a nitrogen atmosphere to the vigorously stirred solution. A small amount of CH_2Cl_2 was used to rinse the last traces of **2** into the reaction mixture. The mixture was stirred vigorously overnight and allowed to warm gradually to room temperature. The reaction was quenched by the addition of $NaHSO_3$ (10 g) and extracted with ether to remove any remaining ketone **2**. The aqueous solution was acidified to a Congo Red endpoint by the addition of 12 M HCl and extracted five times with 100 mL of CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and concentrated to yield 8.12 g (80% yield) of acid **1**: ^1H NMR ($CDCl_3$, 90 MHz) δ 1.6–2.1 (m, 2 H), 2.1–2.2 (m, allylic CH_3), 2.3–2.8 (m, 4 H); ^{13}C NMR ($CDCl_3$, 50.31 MHz) δ 16.6 (CH_3), 21.3 (C-4), 33.3 and 41.2 (C-3 and C-5), 126.9 (C-1), 159.3 (C-2), 172.2 (CO_2H). This material was generally used without further purification. Purification could be effected by chromatography with silica gel (ethyl acetate:hexane, 15:85) or by crystallization from a solution of slowly evaporating methylene chloride. Recrystallization from hexane or sublimation gives analytically pure material: mp 129.5–130.0 °C (lit.[3d] 129–130 °C).

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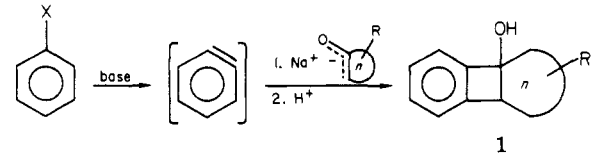
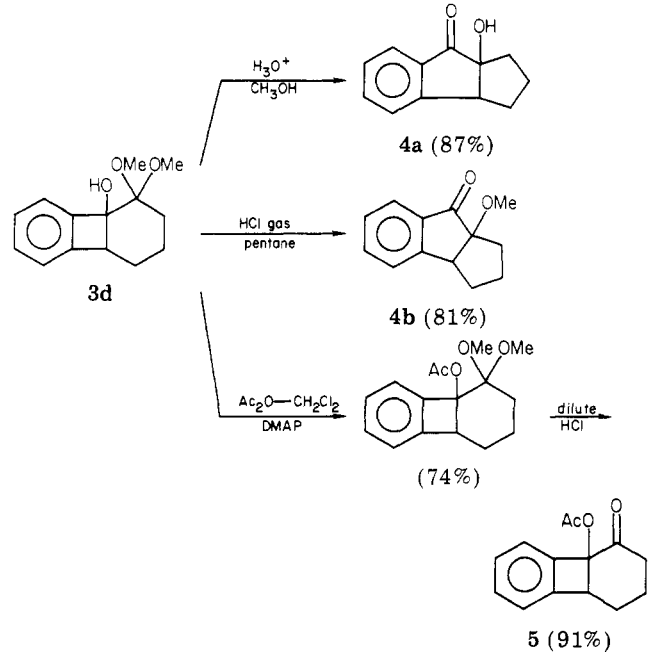
Registry No. **1**, 67209-77-2; **2**, 3168-90-9; $CH_3C(O)Cl$, 75-36-5; cyclohexane, 110-82-7.

Scheme I



1

Scheme II



Arynic Condensation of Ketone Enolates. 16.[1] Efficient Access to a New Series of Benzocyclobutenols

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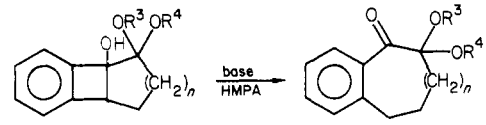
Benzocyclobutenes constitute an important family of starting materials for the synthesis of a large variety of very interesting polycyclic compounds,[2] and convenient access to these structures is always appreciated.

Our laboratory has been interested in the synthesis of benzocyclobutenes for some years and we have already published[3] that benzocyclobutenols **1** could be easily obtained through arynic condensations of ketone enolates (Scheme I).

However these reactions suffer from some limitations. Indeed with a few exception,[4] alcohols **1** were obtained only from cyclic ketone enolates for which $5 \leq n \leq 7$.[5] Linear ketone enolates never led to the desired alcohols with these conditions.

Scheme III



3d,f-i

6d, n = 2 (71%)
6e, n = 2 (83%)
6f, n = 3 (80%)
6g, n = 3 (96%)
6h, n = 4 (90%)
6i, n = 8 (90%)

As part of our program aimed at improving these results as well as at obtaining benzocyclobutenols bearing a function on the saturated ring, we undertook the study of arynic condensations of functionalized ketone enolates. We report here the first results obtained with 1,2-diketone monoketal enolates.

Preliminary experiments showed that instead of $NaNH_2$,[6] the complex base[7] $NaNH_2$–Bu-*t*-ONa must be used to generate the benzyne. The results obtained are grouped in Table I. Unexpectedly the presence of the ketal group dramatically favors the formation of the benzocyclobutenols **3** which were obtained, in good to excellent yields for medium sized cyclic ketone enolates **2c–h** as well as for a linear one (**2a**). With a large ring and a linear ketone enolate, **2i** and **2b** respectively, alcohols **3** were still formed

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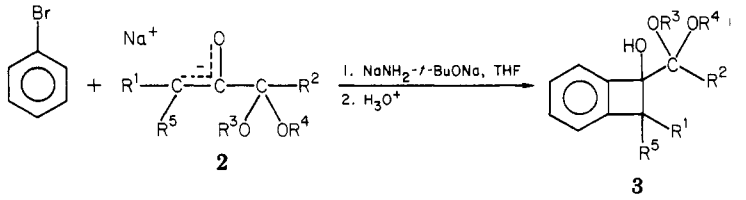
0022-3263/84/1949-2050$01.50/0

Table I



2 3

compd	R^1	R^2	R^3	R^4	R^5	t, h	yield of 3,[a] %
a	H	CH_3	$-(CH_2)_2-$		Et	24	85
b	CH_3	CH_3	$-(CH_2)_2-$		CH_3	17	40[b]
c	$-(CH_2)_2-$		CH_3	CH_3	H	2.25	75
d	$-(CH_2)_3-$		CH_3	CH_3	H	1	76
e	$-(CH_2)_3-$		$-(CH_2)_2-$		H	1	65
f	$-(CH_2)_4-$		CH_3	CH_3	H	2	92
g	$-(CH_2)_4-$		$-(CH_2)_2-$		H	0.75	85
h	$-(CH_2)_5-$		$-(CH_2)_2-$		H	1.75	93
i	$-(CH_2)_9-$		$-(CH_2)_2-$		H	5[c]	33[d]

[a] Yield of isolated alcohol **3** with respect to C_6H_5Br. [b] 10% of unreacted C_6H_5Br recovered and formation of an ethylenic alcohol in 14% yield. [c] Temperature of condensation: 0 °C. [d] Formation of corresponding benzocyclenedione in 33% yield.

but the yields have to be improved. The stereochemistry of the ring fusion of **3** has not yet been established. However, it is clear, from our preceding results,[3] that at least alcohols **3c–h** are certainly cis.

The chemical properties of these new alcohols have been briefly explored and the results obtained are very promising for further synthetic applications (Scheme II): for example, acidic treatment of **3d** led in protic solvent to transposed hydroxy indanone **4a**. On the contrary, under dry conditions alkoxy indanone **4b** was obtained. After acetylation of the hydroxyl group of **3d** the corresponding ketone **5** may be easily obtained. These derivatives constitute a good starting material for the synthesis of new benzocyclobutenols.

Finally we have shown that alcohols **1** were easily opened by bases to give the corresponding benzocyclenones.[8] With alcohols **3** this reaction led to the interesting monoprotected benzocyclenediones **6** (Scheme III).

Conclusion

From the above results, it appears that arynic condensation of 1,2-diketone monoketal enolates constitute a very simple pathway to a large family of benzocyclobutenols. The latter may be used as starting materials to easily obtain various interesting structures. Generalization as well as applications of these reactions are presently being intensively studied in our laboratory and will be the subject of further publications.

Experimental Section

Materials. Degussa powder sodamide was used. Badische Anilin reagent-grade THF was distilled from sodium and stored over sodium wire. *tert*-Butyl alcohol was distilled from sodium before use. Cycladiones[9] and monoketals of diketones[10] were prepared following procedures described in the literature.

2-Butyryl-2-methyl-1,3-dioxolane and 2-methyl-2-(2-methylpropionyl)-1,3-dioxolane were synthetized as described by Conia et al.[10a] 2,2-Dimethoxycyclopentanone was prepared by an oxidation of the 2-(methylthio)cyclopentanone with thallium trinitrate in MeOH following a procedure described in the literature.[10b] Its spectroscopic data (IR, NMR) are identical with those described.[10a]

1,4-Dioxaspiro[4,5]decan-6-one was obtained by following ref 10c.

2,2-Dimethoxycyclohexanone and 2,2-dimethoxycycloheptanone were prepared in 63% and 50% yield, respectively, as follows: To a solution of MeOH (30 mL) at room temperature through which was bubbled a slow stream of HCl was added simultaneously and dropwise a mixture of 100 mmol of diketone and 110 mmol of $HC(OCH_3)_3$. Completion of the reaction was followed by GLC. After usual workup, the diketone monoketal was chromatographed.

1,4-Dioxaspiro[4,6]undecan-6-one and 1,4-dioxaspiro[4,7]dodecan-6-one were obtained in 50% and 70% yield respectively, as follows: To a solution of CH_2Cl_2 (100 mL) and $BF_3{\cdot}Et_2O$ (6 mL) maintained at 5 °C were added simultaneously dropwise 100 mmol of diketone and 100 mmol of ethylene glycol. Completion of the reaction was monitored by TLC. After usual workup, the product was distilled.

1,4-Dioxaspiro[4,11]hexadecan-6-one was obtained in 55% as follows: Through a solution of diketone (38 mmol) and ethylene glycol (42 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL) was bubbled at room temperature a slow stream of HCl (to initiate the reaction). Stirring was continued for 24 h. After usual workup, the diketone monoketal was purified by chromatography.

General Methods. All products were characterized by analytical and spectral data, whose main characteristics will be given only for representative products. ^1H NMR spectra were recorded on a Perkin-Elmer R 12 B and ^{13}C NMR spectra on a Bruker W.P. 80 spectrometer, using Me_4Si as internal standard. Infrared spectra were obtained on a Perkin-Elmer R 457 instrument. UV spectra were carried out with a Beckman DK 2A spectrometer. GLC analyses were carried out with a Girdel 300 instrument with a 15% SE-30 column (Chromosorb WDMCS). TLC was carried out on silica gel Merck G, normally using cyclohexane–ethyl acetate. Column chromatography was run on silica gel Merck (0.05–0.2 mm), normally using light petroleum ether. For difficult separations, preparative LC 500 Waters instrument was used.

General Procedure for Arynic Condensation of 1,2-Diketone Monoketal Enolates (Table I). A typical experimental procedure was as follows: a solution of *t*-BuOH (50 mmol) in THF (10 mL) was added dropwise to a suspension of $NaNH_2$ (200 mmol) in THF (20 mL). The mixture was then heated for 2 h at 40–45 °C. After the mixture cooled, 2,2-dimethoxycyclo-

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hexanone (50 mmol) in THF (10 mL) was added dropwise and the mixture was stirred at room temperature for 2 h. Bromobenzene (25 mmol) in THF (10 mL) was then added and stirring was continued for 1 h. The mixture was poured into ice, extracted with diethyl ether, and dried over $MgSO_4$. After removal of the solvents under reduced pressure, the residual oil was chromatographed on HPLC preparative apparatus to yield **3d**.

3d: $C_{14}H_{18}O_3$; IR (film) 3660–3240 cm^{-1} (OH); UV (MeOH) λ nm (log ε) 274 (3.20), 267 (3.22), 260 (3.07), ^1H NMR (CCl_4) δ 0.76–2.36 (6 H, m, 3 × CH_2); 3.18–3.76 (8 H, m, with s at 3.32 and 3.49, 2 × OCH_3, benzylic H and OH, exchanged with D_2O), 7.00–7.56 (4 H, m, with br s at 7.24, Ar); ^{13}C NMR ($CDCl_3$) δ (aromatic carbons) 147.39, 144.73, 129.34, 127.52, 122.92, 122.13, (aliphatic carbons) 101.41 (>$C(OCH_3)_2$), 82.33 (ArCOH), 54.95 (ArCH), 51.37 and 49.01 (2 × OCH_3), 25.56, 22.41 and 17.81 (cyclic -CH_2).

3e: $C_{14}H_{16}O_3$; mp 94 °C (light petroleum); IR (CCl_4) 3640–3220 cm^{-1} (OH); UV (MeOH) λ nm (log ε) 273 (3.23), 266 (3.25), 260 (3.07); ^1H NMR (CCl_4) δ 0.93–2.31 (6 H, m, 3 × CH_2), 2.87 (1 H, br s, OH, exchanged with D_2O), 3.33–3.57 (1 H, pseudo t, benzylic H), 3.82–4.27 (4 H, m, >$\overline{COCH_2CH_2O}$); 6.96–7.39 (4 H, m with s at 7.16, Ar); ^{13}C NMR ($CDCl_3$) δ aromatic carbons 145.88, 144.97, 129.58, 127.77, 122.86, 122.62; aliphatic carbons 111.53 (>$\overline{COCH_2CH_2O}$); 80.82 (ArCOH), 65.79 and 65.55 (>$\overline{COCH_2CH_2O}$); 54.28 (ArCH), 28.35, 22.90 and 17.57 (cyclic CH_2).

3a: $C_{14}H_{18}O_3$; mp 72 °C (light petroleum); IR (KBr) 3600–3300 cm^{-1} (OH); UV (MeOH) λ nm (log ε) 272 (3.30), 266.5 (3.32), 260.5 (3.17), ^1H NMR (CCl_4) δ 0.78–1.98 (8 H, m, CH_2CH_3, with t at 1.07, J = 6.66 Hz, CH_2CH_3 and s at 1.30, CH_3), 2.97 (1 H, br s, OH, exchanged with D_2O), 3.20–4.04 (5 H, m, >$\overline{COCH_2CH_2O}$ and benzylic H), 7.06 (4 H, br s, Ar); ^{13}C NMR ($CDCl_3$) δ aromatic carbons, 148.24, 145.64, 129.40, 127.40, 122.49, 121.95; aliphatic carbons 111.05 (>$\overline{COCH_2CH_2O}$), 84.51 (ArCOH), 65.67 and 65.55 (>$\overline{COCH_2CH_2O}$), 52.83 (ArCH), 22.90, 20.36, 12.54 (CH_2, CH_3).

3b: $C_{14}H_{18}O_3$; mp 70 °C (pentane); IR (KBr) 3640–3300 cm^{-1} (OH); UV (MeOH) λ nm (log ε) 272.5 (3.23), 266 (3.24), 260 (3.09); ^1H NMR (CCl_4) δ 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, br s, OH, exchanged with D_2O), 3.27–4.02 (4 H, m, >$\overline{COCH_2CH_2O}$), 6.79–7.39 (4 H, m with br s at 7.07, Ar); ^{13}C NMR ($CDCl_3$) δ aromatic carbons 153.57, 144.73, 129.40, 127.34, 122.01, 119.83; aliphatic carbons 111.77 (>$\overline{COCH_2CH_2O}$), 86.33 (ArCOH), 65.91 and 64.22 (>$\overline{COCH_2CH_2O}$), 52.92 (ArCH), 25.44, 23.38 and 20.84 (CH_3).

Chemical properties of alcohols **3** are shown on one example, **3d** (Scheme II).

Reaction of 3d in Acidic Pentane. Through a solution of alcohol **3d** (500 mg, 2.14 mmol) in pentane (30 mL) was bubbled a slow stream of HCl. The reaction was instantaneous (monitored by TLC), and the mixture was poured into water and extracted with ether. The organic layer was then washed with a saturated solution of $NaHCO_3$, dried over $MgSO_4$, and evaporated under reduced pressure. A rapid filtration on column chromatography gave the keto ether **4b** (350 mg, 1.73 mmol; yield 81%): IR (film) 1715 cm^{-1} (C=O); UV (MeOH) λ nm (log ε) 295 (3.42), 249 (4.14); ^1H NMR (CCl_4) δ 0.97–2.47 (6 H, m, 3 × CH_2), 3.22 (3 H, s, OCH_3), 3.33–3.69 (1 H, m, benzylic H), 7.16–7.96 (4 H, m, Ar); CI mass spectrum (NH_3, pos), appropriate clusters at m/e 220 ($M + NH_4^+$), 203 ($M + H^+$).

Reaction of 3d in Acidic MeOH. The alcohol **3d** (500 mg, 2.14 mmol) was added to a mixture (50:50) of CH_3OH and dilute H_2SO_4 (30 mL). The reaction was instantaneous, and the mixture was worked up as above. After short chromatography, the keto alcohol **4a** was obtained (350 mg, 1.86 mmol; yield 87%): $C_{12}H_{12}O_2$; mp 84 °C (light petroleum); IR (film) 3660–3100 (OH), 1715 cm^{-1} (C=O); UV (MeOH) λ nm (log ε) 294 (3.39), 248 (4.14); ^1H NMR (CCl_4) δ 0.89–2.71 (6 H, m, 3 × CH_2), 3.31–3.62 (1 H, m, pseudo d, benzylic H), 4.24 (1 H, br s, OH, exchanged with D_2O), 6.98–7.78 (4 H, m, Ar).

Passage of 3d to 5. The acetate was prepared following a procedure described by Vorbrügger et al.[11] A mixture of alcohol **3d** (1.53 g, 6.5 mmol), acetic anhydride (760 mg, 7.5 mmol), and DMAP (1.125 g, 7.5 mmol) in CH_2Cl_2 (7 mL) was allowed to stand for 31 h at 25 °C. The solution was partitioned between ether and citric acid solution; the organic phase was washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and evaporated in vacuo. The residue was purified by chromatography: the ketal acetate was eluted (1.33 g, 4.82 mmol; yield 74%): IR (film) 1740 cm^{-1} (C=O); UV (MeOH) λ nm (log ε) 274 (3.27), 267.5 (3.29), 261.5 (3.13); ^1H NMR (CCl_4) δ 0.91–2.38 (9 H, m, 3 × CH_2, with s at 1.98, $OCOCH_3$), 3.18 and 3.31 (6 H, 2 s, 2 × OCH_3) 3.74–4.11 (1 H, m, benzylic H), 6.87–7.44 (4 H, m, Ar).

The ketal acetate (1.23 g, 4.46 mmol) in acetone (20 mL) and few drops of dilute HCl led to keto acetate **5** (930 mg, 4.04 mmol; yield 91%): $C_{14}H_{14}O_3$; IR (film) 1740–1715 cm^{-1} (C=O); UV (MeOH) λ nm (log ε) 275 (3.35), 268.5 (3.36), 263.5 (sh, 3.21); ^1H NMR (CCl_4) δ 1.04–2.56 (9 H, m, 3 × CH_2 with s at 2.04, $OCOCH_3$), 3.69–3.98 (1 H, m, benzylic H), 6.98–7.54 (4 H, m, Ar).

General Procedure for the Ring Opening of 3 (Scheme III). Typically, **3d** (1 mmol) in 10 mL of HMPA was added to a suspension of $NaNH_2$ (2 mmol) in 10 mL of HMPA at room temperature. After 15 min, the reaction was complete; classical workup and column chromatography yielded ketone **6d**.

6d: $C_{14}H_{18}O_3$; IR (film) 1715 cm^{-1} (C=O); UV (MeOH) λ nm (log ε) 244 (sh, 3.19); ^1H NMR (CCl_4) δ 1–2.13 (6 H, m, 3 × CH_2), 2.36–2.82 (2 H, m, benzylic CH_2), 3.16 (6 H, s, 2 × OCH_3), 6.86–7.36 (4 H, m, Ar).

6e: $C_{14}H_{16}O_3$; mp 78 °C (ethyl acetate–light petroleum); IR (KBr) 1720 cm^{-1} (C=O); UV (MeOH) λ nm (log ε) 245 (sh, 3.25); ^1H NMR (CCl_4) δ 1.41–2.11 (6 H, m, 3 × CH_2), 2.51–2.89 (2 H, m, benzylic CH_2), 4.00 (4 H, s, >$\overline{COCH_2CH_2O}$), 6.89–7.51 (4 H, m, Ar).

Acknowledgment. This work was partly supported by INSERM (Contract No. 81 3005). M.C.C. gratefully acknowledges the INSERM for financial support.

Registry No. **2a**, 61784-38-1; **2b**, 61784-40-5; **2c**, 66057-04-3; **2d**, 38461-13-1; **2e**, 4746-96-7; **2f**, 89874-31-7; **2g**, 89874-32-8; **2h**, 89874-33-9; **2i**, 89874-34-0; **3a**, 89874-22-6; **3b**, 89874-23-7; **3c**, 89874-24-8; **3d**, 89874-25-9; **3e**, 89874-26-0; **3f**, 89874-27-1; **3g**, 89874-28-2; **3h**, 89874-29-3; **3i**, 89874-30-6; **4a**, 89874-35-1; **4b**, 89874-36-2; **5**, 89874-38-4; **6d**, 88021-68-5; **6e**, 89874-39-5; **6f**, 89874-40-8; **6g**, 89874-41-9; **6h**, 89874-42-0; **6i**, 89874-43-1; PhBr, 108-86-1; $NaNH_2$, 7782-92-5; *t*-BuOH·Na, 865-48-5; benzyne, 462-80-6; 8b-acetoxy-1,1-dimethoxy-1,2,3,4,4a,8b-hexahydrobiphenylene, 89874-37-3; 2-(methylthio)cyclopentanone, 52190-35-9; 1,2-cyclohexanedione, 765-87-7; 1,2-cycloheptanedione, 3008-39-7; 1,2-cyclooctanedione, 3008-37-5; 1,2-cyclododecanedione, 3008-41-1.

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Construction of the Hibaene Skeleton by way of an Abnormal Wolff Reaction

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In connection with a diterpene synthesis problem, a pimaradiene with an acetic acid moiety in place of its vinyl group was needed as starting material. As a consequence it was decided to degrade the 13β-vinyl side chain to a carboxylic acid unit and to carry out a homologation by the standard Arndt–Eisert synthesis. As the following discussion illustrates, an unusual result was obtained.

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