THE JOURNAL OF Organic Chemistry®

VOLUME 40, NUMBER 20

OCTOBER 3, 1975

Arynic and SNAr Reactions of Polyhalogenobenzenes. IV.[1,2] Condensation of Ketone Enolates

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Received January 28, 1975

Condensations of aliphatic or alicyclic ketone enolates with miscellaneous dialkylaminochlorobenzenes in the presence of base and in aprotic media lead, chiefly, to corresponding amino chloro phenyl ketones and benzocyclobutenols. Relative ratios of these last two products depend mainly on experimental conditions and on the relative substituent positions in the starting halo compounds. In two cases, benzofuran formation, in low yields, is observed. Ring opening by bases of benzocyclobutenols thus synthesized was briefly studied. In all these reactions arynes seem to be the major reaction intermediates.

It is well known that condensations of amines with 1,2,4- and 1,2,3-trichlorobenzene as well as with dialkylaminochlorobenzenes, in the presence of bases, involve arynic (EA) and/or SNAr mechanisms.[2]

On the other hand, we have also shown that ketone enolates condense with arynes in aprotic media to lead to aromatic ketones, and, in some cases, to benzocyclobutenols.[3]

The results thus obtained prompted us to study the condensation of ketone enolates with some dialkylaminodichlorobenzenes. Our purpose was to investigate the behavior of these polyhalogeno compounds in these reactions and to synthesize some new derivatives with substituents on the aromatic ring, the properties of which we wanted to study. The present paper discloses the results obtained.

I. Condensation of Ketone Enolates with *N,N*-Diethylamino-3,4-dichlorobenzene. A. Condensation of Alicyclic Ketone Enolates. Scheme I gives a general summary of the results obtained in this series of reactions.

In fact, the results are much less complex than it might at first seem. By varying experimental conditions, it is possible to make these reactions fairly selective, and we report in Table I the essential results.

From this set of results, we can make some general remarks. Obviously, under our basic conditions, the chloro derivative **1** is converted into the aryne **7**.[2]

After the ketone enolate condensation, one obtains compounds **3**, **4**, and **5**, a result in agreement with our previous work.[2,3] The formation of the benzofurans **6** can be attributed only to further reaction, in basic medium, of the ketones **3**. We shall see in the next paper that this hypothesis is verified and that the "side" reaction (here) is in fact a good approach to the heterocycles **6**.

From Table I and from a systematic study, the following essential features can be pointed out.

Scheme I

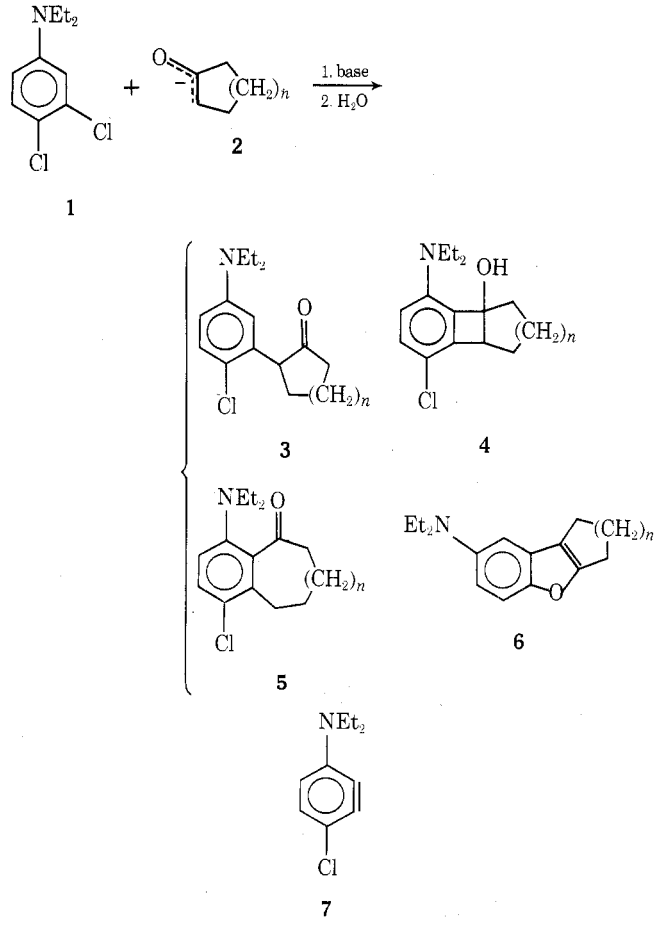
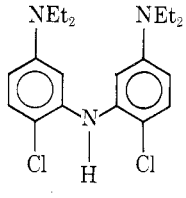


Table I
Condensation of Ketone Enolates 2 with *N,N*-Diethylamino-3,4-dichlorobenzene (1) in THF (Unless Otherwise Mentioned) in the Presence of a Base

No.	*n*	Temp, °C	Time, hr	Base	3, % [a]	4, % [a]	5, % [a]	6, % [a]	Total yield, % [b]
1	1	−15	16	Complex base[c]	88	5	7		85
2	1	22	2	Complex base	61-80	26-10	13-8		80-90
3	1	45-50	1.25	Complex base	63		37		90
4	2	25	7	Complex base	100				77
5	2	45	2	$NaNH_2$	87			13	61
6	3	−10	40	Complex base	45	55			70
7	3	55	1.25	Complex base	18	82			80
8	4	20	4	Complex base	54	46			70
9	4	48	1.25	Complex base	80	20			70
10[d]	4	40-45	2	Complex base	75			25	50

[a] Relative ratios as determined by VPC analysis. [b] Yields obtained after column chromatography of the crude product. [c] For a general review on complex bases, see ref 5. [d] The reaction solvent is DME.

(1) Amine formation, issuing from NH_2^- condensation, is sometimes observed.



(2) The use of the complex base $NaNH_2$–*t*-BuONa[5] often leads to greater total yields than does the use of $NaNH_2$ alone; however, this difference is markedly apparent only for n = 1 and 4.

(3) These condensations are a good approach to the aryl ketones **3** but not to the benzocyclenones **5**; however, the latter are sometimes accessible by ring opening of the alcohols **4** (see below).

As for the formation of the alcohols **4**, some marked differences are observed in comparison with the nonsubstituted arynes. Thus, for n = 1, yields are markedly better than those obtained with benzyne itself.[4] (Note: with n = 1 and below 20° the reactions are not always completely reproducible.) In contrast, with n = 2, it has not been possible to synthesize the corresponding alcohol, whereas it is obtained with a 45% yield in the nonsubstituted series.[4] This result does not seem due to some instability of the corresponding alcoholate, but rather to the fact that cyclization does not take place. A temperature lowering, indeed, only stops the condensation [without the appearance of **4** (n = 2)] and a temperature increase only leads to formation of the benzofuran **6** (n = 2) at the expense of **3**.

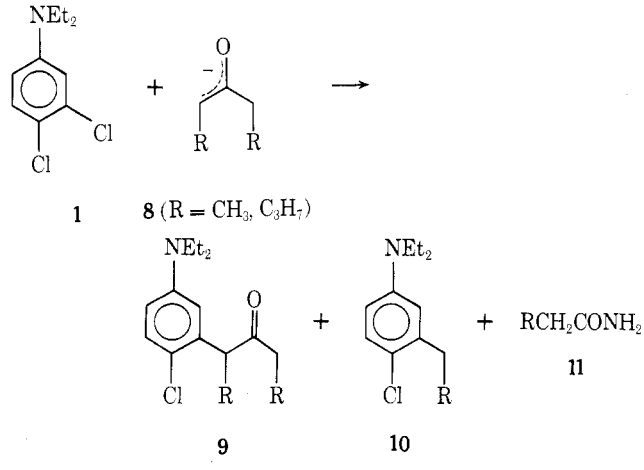
In the case where n = 3, observations are much the same as for those described for n = 2 in the nonsubstituted series[4] for which, in THF medium, only formation of the alcohol **4** is observed. Here, it has been impossible to avoid some formation of the ketone **3** (n = 3).

Lastly, with n = 4, we could never prove the existence of a benzocyclobutenol from benzyne itself.[6] Here, contrary to what we expected, the alcohol **4** (n = 4) can be obtained with a satisfactory yield.

For the moment, we have no ready rational explanation concerning these different observations. However, one point needs to be emphasized: after cyclization occurs, the alcoholates corresponding to **4** should be more stable than the unsubstituted ones.

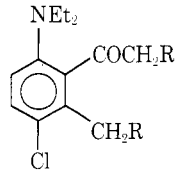
This led us to think that this particular stabilization could perhaps enable us to prepare benzocyclobutenols from aliphatic ketones, a reaction that is not possible with benzyne itself.[7] We shall see below that this hope has been only partially fulfilled.

Scheme II



B. Condensation of Aliphatic Ketone Enolates. Linear ketones condense with **1** according to the reaction of Scheme II.

Amide **11** and chloroaniline **10** are always obtained in equivalent quantities. These derivatives originate from a Haller–Bauer splitting,[8] met before in several cases.[3,9] We shall see in the next paper that the ketone **9**, put again into the reaction medium, undergoes no splitting. Thus we think that **12** is the degradate ketone (we never have been able to isolate it).



12

Various experiments showed us that the condensation results are not markedly dependent on the nature of the base used ($NaNH_2$ or $NaNH_2$–*t*-BuONa), nor on the solvent (THF or DME). We record the best two results we have obtained.

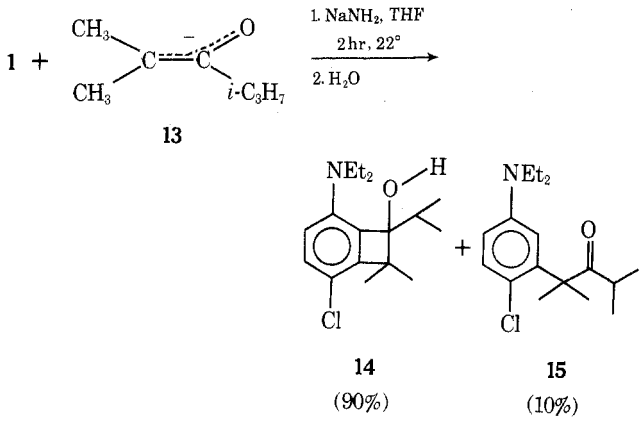
(1) With R = CH_3, in DME, and in the presence of $NaNH_2$–*t*-BuONa an 85% total yield is reached, with a ratio **9**:**10** = 65:35 (25°, 1 hr).

(2) With R = Pr, in THF and in the presence of $NaNH_2$

or $NaNH_2$–*t*-BuONa, an 80% total yield is reached, with **9:10** = 60:40 (25°, 2 hr).

The condensation of diisopropyl ketone enolate (Scheme III) leads to a quite different result shown in Scheme III.

Scheme III



total yield 60%

The temperature and the nature of the base have little effect upon the total yield and the ratio **14:15.**

The high proportion of alcohol **14** is certainly a consequence of the presence of the *gem*-dimethyl group which favors small ring closure and of the fact that the corresponding alcoholates should be particularly stable.

II. Condensation of Ketone Enolates with Various Aminochlorobenzenes. Taking into account the large variety of aminochloroaromatic compounds previously obtained,[2] it is clear that the applications of the condensations described above could lead to a large number of new products. As this kind of work offers no wide interest from a fundamental basic point of view, we limited ourselves to some typical condensations, in order to examine the generality of the method.

The Case of Morpholino-3,4-dichlorobenzene. Condensations of cycloheptanone and diisopropyl ketone enolates lead to the following results (Scheme IV).

It clearly appears that changes of substituents on the nitrogen atom do not modify the results obtained above, which can be considered as general.

The Case of Diethylamino-3,5-dichlorobenzene. Here we have modified the relative positions of the chlorine atom and the amino group. The results are summarized in Scheme V.

Qualitatively, the results agree with those we have described above; however, the propensity for benzocyclenol formation is much smaller. This may be due to several factors.

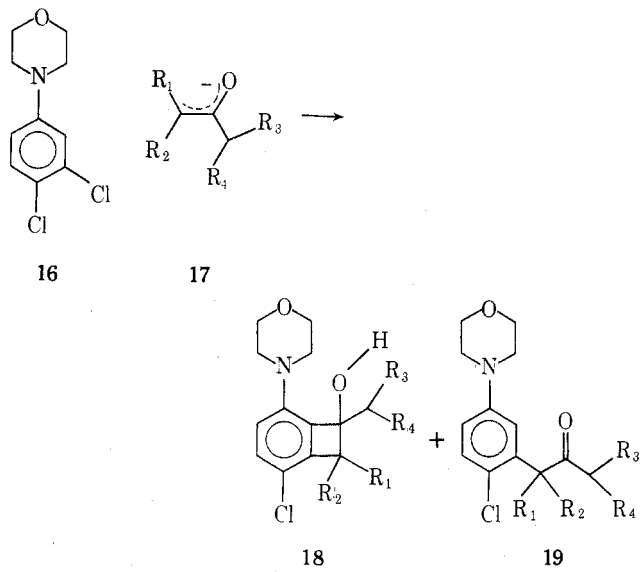
(1) A SNAr reaction may be involved in the formation of **22,** which precludes, of course, any subsequent cyclization.

(2) The stability of alcoholates corresponding to **21** is lower. This is particularly clear from examination of the nature of the products formed from diisopropyl ketone enolate. No alcohol is observed, but rather a transposed ketone **23,** coming from the intermediate alcoholate.

Furthermore, in the case of diisopropyl ketone, a new side reaction appears, namely, the condensation of the enolate with the product of Haller–Bauer splitting, **24,** leading to the alkylamino ketone **25.**

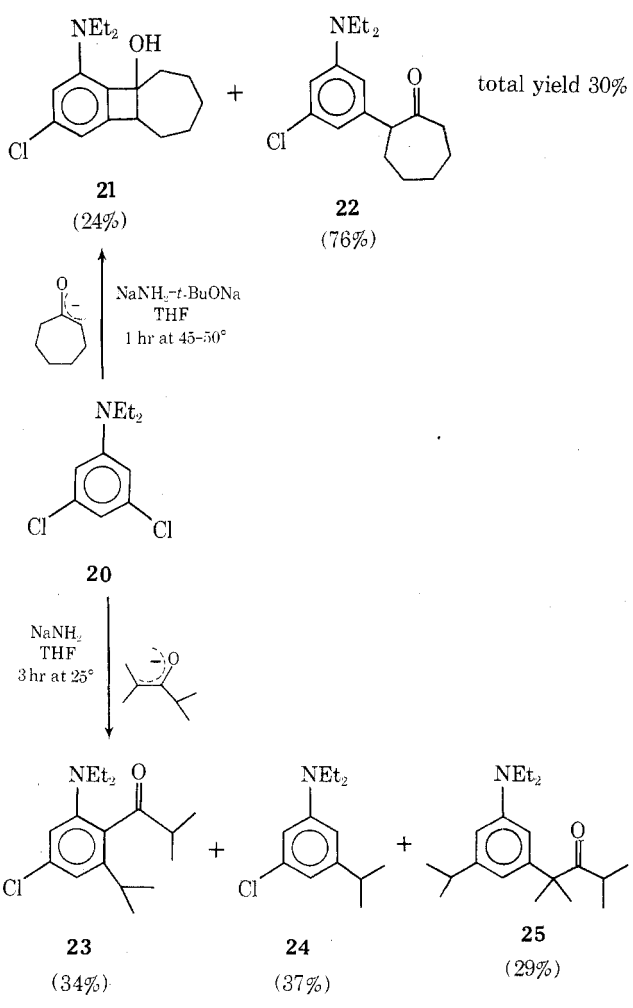
The Case of *N,N,N′,N′*-Tetraalkyl-1,3-diamino-4-chlorobenzene. We have condensed cycloheptanone (the ketone showing the greatest tendency to lead to benzocyclobutenols) with two amines of this type. The only observed reaction is depicted in Scheme VI.

Scheme IV



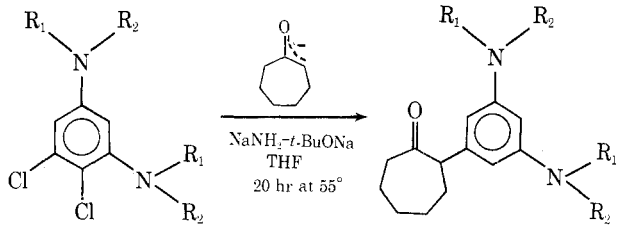
	Relative ratios, % 18	19	Total yield, %
$R_1 = R_3 = H$; $R_2, R_4 = (CH_2)_4$	80	20	80
$R_1 = R_2 = R_3 = R_4 = CH_3$	95	5	55

Scheme V



total yield 68%

Scheme VI



26

$R_1 = R_2 = Et$

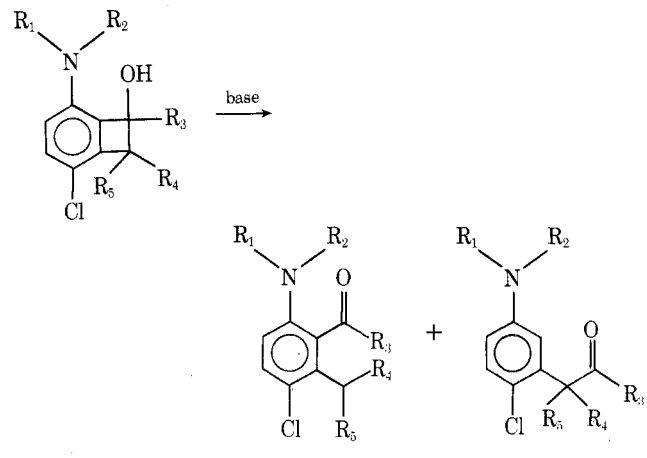
$R_1, R_2 = (CH_2CH_2)_2O$

27

28

yield 75-83%

Scheme VII



29 30

An arynic pathway is followed, certainly, but the keto anion formed shows no propensity for cyclization.

Whatever the aminochlorobenzenes studied, condensation products of ketone enolates are always the result of one or several reactions described in Scheme I of the present work.

Taking into account the great number of parameters we cannot control for the moment, the nature of the product(s) formed and, much less, their relative ratios are not easy to predict.

III. Ring Opening of Benzocyclobutenols 4, 14 and 18 by Bases. In previous work[10] we have shown that benzocyclobutenols are opened by the action of bases, to lead to "normal" ketones **30** or "transposed" ketones **29** or their mixture.

We have subjected some of the alcohols described in the present work to the action of bases, in order to determine the reactivity of the new alcohols. Moreover, these reactions should allow us to obtain by an unequivocal way the ketones isolated from the arynic condensation, and, thus, complete their structural assignment. The results are given in Scheme VII and Table II.

the substituents on the aromatic ring. Therefore, in the present state of our knowledge, we can give no consistent explanation for our results.

Practically, this short study shows that the ring opening of these alcohols leads to transposed ketones (particularly benzocyclenones), which were not accessible by direct condensations. These ring openings enable us, too, to increase the yields of "normal" phenyl ketones obtained in the direct condensation. We shall see in the next paper that the latter are interesting starting materials.

Structural Elucidation. Taking into account the reactivity of 1,[2] the alcohols 4 can correspond to the structure shown in Scheme I only. This structure is confirmed by the aromatic part of the NMR spectrum (AB, J = 8–9 Hz) and by the ring opening in basic medium of the alcohols, leading to the α-phenylated ketones 3. The structure of the latter is determined, too, long-range irradiation at the level of

Table II
Ring Opening in Basic Medium of Benzocyclobutenols 4, 14, and 18 in HMPA and DME

Run	R_1	R_2	R_3	R_4	R_5	Solvent	Base	Temp, °C	Time, hr	Total yield, %	30, %	29, %
11	Et	Et	$(CH_2)_3$		H	HMPA	$NaNH_2$	25	1	80	100	0
12	Et	Et	$(CH_2)_3$		H	DME	NaH	25	2	80	0	100
13	Et	Et	$(CH_2)_5$		H	HMPA	$NaNH_2$	25	2	80	100	0
14	Et	Et	$(CH_2)_5$		H	DME[a]	NaH	50[a]	3	85	100	0
15	Et	Et	$(CH_2)_6$		H	HMPA	NaH	25	1	70	0	100
16	Et	Et	*i*-Pr	CH_3	CH_3	HMPA	$NaNH_2$	25	4	95	75	25
17	Et	Et	*i*-Pr	CH_3	CH_3	DME[a]	$NaNH_2$	50[a]	0.5	85	79	21
18	OC_4H_8		$(CH_2)_5$		H	HMPA	$NaNH_2$	25	2.5	80	75	25
19	OC_4H_8		*i*-Pr	CH_3	CH_3	HMPA	$NaNH_2$	25	2	90	55	45
20	OC_4H_8		*i*-Pr	CH_3	CH_3	DME[a]	$NaNH_2$	50[a]	0.6	80	95	5

[a] The ring opening does not occur at room temperature.

It is clear that the behavior of these alcohols is different from that which we have seen with the alcohols lacking substitution on the aromatic ring.[10] With the latter, indeed, HMPA greatly favors ring opening to give "transposed" ketones, whereas in the present work, run no. 15 excepted, the reverse is observed. On the other hand, if polarity of the solvent is decreased, the direction of the ring opening becomes strongly dependent on the nature of the starting alcohol. Let us remember that, in the nonsubstituted series, an increased yield of the "normal" ketone is observed.

The discussion we have given previously[10] about the direction of the ring opening of alcohols shows that many factors may be involved. Moreover, we have here the effects of the methylenes of the diethylamino groups always showing a sharpening of the signals of two aromatic protons (ortho and ortho').[2]

The structure of the transposed ketones 5 is deduced from that of the alcohols 4, taking into account the ring cleavage reaction of the latter.

Conclusion

The present work shows that the observed reactions are satisfactorily explained by the mechanisms established previously, but that substitution in the aromatic ring brings some marked differences in the stability and the reactivity of the products formed, particularly for the benzo-

cyclobutenols. Moreover, we have observed, in two cases, the formation of small amounts of benzofurans.

We shall show in the next paper that the arylation products we have obtained here can be readily cyclized into aminobenzofurans, by what will be a new route to these heterocycles.

Experimental Section

Ir spectra were recorded with a Perkin-Elmer R-457 spectrophotometer; NMR spectra were carried out with Bruker HX 90 MHz, Varian A-60, or Jeol C-60 HL instruments. Chemical shifts are given in 10^{-6} δ units with respect to Me_4Si as internal standard. Analytical VPC analyses were carried out at 220° with a Carlo Erba GI 452 instrument, flame ionization detector, and SE-30 15% column (Chromosorb W DMCS). The silica gels used for liquid phase and thin layer chromatography were Kieselgel 0.05–0.2 mm and Kieselgel G (Merck), respectively, unless otherwise stated. Eluents were petroleum ether (bp 45–60°)–ether mixtures. We used Fluka brocken sodium amide, washed several times and ground in a mortar, under solvent. All reactions were carried out under a nitrogen atmosphere. Melting points are noninstantaneous and uncorrected.

All new compounds have satisfactory carbon, hydrogen, nitrogen and chlorine microanalyses and infrared spectra which were submitted to referees.

General Procedure. Reaction times and temperatures are indicated in Tables I and II and Schemes III, IV, VI, and VII. Reactions were carried out with magnetic stirring.

Reactions Carried Out in the Presence of the Complex Base $NaNH_2$–*t*-BuONa. To a suspension of $NaNH_2$ (125 mmol) in THF (30 ml), was added, dropwise, a solution of *t*-BuOH (25 mmol) in THF (10 ml); the mixture was heated at 40° for 2 hr; the ketone (50 mmol) in solution in THF (10 ml) was added at room temperature, and the mass was heated at 35–40° for 2 hr. To the mixture thus obtained, heated at the desired temperature, was added a solution of the halogenobenzene derivative (18 mmol) in THF (10 ml). After the end of the reaction, the mass was poured onto ice, extracted with ether, and dried over K_2CO_3. After evaporation of the solvents under reduced pressure, the different components of the mixture were separated by chromatography through a silica gel column (unless otherwise stated).

Reactions Carried Out in the Presence of $NaNH_2$. To a suspension of $NaNH_2$ (100 mmol) in THF (40 ml) the ketone (50 mmol) dissolved in THF (10 ml) was added at room temperature, and the mass was heated at 35–40° for 2 hr. The mixture was heated to the desired temperature and the halogeno derivative (18 mmol) dissolved in THF (10 ml) was added dropwise. After the end of the reaction, the mass was poured onto ice, etc. (see above).

Condensation of Ketone Enolates (50 mmol) with 1 in the Presence of a Base. Condensation of Cyclopentanone Enolates. The reaction mixture was fractionated by means of chromatography through a column filled with a 1:1 mixture of neutral alumina–silica gel. The following products were isolated successively.

5 (n = 1): NMR (CCl_4) 0.94 (t, J = 7 Hz, 6 H), 2.45 (m, 2 H), 2.92 (6 H, multiplet, including a q, J = 7 Hz), 1.72 ppm (4 H, multiplet); aromatic protons, AB spectrum, 6.87 (d, J = 9 Hz, 1 H), 7.20 ppm (d, J = 9 Hz, 1 H).

3 (n = 1): NMR ($CDCl_3$) 1.09 (t, J = 7 Hz, 6 H), 2.70–1.50 (6 H, multiplet), 3.00–3.60 ppm (5 H, multiplet including a quartet at 3.23, J = 7.5 Hz); aromatic H's, ABX spectrum, 7.03 (d, J = 8.75 Hz, 1 H), 6.40 (dd, J = 8.5, 3.0 Hz, 1 H), 6.24 ppm (d, J = 3.0 Hz, 1 H). Irradiation at 3.23 ppm results in the sharpening of the dd (6.40) and the d (6.24).

4 (n = 1): mp 122–123°; NMR ($CDCl_3$) 1.11 (t, J = 7 Hz, 6 H), 1.20–2.25 (6 H, multiplet), 3.38 (6 H, multiplet, becoming a 5 H after addition of D_2O), 3.38 ppm (q, J = 7 Hz); aromatic H's, AB spectrum, 6.30 (d, J = 9 Hz, 1 H), 6.99 ppm (d, J = 9 Hz, 1 H).

Condensation of Cyclohexanone Enolate. By means of chromatography through a silica gel column, the following products were isolated successively.

6 (n = 2): mp 25–26°; NMR ($CDCl_3$) 3.22 (q, J = 7 Hz, 4 H), 1.07 (t, J = 7 Hz, 6 H), 2.40–2.80 (4 H, multiplet), 1.65–2.0 ppm (4 H, m); aromatic H's, ABX spectrum, 7.08 (d, J = 9.5 Hz, 1 H), 6.40–6.70 ppm (four signals, 2 H). Irradiations at 3.22 and 2.60 ppm result in the sharpening of the peak (6.40–6.70).

3 (n = 2): NMR ($CDCl_3$) 3.91 (1 H, multiplet), 3.28 (q, J = 7.5 Hz, 4 H), 1.5–2.6 (8 H, multiplet), 1.14 ppm (t, J = 7.5 Hz, 6 H); aromatic protons, ABX spectrum, 7.03 (d, J = 9.5 Hz, 1 H), 6.30–6.50 ppm (multiplet, five signals, 2 H). Irradiation at 3.28 ppm results in the sharpening of the peak (6.30–6.50).

Condensation of Cycloheptanone Enolate. The reaction mixture was fractionned through a column filled with a 1:1 mixture of neutral alumina–silica gel. The following products were isolated successively.

3 (n = 3): NMR ($CDCl_3$) 1.13 (t, J = 7 Hz, 6 H), 1.20–2.90 (10 H, multiplet with strong resonance at 2.37 and 3.13), 3.31 (q, J = 7 Hz, 4 H), 4.22 ppm (multiplet, 1 H); aromatic protons, ABX spectrum, 7.12 (d, J = 9 Hz, 1 H), 6.40–6.60 ppm (multiplet with three peaks, 2 H). Irradiation at 3.31 ppm results in the sharpening of the peaks (6.40–6.60).

4 (n = 3): mp 89–90°; NMR (CCl_4) 1.09 (t, J = 7 Hz, 6 H), 1.20–2.5 (10 h, multiplet with strong resonance at 1.50 and 1.85), 2.48 (s, 1 H, disappears after addition of D_2O), 3.30 ppm (5 H, multiplet with q, J = 7 Hz); aromatic protons, AB spectrum, 6.19 (d, J = 9 Hz, 1 H), 6.84 ppm (d, J = 9 Hz, 1 H).

Condensation of Cyclooctanone Enolate. The reaction mixture was fractioned through a column filled with a 1:1 mixture of neutral alumina–silica gel. The following products were isolated successively.

6 (n = 4): $n^{24}D$ 1.5765; NMR ($CDCl_3$) 3.28 (q, J = 7 Hz, 4 H), 2.34 (multiplet with six peaks, 4 H), 1.10 (t, J = 7 Hz, 6 H), 1.20–1.90 ppm (two multiplets, 8 H); aromatic protons, ABX spectrum, 7.13 (d, J = 8 Hz, 1 H), 6.40–6.70 ppm (2 H, multiplet). Irradiations at 3.28 and 2.34 result in the sharpening of the peaks (6.40–6.70).

3 (n = 4): mp 52–54°; NMR ($CDCl_3$) 3.0–0.75 (18 H, multiplet including a triplet, J = 7.5 Hz at 1.18), 3.33 (q, J = 7 Hz, 4 H), 4.55 ppm (1 H, multiplet); aromatic protons, ABX spectrum, 7.02 (d, J = 8.5 Hz, 1 H), 6.75 (d, J = 3 Hz, 1 H), 6.40 ppm (dd, J = 9, 2.5 Hz). Irradiation at 3.31 ppm results in the sharpening of d (6.75) and dd (6.40).

4 (n = 4): NMR ($CDCl_3$) 1.10 (t, J = 7 Hz, 6 H), 1.20–2.60 (13 H, multiplet becoming a 12 H after addition of D_2O, with strong resonance at 1.58 and 2.30), 2.95 (m, 1 H), 3.38 ppm (split q, J = 7 Hz, 4 H); aromatic H, AB spectrum, 6.32 (d, J = 9 Hz, 1 H), 6.98 ppm (d, J = 9 Hz, 1 H).

Condensation of Diethyl Ketone Enolate. By means of chromatography on silica gel, the following products were isolated successively.

10 (R = CH_3): NMR ($CDCl_3$) 1.10 (t, J = 7 Hz, 6 H), 1.20 (t, J = 7 Hz, 3 H), 2.66 (q, J = 7.5 Hz, 2 H), 3.28 ppm (q, J = 7.5 Hz, 4 H); aromatic protons, ABX spectrum, 7.11 (d, J = 8.5 Hz, 1 H), 6.30–6.5 ppm (2 H, multiplet, three peaks). Irradiation at 3.28 ppm results in the sharpening of the peaks (6.30–6.55).

9 (R = CH_3): NMR ($CDCl_3$) 0.98 (t, J = 7 Hz, 3 H), 1.11 (t, J = 7 Hz, 6 H), 1.33 (d, J = 7 Hz, 3 H), 2.41 (q, J = 7 Hz, 2 H), 3.31 (q, J = 7 Hz, 4 H), 4.22 ppm (q, J = 7 Hz, 1 H); aromatic H, ABX spectrum, 6.35 (d, J = 3 Hz, 1 H), 6.49 (dd, J = 8.75, 3 Hz, 1 H), 7.16 ppm (d, J = 8.75 Hz, 1 H). Irradiation at 3.31 ppm results in the sharpening of d (6.35) and dd (6.49).

Condensation of Dibutyl Ketone Enolate. 10 (R = C_3H_7): NMR ($CDCl_3$) 0.6–2 (13 H, multiplet including a triplet at 1.15, J = 7 Hz), 2.70 (2 H, multiplet), 3.39 ppm (q, J = 7 Hz, 4 H); aromatic protons, ABX spectrum, 7.3 (d, J = 7.5 Hz, 1 H), 6.35–6.85 ppm (multiplet with three peaks, 2 H).

9 (R = C_3H_7): NMR ($CDCl_3$) 2.20–0.70 (20 H, multiplet), 2.33 (t, J = 7 Hz, 2 H), 3.26 (q, J = 7 Hz, 4 H), 4.24 ppm (t, J = 7 Hz, 1 H); ABX spectrum, 7.18 (d, J = 8.5 Hz, 1 H), 6.65–6.35 ppm (multiplet with four peaks, 2 H). Irradiation at 3.26 ppm results in the sharpening of the multiplet (6.65–6.35).

Condensation of Diisopropyl Ketone Enolate. By means of chromatography on silica gel, the following products were isolated successively.

15: mp 58–59°; NMR ($CDCl_3$) 1.05 (d, J = 7 Hz, 6 H), 1.20 (t, J = 7 Hz, 6 H), 1.55 (s, 6 H), 2.77 (septet, J = 7 Hz, 1 H), 3.38 ppm (q, J = 7 Hz, 4 H); aromatic protons, ABX spectrum, 7.12 (d, J = 9 Hz, 1 H), 6.78 (d, J = 3 Hz, 1 H), 6.52 ppm (dd, J = 9, 3 Hz, 1 H). Irradiation at 3.38 ppm results in the sharpening of d (6.78) and dd (6.52).

14: mp 65–66°; NMR ($CDCl_3$) 1.00 (d, J = 7 Hz), 1.05 (t, J = 7.5 Hz) (9 H), 1.22 (d, J = 7 Hz, 3 H), 1.41 (s, 3 H), 1.52 (s, 3 H), 2.10 (s, 1 H, disappears after addition of D_2O), 2.18 (septet, J = 7 Hz, 1 H), 3.13 (sextet, J = 7 Hz, 2 H), 3.55 ppm (sextet, J = 7 Hz, 2 H); aromatic protons, AB spectrum, 6.44 (d, J = 9 Hz, 1 H), 7.00 ppm (d, J = 9 Hz, 1 H).

Condensation of Ketone Enolates (50 mmol) with 16 (18 mmol). Condensation of Cycloheptanone Enolate (50 min at

45–50°). By means of chromatography on silica gel, the following products were isolated successively.

19 [$R_1 = R_3 = H$; $R_2 = R_4 = (CH_2)_4$]: NMR ($CDCl_3$) 0.8–2.4 (8 H, multiplet with strong resonance at 1.96), 2.70 (2 H, multiplet), 3.11 (4 H, multiplet), 3.76 (4 H, multiplet), 4.24 ppm (1 H, multiplet); aromatic protons, ABX spectrum, 7.18 (d, J = 8.5 Hz, 1 H), 6.8 (d, J = 3 Hz, 1 H), 6.69 ppm (dd, J = 8.5, 3 Hz, 1 H). Irradiation at 3.11 ppm results in the sharpening of d (6.8) and dd (6.69); irradiation at 4.24 ppm results in the sharpening of d(6.80).

18 [$R_1 = R_3 = H$; $R_2, R_4 = (CH_2)_4$]: mp 132–134°; NMR ($CDCl_3$) 1.00–2.6 (10 H, multiplet), 2.98 (s, 1 H, disappears after addition of D_2O), 3.00–3.60 (5 H, multiplet), 3.90 ppm (4 H, multiplet); aromatic protons, AB spectrum, 6.68 (d, J = 8.75 Hz, 1 H), 7.30 ppm (d, J = 8.75 Hz, 1 H).

Condensation of Diisopropyl Ketone Enolate (1.5 hr at 25°). **19** ($R_1 = R_2 = R_3 = R_4 = CH_3$): NMR ($CDCl_3$) 1.02 (d, J = 6.5 Hz, 6 H), 1.56 (s, 6 H), 2.71 (septet, J = 6.5 Hz, 1 H), 3.2 ppm (4 H, multiplet); aromatic protons, ABX spectrum, 7.22 (d, J = 8.5 Hz, 1 H), 7.08 (d, J = 2.75 Hz, 1 H), 6.77 ppm (dd, J = 8.5, 2.75 Hz, 1 H). Irradiation at 3.20 ppm results in the sharpening of d (7.08) and dd (6.77); irradiation at 1.56 ppm results in the sharpening of d (7.08).

18 ($R_1 = R_2 = R_3 = R_4 = CH_3$): mp 178–179°; NMR ($CDCl_3$) 1.02 (d, J = 7 Hz, 3 H), 1.27 (d, J = 7 Hz, 3 H), 1.4 (s, 3 H), 1.51 (s, 3 H), 2.20 (septet, J = 7 Hz, 1 H), 2.25 (s, 1 H, disappears after addition of D_2O), 2.96 (2 H, multiplet), 3.38 (2 H, multiplet), 3.78 ppm (4 H, multiplet), aromatic H's AB spectrum, 6.47 (d, J = 8.5 Hz, 1 H), 7.00 ppm (d, J = 8.5 Hz, 1 H).

Condensation of Ketone Enolates (50 mmol) with 20 (18 mmol). Condensation of Cycloheptanone. By means of chromatography on silica gel, the following products were isolated successively.

22: NMR ($CDCl_3$) 1.16 (t, J = 7 Hz, 6 H), 1–3 (10 H, multiplet with strong resonance at 2.02 and 2.60), 3.37 ppm (5 H, multiplet including a quartet, J = 7 Hz); aromatic protons, AB_2 spectrum, 6.53 (t, J = 2 Hz, 1 H), 6.63 (d, J = 2 Hz, 2 H).

21: NMR ($CDCl_3$) 1.15 (t, J = 7.5 Hz, 6 H), 1–2.5 (10 H, multiplet with strong resonance at 1.92 and 1.57), 3.40 ppm (6 H, multiplet, becoming 5 H after addition of D_2O, including quartet, J = 7 Hz), aromatic protons, AB spectrum, 6.60 (d, J = 3 Hz, 1 H), 6.68 ppm (d, J = 3 Hz, 1 H).

Condensation of Diisopropyl Ketone Enolate. By means of chromatography on silica gel, the following products were isolated successively.

24: NMR ($CDCl_3$) 1.14 (t, J = 6 Hz, 6 H), 1.24 (d, J = 7 Hz, 6 H), 2.85 (septet, J = 7 Hz, 1 H), 3.36 ppm (q, J = 7 Hz, 4 H); aromatic protons 6.50–6.75 ppm (3 H, multiplet).

23: NMR ($CDCl_3$) 0.99 (t, J = 7 Hz, 6 H), 1.12 (d, J = 7 Hz, 6 H), 1.21 (d, J = 7 Hz, 6 H), 2.69 (septet, J = 7 Hz, 1 H), 2.96 (q, J = 7 Hz, 4 H), 3.20 ppm (septet, J = 7 Hz, 1 H); aromatic H, AB spectrum, 6.94 (d, J = 2 Hz, 1 H), 7.06 ppm (d, J = 2 Hz, 1 H). Irradiation at 3.20 ppm results in the sharpening of d (6.94); irradiation at 2.69 ppm results in sharpening of d (7.06).

25: NMR ($CDCl_3$) 0.90 (split d, J = 7 Hz, 6 H), 1.16 (split t, J = 7 Hz, 6 H), 1.23 (d, J = 7 Hz, 6 H), 1.46 (s, 6 H), 2.74 (septet, J = 7 Hz, 2 H), 3.32 ppm (split q, J = 7 Hz, 4 H); aromatic protons 6.62–6.25 ppm (3 H, multiplet).

Condensation of Ketone Enolates (50 mmol) with 1.3-Bis(*N,N*-dialkylamino)-4-chlorobenzene (18 mmol) (26). Condensation of Cycloheptanone Enolate. After filtration through a silica gel column, the following products were isolated.

27 [α-3.5-bis(*N,N*-diethylamino)phenylcycloheptanone]: NMR (CCl_4) 1.11 (t, J = 7.5 Hz, 12 H), 2.8–1 (10 H, multiplet), 3.28 ppm (5 H, multiplet including quartet, J = 7.5 Hz); aromatic protons, A_3 spectrum, 5.87 ppm (s, 3 H).

28 [α-3.5-di(*N*-morpholino)phenylcycloheptanone]: mp 117–118°; NMR ($CDCl_3$) 1–3 (10 H, multiplet), 3.17 (8 H, multiplet), 3.5–3.7 (1 H, multiplet), 3.82 ppm (8 H, multiplet); aromatic protons, A_3 spectrum, 6.33 ppm(s, 3 H).

Basic Ring Cleavage of Benzocyclobutenols 4, 14, and 18. Solvents, reaction times, and temperatures are indicated in Table II. An excess of base was used.

Ring cleavage products were described above, except for the following.

29 [$R_1 = R_2 =$ Et; $R_3, R_4 = (CH_2)_6$; $R_5 = H$]: mp 56–57°; NMR ($CDCl_3$) 0.95 (t, J = 7.5 Hz, 6 H), 2.5–0.6 (10 H, multiplet) 2.5–3.8 ppm (8 H, multiplet including quartet at 2.93, J = 7.5 Hz); aromatic H, AB spectrum, 6.93 (d, J = 8.75 Hz, 1 H), 7.30 ppm (d, J = 8.75 Hz, 1 H).

29 ($R_1 = R_2 =$ Et; $R_3 = i$-Pr; $R_4 = R_5 = CH_3$): NMR ($CDCl_3$) 0.8–1.5 (18 H, multiplet including t at 0.98, J = 7.5 Hz, d at 1.17, J = 7.5 Hz, d at 1.40, J = 7.5 Hz), 2.5–3.5 (6 H, multiplet including a quartet at 2.90, J = 7.5 Hz); aromatic H, AB spectrum, 6.92 (d, J = 9 Hz, 1 H), 7.24 (d, J = 9 Hz, 1 H).

29 [$R_1, R_2 = OC_4H_8$; $R_3, R_4 = (CH_2)_5$; $R_5 = H$]: mp 114–116°; NMR ($CDCl_3$) 1–2 (10 H, multiplet), 2.2–3.5 (8 H, multiplet), 3.82 ppm (4 H, multiplet); aromatic H, 7.12 (d, J = 8 Hz, 1 H), 7.52 ppm (d, J = 8 Hz, 1 H).

29 ($R_1, R_2 = OC_4H_8$; $R_3 = i$-Pr; $R_4 = R_5 = CH_3$): mp 65–67°; NMR ($CDCl_3$) 1.21 (d, J = 7 Hz, 6 H), 1.32 (d, J = 7 Hz, 6 H), 2.3–4 ppm (10 H, multiplet with strong resonance at 2.95 and 3.80); aromatic protons, AB spectrum, 7.15 (d, J = 7.5 Hz, 1 H), 7.46 ppm (d, J = 7.5 Hz, 1 H).

Acknowledgments. We are grateful to K. G. Taylor, visiting Professor in Nancy University, and the referees for discussing this manuscript, to Produits Chimiques Ugine Kuhlmann for financial support, and to M. Dorme (Laboratoire de Microanalyse, Paris VI) for the microanalyses.

Registry No.—**1**, 55039-58-2; **2** (n = 1), 55886-83-4; **2** (n = 2), 55886-84-5; **2** (n = 3), 55886-85-6; **2** (n = 4), 55886-86-7; **3** (n = 1), 55887-02-0; **3** (n = 2), 55887-03-1; **3** (n = 3), 55887-04-2; **3** (n = 4), 55887-05-3; **4** (n = 1), 55887-06-4; **4** (n = 3), 55887-07-5; **4** (n = 4), 55887-08-6; **5** (n = 1), 55887-09-7; **6** (n = 2), 55887-10-0; **6** (n = 4), 55887-11-1; **8** ($R = CH_3$), 29263-72-7; **8** ($R = C_3H_7$), 55887-12-2; **9** ($R = CH_3$), 55887-13-3; **9** ($R = C_3H_7$), 55887-14-4; **10** ($R = CH_3$), 55887-15-5; **10** ($R = C_3H_7$), 55887-16-6; **13**, 55887-17-7; **14**, 55887-18-8; **15**, 55887-19-9; **16**, 55039-68-4; **18** [$R_1 = R_3 = H$; $R_2, R_4 = (CH_2)_4$], 55887-20-2; **18** ($R_1 = R_2 = R_3 = R_4 = CH_3$), 55887-21-3; **19** [$R_1 = R_3 = H$; $R_2, R_4 = (CH_2)_4$], 55887-22-4; **19** ($R_1 = R_2 = R_3 = R_4 = CH_3$), 55887-23-5; **20**, 55039-56-0; **21**, 55887-24-6; **22**, 55887-25-7; **23**, 55887-26-8; **24**, 55887-27-9; **25**, 55887-28-0; **26** ($R_1 = R_2 =$ Et), 55039-60-6; **26** [$R_1, R_2 = (CH_2CH_2)_2O$], 55039-70-8; **27**, 55887-29-1; **28**, 55887-30-4; **29** [$R_1 = R_2 =$ Et; $R_3, R_4 = (CH_2)_6$; $R_5 = H$], 55887-31-5; **29** ($R_1 = R_2 =$ Et; $R_3 = i$-Pr; $R_4 = R_5 = CH_3$), 55887-32-6; **29** [$R_1, R_2 = OC_4H_8$; $R_3, R_4 = (CH_2)_5$; $R_5 = H$], 55887-33-7; **29** ($R_1, R_2 = OC_4H_8$; $R_3 = i$-Pr; $R_4 = R_5 = CH_3$), 55887-34-8; $NaNH_2$, 7782-92-5; t-BuOH, 75-65-0.

References and Notes

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