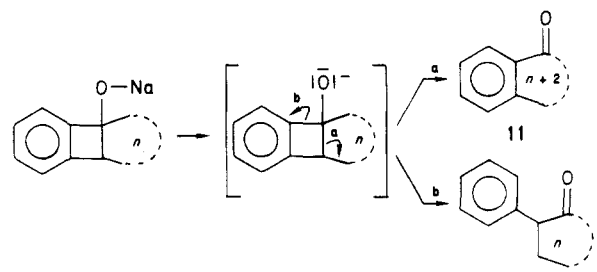
The origin of this lack of stability has not been completely clarified. However, the numerous experiments previously performed in our laboratory give interesting information.

Thus the stability of the sodium alkoxide formed during arynic condensations has a steric component. Indeed we always observed that the presence of methyl groups in the α and/or α' position of the starting ketone strongly favors the formation of benzocyclobutenols.

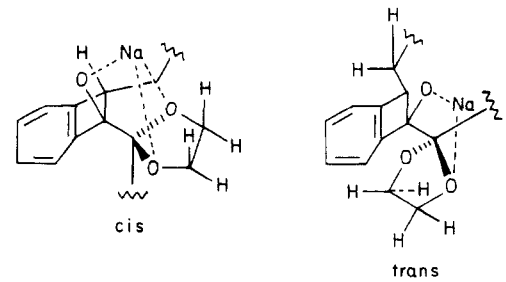
Another important component of the stability deals with electronic effects.

When the sodium cation of the alkoxide was completely removed or moved further from the oxygen, liberation of the electrons led to the opening of benzocyclobutenol (Scheme II).[24]

Scheme II



Scheme III



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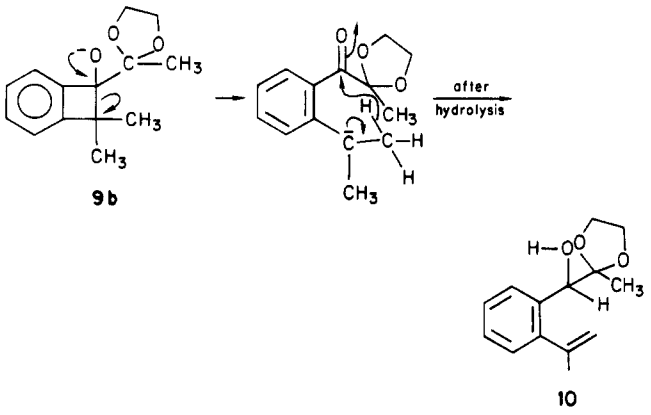
(23) Caubere, P. *Acc. Chem Res.* **1974**, *7*, 301.

Scheme IV



9b **10**

Coming back to the problem of 1,2-diketone monoketals, it may be concluded that the two alkoxy groups must play the part of the methyl groups cited above and then participate in the stabilization of benzocyclobutenols.

Moreover the Dreiding models show (see Scheme III) that oxygens of the ketal function can contribute to the stabilization of the alkoxide by complexation of the sodium cation. Taking into account of the structure (see later) this stabilization must be more significant in the cis isomer than in the trans one (see Scheme III).

The combined effects of steric and electronic stabilization nicely explain the results obtained.

Considering Table III, the 40% yields observed with the 3-methyl-1,2-butanedione monoketal **8b** were partially due to an internal hydride transfer leading to an unsaturated alcohol **10** (Scheme IV).

This kind of side reaction has already been observed with isopropyl ketones.[25] With the other ketones studied, the only byproducts (if formed) were due to the opening of the cyclobutene ring following route a reported in Scheme II.

The structure of benzocyclobutenols has been easily established (see Experimental Section) by comparison of their spectroscopic properties (IR, ^1H and ^{13}C NMR, UV) with those of the numerous benzocyclobutenols previously prepared.[5,26]

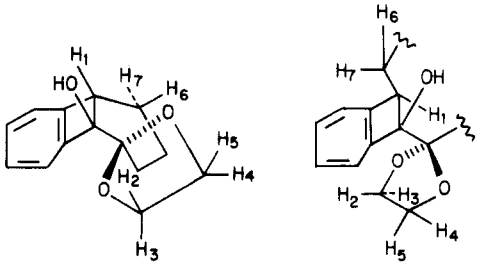
The stereochemistry of the junction between the cyclobutene and the saturated rings is more difficult to determine.

Our previous work on arynic, cycloalkynic, and 1,2-cycloalkadienic[6] condensations of ketone enolates amply demonstrated that benzynes as well as cycloalkynes and 1,2-cycloalkadienes always lead to syn addition to ketone enolates. Thus arynic condensation of cyclopentan-, hexan-, and heptanones, always led to cis junctions. The same was expected with the corresponding monoketal of 1,2-diketones.

However, with larger rings, particularly from nine-membered ones, the stereochemistry of the ring junctions had to be established. We first compared the benzocyclobutenols coming from the 6- and 12-membered ring ketones. The alcohol **9f** is constrained to have a cis junction. Indeed this alcohol is very stable, a property which would be incompatible with a trans stereochemistry.

X-ray diffraction on the 12-membered alcohol **9m** established the trans nature of the ring junction.[27a] However, comparison of ^{13}C NMR and UV spectroscopic data of alcohols **9f** and **9m** disclosed no differences (see Experimental Section).

Scheme V



9f **9m**

Careful study of ^1H NMR spectra at 400 MHz was of considerable help. In order to clarify the present discussion we have reported in Scheme V the Dreiding model representation of alcohols **9f** and **9m**.

The **9m** structure is the one obtained from X-ray diffraction experiments. Of course in solution, conformational equilibrium must be expected. However, our previous study on smaller membered rings showed that in solution the dominant conformation[28] was that found in the solid states. This starting hypothesis helped us to solve a puzzling artifact in the present work.

In alcohol **9f** H_1 corresponds to a pseudo triplet signal at 3.39 ppm in agreement with what is found for other benzocyclobutenols.

The methylene ketal protons (H_2–H_5) were assigned as follows: four quadruplets at 3.85, 3.91, 4.03, and 4.10 ppm with J = 6 Hz. In the corresponding resonance regions alcohol **9m** presents the following data: a quadruplet at 3.07 ppm, J = 7 Hz; a multiplet at 3.65 ppm; two quadruplets at 3.79 and 3.89 ppm, J = 7 Hz.

Irradiation at 3.07 ppm led to no decoupling in the saturated proton region but to a strong decoupling effect on the three other signals. Conversely, irradiation at 3.65 ppm led to a strong decoupling effect on the signals centered at 1.63 ppm which are attributable to H_6 and H_7 protons.

Coming back to the structure of **9m** (Scheme V) it appears that H_2 is situated in the shielding region of the aromatic ring. Approximate calculation from the data given by Elvidge[29] led us to expect a shielding effect of about 0.6 ppm relative to the position of H_2 in **9f**. The value actually found was 0.78 ppm. Moreover, the Dreiding model also showed that H_1 must be deshielded by the proximity of the endo oxygen ketal. Combination of these two effects led to the inversion of signals corresponding to H_1 and H_2 in **9m** compared to the corresponding signals in **9f**.

An identical irradiation study was done on each of the benzocyclobutenols **9h–m**.

The ^1H NMR data obtained for alcohols **9** (see Experimental Section) led to the following conclusions: the ring junctions are cis for the 5–8-membered ring derivatives and they are trans from 9–12.

In order to confirm these conclusions, nine-membered ring alcohol **9j** was studied by X-ray diffraction. As expected from NMR data, a trans junction was found.[27b]

The results given above may be rationalized: (i) a syn addition of benzyne on ketone enolates; (ii) a trans configuration for the ketone enolates of cyclic 1,2-diketone monoketals with ring size larger than eight.

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Table IV.[a] Physical Data for Benzocyclobutenols 9

compd	mp, °C (solv)[b]	IR (solv) ν, cm^{-1}	UV (MeOH) λ, nm (log ϵ)	^1H NMR (solv), δ	^{13}C NMR ($CDCl_3$), δ
9a	72 (PE)	(KBr) 3640–3000 [OH]	272 (3.3), 266.5(3.32), (260.5 (3.17)	(CCl_4) 0.78–1.98 (8 H, m, CH_2CH_3 with t at 1.07, J = 6.66 Hz, and s at 1.3, $CH_3\overline{COCH_2CH_2O}$), 2.96 (1 H, s, OH exchanged with D_2O), 3.26–4.06 (5 H, m, $\overline{COCH_2CH_2O}$, benzylic H), 7.06 (4 H, m, Ar H)	(arom C) 148.2, 145.6, 129.4, 127.4, 122.5, 121.9, (aliph C) 111.0 ($\overline{COCH_2CH_2O}$), 84.5 (COH), 65.7, 65.5 ($\overline{COCH_2CH_2O}$), 52.8 (benzylic C), 22.9, 20.4, 12.5 ($CH_3\overline{COCH_2CH_2O}$, CH_3CH_2)
9b	70 (pentane)	(KBr) 3640–3300 [OH]	272.5 (3.23), 266 (3.24), 260 (3.08)	(CCl_4) 1.31 (3 H, s, CH_3), 1.41 (3 H, s, CH_3), 1.51 (3 H, s, CH_3), 2.96 (1 H, s, OH exchanged with D_2O), 3.27–4.02 (4 H, m, $\overline{COCH_2CH_2O}$), 6.79–7.39 (4 H, m, Ar H)	(arom C) 153.6, 144.7, 129.4, 127.3, 122.0, 119.8, (aliph C) 111.8 ($\overline{COCH_2CH_2O}$), 86.6 (COH), 65.9, 64.2 ($\overline{COCH_2CH_2O}$), 52.9 (benzylic C), 25.4, 23.4, 20.8 (3 × CH_3)
9c	43 (PE)	(NaCl) 3660–3200 [OH]	273 (3.01) 267 (3.05), 261 (2.87)	(CCl_4) 0.80–2.11 (10 H, m, $CH_2CH_2CH_3$ with s at 1.4, $CH_3\overline{COCH_2CH_2O}$), 2.78 (1 H, s, OH exchanged with D_2O), 3.40–4.20 (5 H, m, $\overline{COCH_2CH_2O}$, benzylic H), 7.0–7.51 (4 H, m, Ar H)	(arom C) 147.5, 144.8, 128.5, 126.3, 121.9, 121.0, (aliph C) 110.6 ($\overline{COCH_2CH_2O}$), 84.5 (COH), 65.9 ($\overline{COCH_2CH_2O}$), 51.3 (benzylic C), 32.6, 22.0, 21.1, 15.4 ($CH_2CH_2CH_3$, CH_3)
9d	oil	(NaCl) 3700–3260 [OH]	273 (2.86), 267 (2.86), 260 (2.72)	(CCl_4) 1.09–2.09 (4 H, m, 2 × CH_2), 3.18–3.69 (8 H, m, OH exchanged with D_2O, benzylic H, with 2 s at 3.28 and 3.46), 6.88–7.41 (4 H, m, Ar H)	(arom C) 144.5, 143.7, 129.9, 128.0, 122.7, 122.4 (aliph C) 105.3 ($C(OMe)_2$), 88.3 (COH), 56.2 (benzylic C), 51.5, 48.8 ($C(OCH_3)_2$), 29.2, 23.7 (2 × CH_2)
9e	oil	(NaCl) 3660–3240 [OH]	274 (3.39), 267 (3.22), 260 (3.00)	(CCl_4) 0.76–2.36 (6 H, m, 3 × CH_2), 3.18–3.66 (8 H, m, benzylic H, OH exchanged with D_2O, with 2 s at 3.3 and 3.49, 2 × OCH_3), 7.00–7.54 (4 H, m, Ar H)	(arom C) 147.4, 144.7, 129.3, 127.5, 122.9, 122.1, (aliph C) 101.4 ($C(OCH_3)_2$), 82.3 (COH), 54.9 (benzylic C), 51.4; 49.0 ($C(OCH_3)_2$), 25.6, 22.4, 17.8 (3 × CH_2)
9f	oil	(NaCl) 3640–3220 [OH]	273 (3.23), 266 (3.25), 260 (3.07)	(Me_2SO)[a] 0.84–2.13 (6 H, m, 3 × CH_2), 3.28 (1 H, s, OH exchanged with D_2O), 3.39 (1 H, pseudo t, benzylic H), 3.85, 3.91, 4.03, 4.10 (4 H, 4 q, J = 6 Hz, $\overline{COCH_2CH_2O}$), 6.97–7.31 (4 H, m, Ar H)	(arom C) 145.9, 144.9, 129.6, 127.8, 122.8, 122.6, (aliph C) 111.5 $\overline{COCH_2CH_2O}$), 80.8 (COH), 65.8, 65.5 $\overline{COCH_2CH_2O}$), 54.3 (benzylic C), 28.3, 22.9, 17.6 (3 × CH_2)
9g	oil	(NaCl) 3700–3140 [OH]	274 (3.25), 267.5 (3.27), 261 (3.11)	(CCl_4) 1.02–2.31 (8 H, m, 4 × CH_2), 2.98–3.71 (8 H, m, with 2 s at 3.11 and 3.31, 2 × OCH_3, benzylic H, OH exchanged with D_2O), 6.82– 7.58 (4 H, m, Ar H)	(arom C) 147.0, 146.1, 128.7, 127.2, 123.2, 121.9, (aliph C) 103.7 ($C(OMe)_2$), 85.8 (COH), 58.5 (benzylic C), 50.0, 49.7 ($C(OCH_3)_2$), 32.8, 30.1, 26.9, 24.7 (4 × CH_2)
9h	oil	(NaCl) 3700–3140 [OH]	273 (3.39), 267 (3.40), 261 (3.28)	(Me_2SO)[a] 1.19–1.66, 1.74–2.14 (8 H, 2 m, 4 × CH_2), 3.33 (1 H, m, benzylic H), 3.52 (1 H, m, OH), 3.64–3.85, 3.90–4.05 (4 H, 2 m, $\overline{COCH_2CH_2O}$), 6.93–7.21 (4 H, m, Ar H)	(arom C) 146.5, 145.9, 129.1, 127.3, 122.3, 121.5, (aliph C) 112.3 ($\overline{COCH_2CH_2O}$), 85.4 (COH), 65.5 ($\overline{COCH_2CH_2O}$), 56.0 (benzylic C), 33.9, 29.3, 26.2, 24.5 (4 × CH_2)
9i	78 (PE)	(KBr) 3700–3140 [OH]	273 (3.25), 267 (3.26), 260.5 (3.11)	($CDCl_3$)[a] 1.22–1.95 (8 H, m, 4 × CH_2), 2.26 and 2.48 (2 H, dt and dq, J = 2 Hz, J = 12 Hz, CH_2), 3.25 (1 H, d, J = 12 Hz, benzylic H), 3.30 (1 H, m, OH exchanged with D_2O), 3.36 (1 H, m, $\overline{COCH_2CHHO}$), 3.77–3.86 (2 H, m $\overline{COCH_2CH_2O}$), 3.87–3.96 (1 H, m, $\overline{COCH_2CHHO}$), 7.00–7.31 (4 H, m, Ar H)	(arom C) 147.4, 146.2, 129.1, 127.0, 121.9, 121.2, (aliph C) 113.6 $\overline{COCH_2CH_2O}$), 85.1 (COH), 66.2, 63.7 $\overline{COCH_2CH_2O}$), 57.7 (benzylic C), 35.4, 28.5, 25.4, 24.1, 19.9 (5 × CH_2)
9j	140 (PE)	(KBr) 3700–3220 [OH]	273 (3.29), 267 (3.31), 261 (3.14)	(Me_2SO)[a] 1.00–2.04 (12 H, m, 6 × CH_2), 3.21 (1 H, q, J = 7 Hz, $\overline{COCHHCH_2O}$), 3.33 (1 H, m, OH), 3.64–3.95 (4 H, m, benzylic H, $\overline{COCHHCH_2O}$), 6.97–7.21 (4 H, m, Ar H)	(arom C) 149.1, 146.5, 129.2, 127.3, 121.6, (aliph C) 112.4 $\overline{COCH_2CH_2O}$), 83.9 (COH), 66.0, 65.0 $\overline{COCH_2CH_2O}$), 53.0 (benzylic C), 31.0, 30.5, 28.4, 27.0, 22.4, 18.7 (6 × CH_2)

Table IV (Continued)

compd	mp, °C (solv)[b]	IR (solv) ν, cm^{-1}	UV (MeOH) λ, nm (log ϵ)	^1H NMR (solv), δ	^{13}C NMR ($CDCl_3$), δ
9k	172 (EtOAc, PE)	(KBr) 3460 [OH]	274 (3.31), 267 (3.33), 261 (3.18)	($CDCl_3$)[a] 1.24–1.94, 2.08–2.28 (14 H, 2 m, 7 × CH_2), 2.58 (1 H, s, OH exchanged with D_2O), 3.33 (1 H, q, J = 7 Hz, 3.8–4.18 (4 H, m, benzylic H, $\overline{COCHHCH_2O}$), 7.06–7.48 (4 H, m, Ar H)	(arom C) 150.1 146.7, 129.7, 127.1, 122.1, 121.3, (aliph C) 113.0 ($\overline{COCH_2CH_2O}$), 84.9 (COH), 66.0, 65.0 ($\overline{COCH_2CH_2O}$), 48.8 (benzylic C), 33.3, 27.7, 26.7, 25.9, 25.6, 22.3, 19.2 (7 × CH_2)
9l	148 (EtOAc, PE)	(KBr) 3700–3200 [OH]	272.5 (3.29), 266 (3.31), 260 (3.16)	(Me_2SO)[a] 1.14–1.73, 1.83–1.95, 2.24–2.36 (16 H, 3 m, 8 × CH_2), 3.16 (1 H, q, J = 7 Hz, $\overline{COCHHCH_2O}$, 3.33 (1 H, s, OH), 3.69, 3.75–3.88 (4 H, 2 m, benzylic H, $\overline{COCHHCH_2O}$), 6.98–7.19 (4 H, m, Ar H)	(arom C) 149.2, 146.9, 129.4, 127.2, 121.8, 121.6, (aliph C) 112.5 ($\overline{COCH_2CH_2O}$), 85.4 (COH), 66.0, 64.8 ($\overline{COCH_2CH_2O}$), 48.9 (benzylic C), 32.8, 28.1, 27.5, 25.1, 24.5, 23.6, 23.2 (8 × CH_2)
9m	136 (PE)	(KBr) 3600–3300 [OH]	273.5 (3.24), 267 (3.27), 261 (3.09)	(Me_2SO)[a] 1.00–1.90 (18 H, m, 9 × CH_2), 3.07 (1 H, q, J = 7 Hz, $\overline{COCHHCH_2O}$), 3.33 (1 H, s, OH), 3.61–3.69 (2 H, m, benzylic H, $\overline{COCHHCH_2O}$), 3.79 (1 H, q, J = 7 Hz, $\overline{COCH_2CH_2O}$), 3.89 (1 H, m, $\overline{COCH_2CH_2O}$), 6.95–7.19 (4 H, m, Ar H)	(arom C) 148.8, 146.7, 129.3, 127.0, 121.6, (aliph C) 112.6 ($\overline{COCH_2CH_2O}$), 86.7 (COH), 65.9, 65.7 $\overline{COCH_2CH_2O}$), 49.2 (benzylic C), 34.4, 29.1, 27.6, 27.2, 24.8, 24.3, 23.3, 22.3 (9 × CH_2)

[a] Spectra recorded at 400 MHz. [b] PE = petroleum ether.

These two hypotheses appear reasonable, taking into account our previous results[6] and the literature data concerning the stereochemistry of cycloalkenes[30] and cyclic 1,2-diketones.[31]

However, we cannot completely exclude that for unknown reasons, benzocyclobutenols with cis junction were unstable and destroyed under the reaction conditions.

Conclusion. Arynic condensation of 1,2-diketone monoketal enolates appears to be a simple means for the synthesis of benzocyclobutenols which may be performed on a large scale. We are presently studying the chemical transformation of the alcohols thus prepared as well as the synthesis of corresponding benzocyclobutenols variously substituted on the aromatic ring. The results will be presented in further publications.

Experimental Section

General Methods. Melting points were determined on a Kofler melting point apparatus and are reported uncorrected. ^{13}C NMR spectra were recorded on a Burker WP 80 spectrometer and ^1H NMR spectra on a Perkin-Elmer R 12 B instrument at 60 MHz and on a Bruker AM 400 instrument at 400 MHz with Me_4Si as internal standard. Ultraviolet spectra were obtained with methanol solutions on a Beckman Model DK 2A instrument. Infrared spectra with NaCl film or KBr pellets were recorded on a Perkin-Elmer 580 instrument. Elemental analyses were performed by CNRS Laboratory (Vernaison) and by François M. (Strasbourg). Thin-layer chromatography was performed by using Kieselgel G (Merck) with a hexane–EtOAc mixture as eluent.

The silica gels used for liquid phase chromatography and flash chromatography were respectively Kieselgel 0.063 (0.2 mm) and Kieselgel 0.04 (0.063 mm). High-pressure liquid chromatography was carried out on a Waters PREP 500 chromatograph with a silica gel column. Analytical HPLC was performed in a Waters Model 6000 A instrument with a stainless steel column Merck Hibar RT 250-4 (Lichrosorb Si 60-5 μM). GLC analyses were carried out with a Girdel Model 300 instrument with a 15% SE-30 column (Chromosorb WDMCS).

Materials. Degussa sodamide was washed with appropriate solvents and finely ground with a mortar under solvent. Badische Anilin reagent-grade THF freshly distilled from a benzophenone–sodium couple and DME distilled on sodium, stored under sodium were used. Cycloalkanones (n = 5–8, 10, 12) were commercial, cycloundecanone was prepared from cyclododecanone by ring contraction via a Favorskii-type rearrangement following the literature procedure,[13a] and cyclononanone was prepared by monohydroboration of cyclononadiene[13b] followed by oxidation as described by Chandrasekaran and co-workers.[13c]

Preparation of Cycloalkanediones 4. (1) By SeO_2 Oxidation. The cyloalkanediones 4 (n = 6–8, 12) were prepared by oxidation of the corresponding cycloalkanone with selenium oxide.[12a] **(2) By the Two-Step Conversion of Cycloalkanone. General Procedure for α-Sulfenylation of Ketone.** To a mechanically stirred suspension of $NaNH_2$ (450 mM) in THF (50 mL) under a nitrogen atmosphere was added dropwise Et-$(OCH_2CH_2)_2OH$ (150 mM) in THF (20 mL), and the mixture was heated at 45 °C for 2 h. Ketone (100 mM) in THF (20 mL) was then added dropwise at the temperature indicated in the Table I and the mixture stirred for 2 h. After the mixture was cooled to 0 °C, dimethyl disulfide (100 mM) in THF (10 mL) was slowly added (0.5 h), and the reaction followed by GLC was complete at the end of the addition. The mixture was poured into ice and extracted with diethyl ether (3 × 100 mL). The combined extracts were washed with diluted HCl, water, and brine, then dried ($MgSO_4$), and filtered. Rotary evaporation left an oil, which was distilled or chromatographed on a silica gel column.

2-(Methylthio)cyclopentanone (3, n = 5): yield, 70%; bp 65–66 °C (5 mmHg) [lit.[32b] bp 84 °C (10.5 mmHg)]; the spectroscopic data obtained for this product were identical with those previously reported.[32a,32b]

2-(Methylthio)cyclohexanone (3, n = 6): prepared from 100 mM of cyclohexanone; yield, 90%; bp 85 °C (7 mmHg) [lit.[32b] bp 83 °C (7 mmHg)]; its spectroscopic data (IR, NMR) were identical with those described.[32]

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2-(Methylthio)cycloheptanone (3, n = 7): prepared from 100 mM of cycloheptanone; yield, 70%; bp 80–81 °C (4 mmHg) [lit.[32b] bp 91 °C (6 mmHg)]; IR (NaCl) 1695 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.16–2.44 (12 H, m, CH_2 with s at δ 2.00, SCH_3), 2.56–3.15 (m, 2 H).

2-(Methylthio)cyclooctanone (3, n = 8): prepared from 100 mM of cyclooctanone; yield, 86%; bp 98 °C (4 mmHg) [lit.[32b] bp 89 °C (2 mmHg)]; IR (NaCl) 1690 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 0.96–2.29 (14 H, m, CH_2 with s at δ 1.93, SCH_3), 2.50–3.11 (m, 2 H).

2-(Methylthio)cyclononanone (3, n = 9): prepared from 17 mM of cyclononanone; the yellow oil was chromatographed on a silica gel column (5% EtOAc in petroleum ether) to yield 76 % of an almost colorless oil; IR (NaCl) 1700 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.11–2.47 (16 H, m, CH_2 with s at δ 1.89, SCH_3), 2.56–3.24 (m, 2 H). Anal. Calcd for $C_{10}H_{18}OS$: C, 64.25; H, 9.95. Found: C, 64.46; H, 9.73.

2-(Methylthio)cyclodecanone (3, n = 10): prepared from 34 mM of cyclodecanone; the yellow oil was chromatographed on HPLC (5% EtOAc in petroleum ether) to yield 90 % of an almost yellow oil; IR (NaCl) 1700 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.20–2.40 (17 H, m, 7 × CH_2 with s at δ 1.95, SCH_3), 2.62–2.91 (2 H, m CH_2C=O), 3.63 (1 H, dd, J = 2 Hz, J = 11 Hz; C*H*(SMe)). Anal. Calcd for $C_{11}H_{20}OS$: C, 65.89; H, 10.39. Found: C, 65.95; H, 10.05.

2-(Methylthio)cycloundecanone (3, n = 11): prepared from 66 mM of cycloundecanone; purified by HPLC (5% EtOAc in petroleum ether); yield, 87%; mp 55 °C (petroleum ether); IR (NaCl) 1700 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.06–2.22 (19 H, m, 8 × CH_2 with s at δ 1.93, SCH_3), 2.47–2.76 (2 H, m, CH_2C=O), 3.33–3.64 (1 H, m, C*H*(SMe)). Anal. Calcd for $C_{12}H_{22}OS$: C, 67.10; H, 10.55. Found: C, 67.23; H, 10.34.

2-(Methylthio)cyclododecanone (3, n = 12): prepared from 25 mM of cyclododecanone; purified on HPLC (5% EtOAc in petroleum ether); yield, 95%; mp 59 °C (petroleum ether) [lit.[32a,b] mp 59 °C (MeOH)]; its spectroscopic data were identical with those previously reported.[32a,b]

General Procedure for the Conversion of 2-Methylthio Ketones 3 into the Corresponding Cycloalkanediones 4. A mixture of the α-methylthio ketone **3** (25 mM) and copper(II) chloride dihydrate/copper(II) oxide in the ratio of 50 mM/100 mM for the method I or 25 mM/50 mM for the method II in aqueous 1% acetone (100 mL) was stirred at the temperature and for the time indicated in the Table I. (Disappearance of the ketone was monitored by GLC or analytical HPLC.) The precipitate was filtered off through Celite, and the filtrate was concentrated under reduced pressure. Diethyl ether was added to the residue, and the resulting precipitate was filtered off. The concentrated filtrate was chromatographed or distilled to give the corresponding 1,2-dicarbonyl compound.

1,2-Cyclopentanedione (4, n = 5) was prepared on a 25 mM scale from 2-(methylthio)cyclopentanone (**3**, n = 5) by method I and purified by HPLC (30% EtOAc in petroleum ether): yield, 60%; IR (NaCl) 1650 (C=C), 1700 (C=O), 3300 cm^{-1} (OH); ^1H NMR (CCl_4) δ 2.20–2.67 (4 H, m, 2 × CH_2), 6.47–6.62 (1 H, m, C=CH), 6.93–7.36 (1 H, m, C=COH).

1,2-Cyclohexanedione (4, n = 6) was obtained from 25 mM of 2-(methylthio)cyclohexanone (**3**, n = 6) by method I and purified by chromatography (50% EtOAc in petroleum ether): yield, 80%; its spectroscopic data (IR, NMR) were identical with those of an authentic sample prepared by SeO_2.[12a]

1,2-Cycloheptanedione (4, n = 7) was prepared on a 25 mM scale from 2-(methylthio)cycloheptanone (**3**, n = 7) by the method II and purified by distillation: yield, 70%; bp 90–95 °C (7 mmHg) [lit.[31] bp 84–85 °C (2.5 mmHg)]; its spectroscopic data (IR, NMR) were identical with those of an authentical sample prepared by SeO_2 oxidation.[12a]

1,2-Cyclooctanedione (4, n = 8) was prepared on a 50 mM scale from 2-(methylthio)cyclooctanone (**3**, n = 8) by the method II and purified by distillation: yield, 87%; bp 85 °C (5 mmHg) [lit.[31] bp 59–60 °C (1.5 mmHg)]; its spectroscopic data were identical with those of an authentic sample prepared by SeO_2 oxidation;[31,12c] mp 169 °C (dioxime) [lit.[31] mp 170 °C].

1,2-Cyclononanedione (4, n = 9) was prepared on a 10 mM scale from 2-(methylthio)cyclononanone (**3**, n = 9) by the method I and purified by silica gel column (5% EtOAc in petroleum ether): yield, 70%; IR (NaCl) 1700 cm^{-1} (C=O), ^1H NMR (CCl_4) δ 1.19–2.10 (10 H, m, 5 × CH_2), 2.46–2.89 (4 H, m, 2 × CH_2C=O); mp 178 °C (dioxime) [lit.[31] mp 178 °C].

1,2-Cyclodecanedione (4, n = 10) was prepared on a 10 mM scale from 2-(methylthio)cyclodecanone (**3**, n = 10) by the method II and purified by silica gel column (5% EtOAc in petroleum ether): yield, 45%; IR (CCl_4) 1705 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.04–2.29 (12 H, m, 6 × CH_2), 2.37–2.91 (4 H, m, 2 × CH_2C=O); mp 190–192 °C (dioxime) [lit.[31] mp 190 °C].

In this reaction, the corresponding monomethylthio enol ether was too isolated: yield, 50%; IR (NaCl) 1690 (C=O), 1610 cm^{-1} (C=C); ^1H NMR (CCl_4) δ 1.02–2.75 (17 H, m, 7 × CH_2 with s at δ 2.13, SCH_3), 5.75 (1 H, t, J = 8.6 Hz, C=CH).

1,2-Cycloundecanedione (4, n = 11) was prepared on a 12.5 mM scale from 2-(methylthio)cycloundecanone (**3**, n = 11) by the method I and purified by silica gel column (5% EtOAc in petroleum ether): yield, 80%; IR (NaCl) 1715 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.04–2.02 (14 H, m, 7 × CH_2), 2.42–2.95 (4 H, m, 2 × CH_2C=O); mp 208 °C (dioxime) [lit.[31] mp 207 °C].

1,2-Cyclododecanedione (4, n = 12) was prepared on a 50 mM scale from 2-(methylthio)cyclododecanone (**3**, n = 12) by the method I and purified by silica gel column (5% EtOAc in petroleum ether): yield, 90%; mp 43 °C [lit.[31] mp 44 °C]; its spectroscopic data were identical with those described in the literature;[12c] mp 214 °C (dioxime) [lit.[31] mp 214 °C].

A Large-Scale Preparation of 1,2-Cyclododecanedione (4, n = 12). The α-(methylthio)cyclododecanone (**3**, n = 12) was prepared on the 500 mM scale as described above (addition of $Et(CH_2CH_2)_2OH$ and cyclododecanone 0.5 h). After the usual workup the residue was crystallized (petroleum ether) to yield 104 g, 91%, of **3**, mp 59 °C [lit.[32a,b] mp 59 °C]. To a mixture of $CuCl_2 \cdot 2\ H_2O$–CuO (0.9 M/1.8M; method I) in 800 mL of 1% aqueous acetone cooled by a water bath was added over 1 h the α-(methylthio)cyclododecanone (450 mM) diluted in 200 mL of 1% aqueous acetone. Then, the reaction mixture was stirred for 6 additional h at 35 °C. After decantation of the salts the supernatent liquid was filtered through a pad of Celite, concentrated, and filtered through a short column of silica gel (5% EtOAc in petroleum ether). Rotary evaporation left a mass which was distilled. **4** (n = 12): yield, 70.3 g, 80%; bp. 135 °C (6 mmHg) [lit.[31] bp 99–101 °C (1.5 mm Hg)].

General Procedure of Monoprotection of Cycloalkanedione 4. Formation of Ethylene Acetal (Method A or B). To a solution containing 100 mM of $BF_3 \cdot OEt_2$ in 100 mL of methylene chloride cooled at 5 °C by an ice bath (method A) or 100 mM of trimethylchlorosilane at 20 °C (method B) was slowly added a mixture containing 100 mM of cycloalkanedione **4** and 100 mM of ethylene glycol. After complete reaction (monitored by TLC or GLC), the solution was poured into water (200 mL) and extracted with methylene chloride (3 × 100 mL). The organic layer was washed with 50 mL of 10% sodium bicarbonate and 50 mL of water. After drying over magnesium sulfate, the solvent was removed in vacuo. The residue was distilled or separated on silica gel column.

Formation of Dimethyl Acetal (Method B). To a solution containing 100 mM of Me_3SiCl in 100 mL of MeOH was added 100 mM of cycloalkanedione **4** slowly at room temperature. After complete reaction (monitored by TLC), the solution was poured into water (200 mL) and extracted with ether (3 × 100 mL). The organic layer was washed with 50 mL of 10% sodium bicarbonate and 50 mL of water. After drying over magnesium sulfate, the solvents were removed in vacuo. The residue was distilled or chromatographed on silica gel column.

2,2-Dimethoxycyclopentanone (6, n = 5; R^1 = Me) was prepared by an oxidation of 30 mM of 2-(methylthio)cyclopentanone (**3**, n = 5) with thallium trinitrate (60 mM) in MeOH following a procedure described in the literature:[10c,d] yield, 56%; its spectroscopic data were identical with those described.[9]

2,2-Dimethoxycyclohexanone (6, n = 6; R^1 = Me) was prepared from cyclohexanedione (**4**, n = 6) by the method B: IR (NaCl) 1735 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.51–2.02 (6 H, m, 3 × CH_2), 2.22–2.64 (2 H, m, CH_2C=O), 3.20 (6 H, s, 2 × OCH_3); its spectroscopic data (IR, NMR) were identical with those described.[9]

2-Oxocyclohexane-1-spiro-2′-(1′,3′-dioxolane) (6, n = 6; $\overline{R^1R^1}$

= $(CH_2)_2$) was prepared from 100 mM of cyclohexanedione (**4**, n = 6) by the method A: IR (NaCl) 1730 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.30–2.00 (6 H, m, 3 × CH_2), 2.20–2.64 (2 H, m, CH_2C=O), 3.85 (4 H, m, $\overline{COCH_2CH_2O}$); bp 80 °C (3 mmHg) [lit.[10a] bp 115 °C (22 mmHg)].

2,2-Dimethoxycycloheptanone (6, n = 7; R^1 = Me) was prepared from 100 mM of cycloheptanedione (**4**, n = 7) by the method B: IR (NaCl) 1735 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.17–2.01 (8 H, m, 4 × CH_2), 2.22–2.63 (2 H, pseudo-t, CH_2C=O), 3.16 (6 H, s, 2 × OCH_3); bp 93 °C (7 mmHg). Anal. Calcd for $C_9H_{16}O_3$: C, 62.76; H, 9.36. Found: C, 62.57; H, 9.53.

2-Oxocycloheptane-1-spiro-2′-(1′,3′-dioxolane) (6, n = 7; $\overline{R^1R^1}$ = $(CH_2)_2$) was prepared from 100 mM of cycloheptanedione (**4**, n = 7) by the method B: IR (NaCl) 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.42–2.09 (8 H, m, 4 × CH_2), 2.27–2.71 (2 H, m, CH_2C=O), 3.92 (4 H, s, $\overline{COCH_2CH_2O}$); bp 105 °C (8 mmHg).

2-Oxocyclooctane-1-spiro-2′-(1′,3′-dioxolane) (6, n = 8; $\overline{R^1R^1}$ = $(CH_2)_2$) was prepared from 100 mM of cyclooctanedione (**4**, n = 8) by the method A: IR (NaCl) 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.10–1.19 (10 H, m, 5 × CH_2), 2.27–2.62 (2 H, m, CH_2C=O), 3.89 (4 H, s, $\overline{COCH_2CH_2O}$); bp 128 °C (8 mmHg). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.00; H, 8.97.

2-Oxocyclononane-1-spiro-2′-(1′,3′-dioxolane) (6, n = 9; $\overline{R^1R^1}$ = $(CH_2)_2$) was prepared from 10 mM of cyclononanedione (**4**, n = 9) by the method A: IR (NaCl) 1730 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.00–2.11 (12 H, m, 6 × CH_2), 2.27–2.62 (2 H, m, CH_2C=O), 3.55–4.04 (4 H, m, $\overline{COCH_2CH_2O}$).

2-Oxocyclodecane-1-spiro-2′-(1′,3′-dioxolane) (6, n = 10; $\overline{R^1R^1}$ = $(CH_2)_2$) was prepared from 7.7 mM of cyclodecanedione (**4**, n = 10) by the method A or from 9 mM of cyclodecanedione by azeotropic distillation in benzene–PTSA mixture: IR (NaCl) 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 1.26–2.11 (14 H, m, 7 × CH_2), 2.62 (2 H, pseudo-t, CH_2C=O), 3.73–4.04 (4 H, m, $\overline{COCH_2CH_2O}$).

2-Oxocycloundecane-1-spiro-2′-(1′,3′-dioxolane) (6, n = 11; $\overline{R^1R^1}$ = $(CH_2)_2$) was prepared from 25 mM of cycloundecanedione (**4**, n = 11) by the method B: IR (NaCl) 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 0.95–2.13 (16 H, m, 8 × CH_2), 2.35–2.77 (2 H, m, CH_2C=O), 3.55–4.05 (4 H, m, $\overline{COCH_2CH_2O}$). Anal. Calcd for $C_{13}H_{22}O_3$: C, 69.06; H, 10.04. Found: C, 68.99; H, 9.80.

2-Oxocyclododecane-1-spiro-2′-(1′,3′-dioxolane) (6, n = 12; $\overline{R^1R^1}$ = $(CH_2)_2$) was prepared from 25 mM of cyclododecanedione (**4**, n = 12) by the method B: IR (KBr) 1720 cm^{-1} (C=O); ^1H NMR (CCl_4) δ 0.84–1.99 (18 H, m, 9 × CH_2 with br s at δ 1.27), 2.36–2.69 (2 H, pseudo t, CH_2C=O), 3.47–4.07 (4 H, m, $\overline{COCH_2CH_2O}$). Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.96; H, 10.07. Found: C, 69.79; H, 10.03.

General Procedure for the Preparation of Benzocyclobutenols 9. Reactions were carried out with magnetic stirring under a nitrogen atmosphere and monitored by GLC analysis.

A solution of t-BuOH (50 mM) in THF (or DME) (10 mL) was added dropwise to a suspension of $NaNH_2$ (200 mM for the ratio **7**/**8** = 0.5/1 or 220 mM for the ratio **7**/**8** = 1.1/1) in THF or DME (30 mL), and the mixture was heated at 45 °C for 2 h; the ketone **4** (50 mM) diluted in THF (or DME) (10 mL) was added at room temperature, and the reaction mixture was stirred for 2 h. A solution of bromobenzene (25 mM for the ratio **7**/**8** = 0.5/1 or 55 mM for the ratio **7**/**8** = 1.1/1) in THF (or DME) (20 mL) was slowly added at the temperature and for the time indicated in the Table III. Upon completion, the mass was poured on ice, extracted with diethyl ether, washed twice with water, and dried over $MgSO_4$. After evaporation of the solvents under reduced pressure, the different components of the mixture were separated by chromatography on a silica gel column or by HPLC for benzocyclobutenol ethylene acetal and only by HPLC for benzocyclobutenol dimethylacetal. Spectral data and melting points for compounds **9** are given in Table IV.

Registry No. **2** (n = 5), 120-92-3; **2** (n = 6), 108-94-1; **2** (n = 7), 502-42-1; **2** (n = 8), 502-49-8; **2** (n = 9), 3350-30-9; **2** (n = 10), 1502-06-3; **2** (n = 11), 878-13-7; **2** (n = 12), 830-13-7; **3** (n = 5), 52190-34-8; **3** (n = 6), 52190-35-9; **3** (n = 7), 52190-36-0; **3** (n = 8), 52190-37-1; **3** (n = 9), 100703-64-8; **3** (n 10), 100703-65-9; **3** (n = 11), 100703-66-0; **3** (n = 12), 52190-38-2; **4** (n = 5), 3008-40-0; **4** (n = 6), 765-87-7; **4** (n = 7), 3008-39-7; **4** (n = 8), 3008-37-5; **4** (n = 9), 3008-36-4; **4** (n = 10), 96-01-5; **4** (n = 11), 3008-34-2; **4** (n = 12), 3008-41-1; **5**, 100703-67-1; **6** (n = 5; R^4 = Me), 66057-04-3; **6** (n = 6; R^1 = Me), 38461-13-1; **6** (n = 6; $\overline{R^1R^1}$ = (CH_2)), 4746-96-7; **6** (n = 7; R^1 = Me), 89874-31-7; **6** (n = 7; $\overline{R^1R^1}$ $(CH_2)_2$), 89874-32-8; **6** (n = 8; $\overline{R^1R^1}$ = $(CH_2)_2$), 89874-33-9; **6** (n = 9; $\overline{R^1R^1}$ = $(CH_2)_2$), 100703-68-2; **6** (n = 10; $\overline{R^1R^2}$ = $(CH_2)_2$), 100703-69-3; **6** (n = 11; $\overline{R^1R^1}$ = $(CH_2)_2$), 100703-70-6; **6** (n = 12; $\overline{R^1R^1}$ = $(CH_2)_2$), 89874-34-0; **7**, 108-86-1; **9a**, 89874-22-6; **9b**, 89874-23-7; **9c**, 100765-51-3; **9d**, 89874-24-8; **9e**, 100703-71-7; **9f**, 100789-70-6; **9g**, 100703-72-8; **9h**, 100703-73-9; **9i**, 100703-74-0; **9j**, 100703-75-1; **9k**, 100703-76-2; **9l**, 100703-77-3; **9m**, 100837-45-4; MeSSMe, 624-92-0; 2-methyl-2-butanoyl-1,3-dioxolane, 61784-38-1; 2-methyl-2-(2-methylpropanoyl)-1,3-dioxolane, 61784-40-5; 2-methyl-2-pentanoyl-1,3-dioxolane, 61784-39-2.

Selective Protection of Carbonyl Compounds. Silica Gel Treated with Thionyl Chloride as an Effective Catalyst for Thioacetalization

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Silica gel treated with thionyl chloride was found to be an effective as well as highly selective catalyst for thioacetalization of aldehydes. With the use of this catalyst 1,3-dithioranes and 1,3-dithianes were obtained in excellent yields from various aldehydes. Under the same conditions ketones were similarly but more slowly thioketalized. This difference in reactivity between aldehydes and ketones was successfully utilized for the thioacetalization of aldehydes in the presence of ketones and also for the chemoselective conversion of keto aldehydes into the corresponding dithioacetals with the keto group remaining intact.

Introduction

The protection of carbonyl groups as acetals or dithioacetals is now commonly used as an important synthetic technique in the course of preparation of many organic compounds including multifunctional complex molecules. For thioacetalization, a number of methods using protic acids, Lewis acids, and some silicon reagents have been developed so far.[1] However, a convenient and at the same time highly chemoselective thioacetalization method capable of discrimination between aldehydes and ketones has not yet been described in spite of its great importance and

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