gruppen *Folkers* und *Wright* die Mevalonsäure (= Hydroxymethyl-glutarsäure) eigentlich zufällig entdeckt hatten. Sehr wichtig war die Beobachtung, dass aus der Mevalonsäure (6 C-Atome), unter Abspaltung des einen Carboxyls und Reduktion des anderen zur CH_2OH-Gruppe, endlich der **hypothetische Isoprenrest in Form des Isopentenols** erhalten wurde. Aus Isopentenol, das die Doppelbindung in β,γ-Stellung zur CH_2OH-Gruppe enthält, wird biogenetisch durch Wanderung der Doppelbindung in α,β-Stellung der **Dimethyl-allylalkohol** gewonnen. Die beiden Alkohole zusammen sind nötig, um biogenetisch Geraniol zu erhalten. Für die Verlängerung des Geraniols zu Farnesol und weiter zu Geranylgeraniol genügt das Isopentenol. Für die biogenetischen Reaktionen werden die Pyrophosphate der Alkohole verwendet. Bemerkenswert ist, dass sich die beiden Varianten des Isoprenrestes schematisch (nicht biogenetisch) durch Anlagerung von Pyrophosphorsäure an Isopren ableiten lassen.

An der Durchführung dieser und anderer dazugehöriger biogenetischer Reaktionen waren zahlreiche Autoren beteiligt. Erwähnt seien besonders die beiden *Nobel*-Preisträger auf diesen Gebieten, *Bloch* und *Lynen*, ebenso auch die Arbeitsgruppe *Popjak-Cornforth*.

Die **Rolle der Riechstoffe Geraniol und Farnesol** bei der Biogenese so vieler verschiedenartiger und z.T. ungemein wichtiger Verbindungen – alle Terpene, Carotinoide und Steroide – steht in sehr scharfer Konkurrenz mit ihrer Rolle in der Parfumerie.

---

188. Mass Spectrometry and Organic Analysis, part 14[1]) The Photolysis and Mass Spectra of Medium and Large Ring Ketones from C_9 to C_{16}

by **K.H. Schulte-Elte, B. Willhalm, A.F. Thomas,**
the late **M. Stoll** and **G. Ohloff**
Firmenich & Cie, Laboratoire de Recherches, Genève

Dedicated to Dr. *Roger Firmenich* on the occasion of his 65th birthday

(14. VII. 71)

Summary. The photolysis of cyclic ketones from C_9 to C_{16} has been carried out, and formation of cyclobutanols observed in only C_{11} to C_{16}. Although in the mass spectrometer cyclobutanols are not formed, an initial transfer of a γ-hydrogen atom to the carbonyl group is shown to occur in the mass spectra of all cyclic ketones higher than C_{10}.

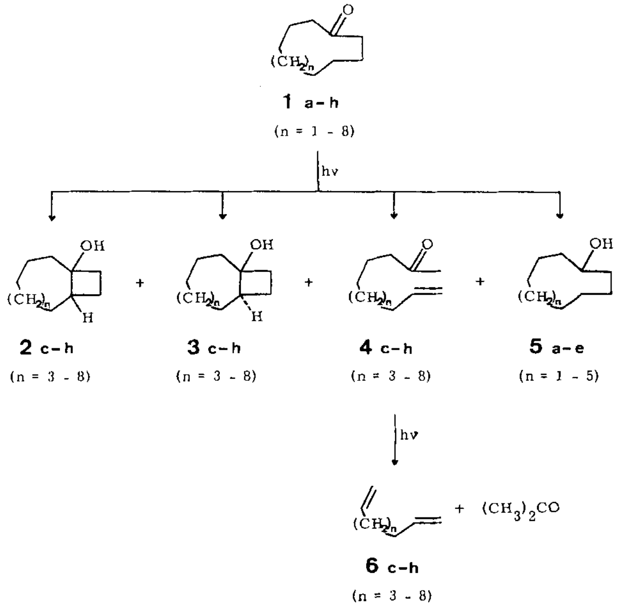
The photolysis of cyclic ketones by direct excitation in solution has already been described for cyclododecanone [2], cycloundecanone [3], cyclodecanone [4], and cyclopentadecanone [5]. We have now examined the photolysis of the C_9, C_{13}, C_{14}, and C_{16} cyclic ketones, and in this note we discuss the analogy which may exist between photochemistry and mass spectrometry in the series of cyclic ketones. That such analogies between photochemistry and mass spectra are possible is well-known; *e.g.*, the site-specific γ-hydrogen transfer to the carbonyl group in ketone mass spectra (often

---

[1]) For part 13, see [1].

called the *McLafferty* rearrangement) [6] corresponds to the *Norrish* type II photochemical decomposition of carbonyl compounds [7].

Scheme 1



Photolysis of the six cyclic ketones (**1c**–**1h**, n = 3 to 8) in cyclohexane[2]) affords in each case varying amounts of the two possible α,β-polymethyleno-cyclobutanols (**2** and **3**), as well as the unsaturated ketone **4** resulting from the *Norrish* type II fission, together with a certain amount of **5** by photoreduction. In contrast, neither cyclononanone (**1a**) nor cyclodecanone (**1b**) exhibit neither polymethyleno-cyclobutanol formation nor *Norrish*-II fission. Cyclodecanone yields a mixture of the stereoisomeric 9-decalols (yields, 31% *cis*, 10% *trans*) [4] in addition to cyclodecanol (**5b**) and 1-cyclohexylcyclodecanol (ca. 12%), whereas cyclononanone (**1a**) is converted almost entirely to cyclononanol (**5a**) and 1-cyclohexylcyclononanol. The relative yields of the photoproducts **2**–**5** (determined by GLPC.[3])) are given in Table 1.

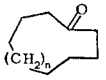
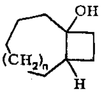
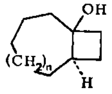
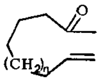
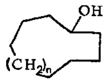
From Table 1, it can be seen that photochemical polymethyleno-cyclobutanol formation was greatest for the C_{12}-ketone (**1d**), and in this case we examined the mass spectrum of the bicyclo[8.2.0]dodecanols **2d** and **3d** formed. Although there were many points common to these spectra, and to that of cyclododecanone (notably formation of an important fragment at *m/e* 58, see Fig. 1), the fragment at *m/e* 154 in the cyclobutanols (18% of the most important fragment), corresponding to loss of ethylene from the molecular ion, see [9], was absent in the case of cyclododecanone. We can be fairly certain that the cyclobutanol pathway is not a major one in any of

---

[2]) It would be preferable to compare *gas-phase* photolysis with mass spectrometry, but on account of the experimental difficulties, we have used solutions.

[3]) Gas-liquid partition chromatography, carried out on Carbowax 20M columns.

Table 1. *Photolysis of cyclic ketones (C-9 to C-16)* [a])

		Reaction products [c]) (%)				
Macrocyclic Ketones	Quantum Yield [b]) Φ (mol/E.)	Bicyclic Alcohols		Norrish II Fission [d])	Monocyclic Alcohols	Unknown Products, Polymers, etc.
 **1**		 **2**	 **3**	 **4**	 **5**	
Cyclononanone **1a** (n = 1)	0.13	–	–	–	42 [e])	20
Cyclodecanone **1b** (n = 2)	0.12	–	–	–	18	12
Cycloundecanone **1c** (n = 3)	0.10	40	14	8	12	26
Cyclododecanone **1d** (n = 4)	0.35	64	11	8	7	10
Cyclotridecanone **1e** (n = 5)	0.38	45	23	18	5	9
Cyclotetradecanone **1f** (n = 6)	0.29	39	12	30	(<1)	20
Cyclopentadecanone **1g** (n = 7)	0.18	17	11	52	(<1)	14
Cyclohexadecanone **1h** (n = 8)	0.14	13	9	58	(<1)	20

[a]) Photolysis of ketones **1** carried out with 120 ml of 0.02 M solutions in pure cyclohexane in quartz apparatus at 15° under N_2, using a central, water-cooled Hg high pressure lamp (*Philips* HPK 125 W), and followed quantitatively by GLPC.

[b]) Measured with a uranyl oxalate actinometer (*Leighton & Forbes* [7]).

[c]) Distilled from the polymeric material, then purified by GLPC., identified *either* by direct comparison with authentic material *or* as previously described for the C_{12} ketone [2a].

[d]) The amount of enones **4** (n = 3 to 8) formed was deduced from the practically linear increase in concentration at the beginning of the irradiation; their photolysis products (including acetone and α,ω-dienes **6**) were only qualitatively identified.

[e]) In addition to **5a**, 28% of 1-cyclohexylcyclononanol was obtained.

the ketones examined here, even when, as in the latter case, this might be expected to be most favourable compared with open-chain ketones, see [10] [4]).

Formation of the ω-unsaturated ketones (**4**) depends on an initial γ-hydrogen transfer, as do cyclobutane ring formation and the *McLafferty* rearrangement. In open-chain ketones, it is known that if there are suitably placed hydrogens on each side of the carbonyl group, a double transfer will occur in the mass spectrometer [5]) leading to a fragment at *m/e* 58. Scheme 2 shows how this might occur in the case of a

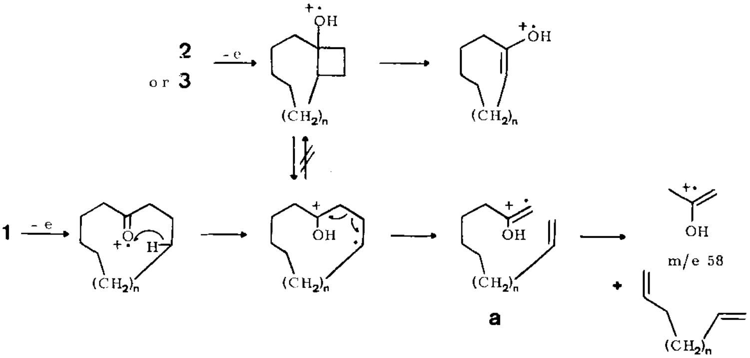
---

[4]) It may also be presumed that cyclobutanol ringformation during photolysis requires the presence of a biradical intermediate. In the mass spectrometer, the species formed from the molecular ion after the initial hydrogen transfer is an ion-radical, and there is no reason to suppose that this would undergo similar reactions.

[5]) Leading references are given in [11].

macrocyclic ketone. The radical ion **a** corresponds to the enol of the unsaturated ketone observed in the photolytic reaction (and can, of course, also be formed in the mass spectrum of the cyclobutanols (**2**)), but cannot be seen as such in the mass spectrometer, since it has the same molecular weight as the original ketone. The amount of the fragment at *m/e* 58, however, will give a measure of the importance of the initial hydrogen transfer reaction, and in Fig. 1 it is shown as a percentage of the total ionization (above *m/e* 40, below which all spectra are the same), compared with the combined yields of **2**, **3** and **4** from the photolysis. It can be seen that whereas a minimum of 11 carbon atoms in the ring is required before any photolytic reaction can take place, there is a measurable amount of γ-hydrogen transfer occurring at C_9 in the mass spectrometer. Photochemically, cyclobutanol formation rather than *Norrish*-II fission is associated with the higher quantum yields of the medium ring ketones; in these cases the steric position of the γ-hydrogen to be transferred is presumably very favourable, and in the biradical intermediates there may be greater overlap of the orbitals involved in formation of the new bond. In the mass spectrometer much more energy is available, and it seems that, at least as low as the C_9-ketones, this is sufficient to overcome steric difficulties and so allows a γ-hydrogen transfer, although other reactions take precedence for smaller rings.

Scheme 2



For the mass spectra of cyclic ketones C_6–C_{16} the principal fragments, of which there are three types, are listed in Table 2. The first type can be illustrated by the molecular ion, which diminishes in intensity (see Fig. 2) as the stability of the ring decreases, to reach a constant value as the compounds approach similarity to open-chain compounds. The main fragment from the lower rings, at *m/e* 55 (mixture of isobaric $C_4H_7^+$ and $C_3H_3O^+$ ions) [12], also decreases in intensity with increasing ring size, although the fraction containing oxygen, arising by initial α-fission [13], falls from 87% of the total intensity of this fragment in cyclohexanone [12], 75% in cycloheptanone [12], to 39% in cyclononanone[6]; this behaviour is characteristic of many fragmentations in homologous series. The second group of fragments clearly is influenced by ring size, and is illustrated by the fragments for 4-methylcyclopentadecanone at

---

[6] We are greatly indebted to Dr. *Aplin, Dyson Perrins* Laboratory, Oxford, for the measurement of the high resolution mass spectrum of cyclononanone.

m/e 98 and *m/e* 111 shown in Fig. 3. The existence of a metastable ion supports the supposition that in spectra with both *m/e* 98 and *m/e* 97 fragments, the former, although not the only source, gives rise to *m/e* 97, which was shown by high resolution measurements to contain 18% of $C_7H_{13}^+$, for cyclononane, the fragments at *m/e* 98 being of only one type and containing oxygen. It is very tempting to ascribe cyclic structures to these ions, and it may be recalled that cyclooctanone and cyclodecanone have both been reported to undergo such photochemical hydrogen transfer [5] 7), but whatever its real structure, the radical ion of *m/e* 98 is unlikely to be that of cyclohexanone enol, which we have observed in the mass spectrum of a different compound (see below), and which does not lose a hydrogen atom to give a fragment of *m/e* 97. The fragments in the

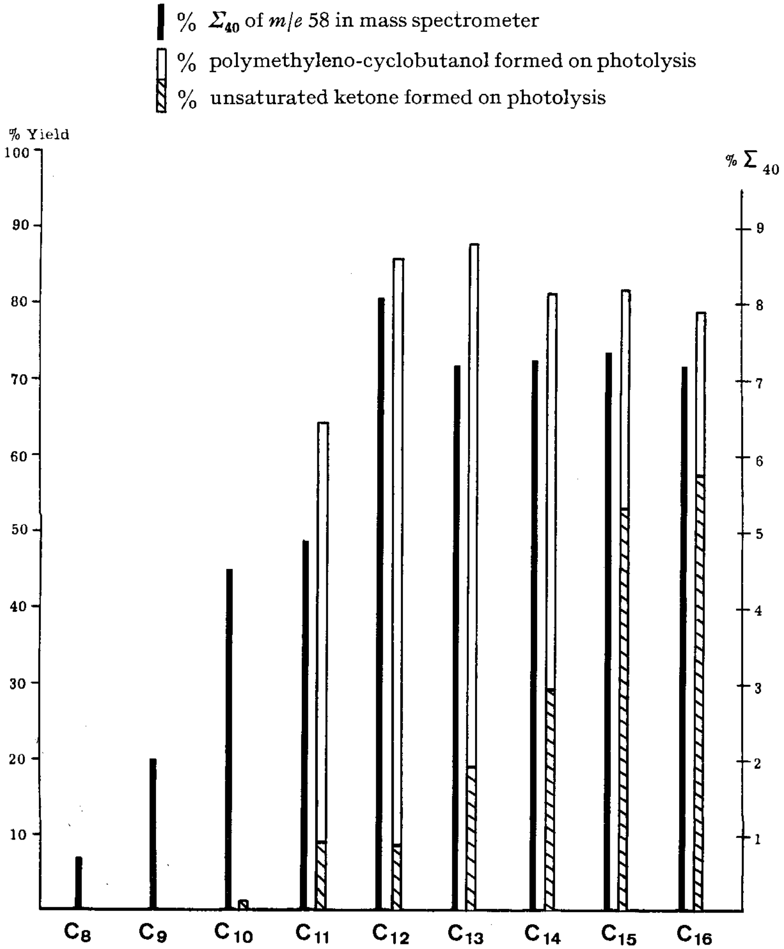


Fig. 1. *Comparison of photochemical and mass spectrometric γ-hydrogen transfer for cyclic ketones*

---

7) Since we were unable to detect any photochemical intramolecular hydrogen transfer for cyclononanone in solution, we feel that the result published for cyclooctanone requires confirmation.

third group are those which increase with increasing ring size, *i.e.* as the system becomes more like an open-chain ketone. In addition to the fragment at *m/e* 58 already mentioned, this group includes the fragment at *m/e* 71.

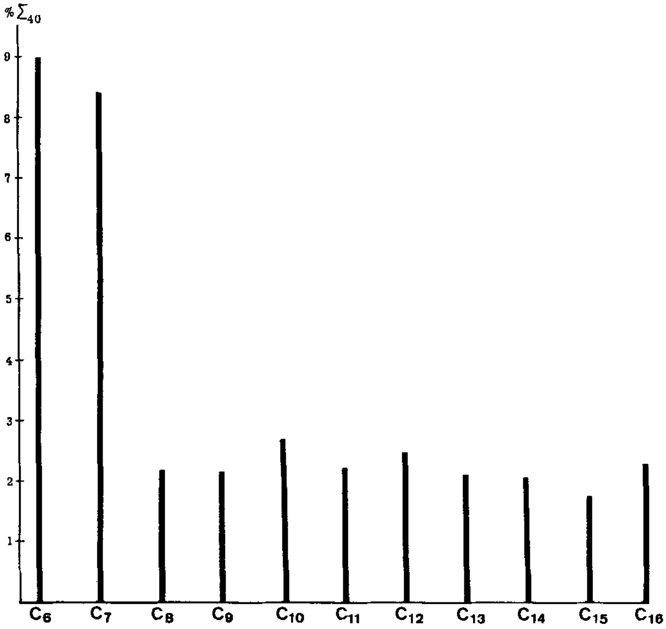


Fig. 2. *Relative molecular intensities* (M^+) *in mass spectra of cyclic ketones* (C_6–C_{16})

Table 2. $\% \Sigma_{40}$ *of main fragments of mass spectra of cyclic ketones* (C_6–C_{16})

m/e	C_6 $M = 98$	C_7 112	C_8 126	C_9 140	C_{10} 154	C_{11} 168	C_{12} 182	C_{13} 196	C_{14} 210	C_{15} 224	C_{16} 238
55	30	18	16	12	11	10	9.5	8.3	8.4	8.4	8.5
56	3.0	9.0	5.4	6.0	4.4	3.0	3.0	2.3	2.0	1.9	2.0
58	0	0.4	0.7	2.0	4.5	4.9	8.1	7.2	7.3	7.4	7.1
68	0.3	16	2.0	1.9	1.6	1.8	1.8	1.9	1.6	1.9	1.8
69	6.8	7.2	4.1	3.8	3.6	3.5	3.5	3.0	3.1	3.9	3.4
70	6.0	4.5	4.2	3.2	3.2	2.7	2.3	2.0	1.8	1.7	1.8
71	0.1	0.8	0.8	1.4	2.9	4.1	7.7	7.6	7.8	7.9	7.7
82	tr[a])	tr	5.4	2.1	1.2	1.9	3.3	3.0	2.4	2.9	3.0
83	2.4	2.6	5.7	4.3	3.3	3.3	3.3	2.8	2.4	2.7	2.8
84	tr	5.8	6.2	5.5	4.2	4.0	2.5	2.0	1.6	1.9	2.2
96	0	tr	tr	1.3	2.2	0.8	1.4	3.0	2.6	2.7	2.9
97	0.2	1.0	2.7	5.0	4.9	3.7	2.7	2.7	2.3	2.3	2.3
98	$= M^+$	tr	12	13	6.2	4.9	4.6	2.8	1.9	2.3	2.9
111	–	tr	0.9	3.2	7.1	5.4	3.2	1.8	1.6	1.7	1.6
112	–	$= M^+$	tr	1.3	2.3	1.8	1.1	0.7	0.5	0.6	0.4
125	–	–	tr	0.6	1.5	3.9	1.9	1.3	1.3	1.6	1.8
$M^{\cdot +}$	9.0	8.4	2.2	2.1	2.6	2.2	2.5	2.1	2.0	1.9	2.4

[a]) Trace = less than 0.2% Σ_{40}.

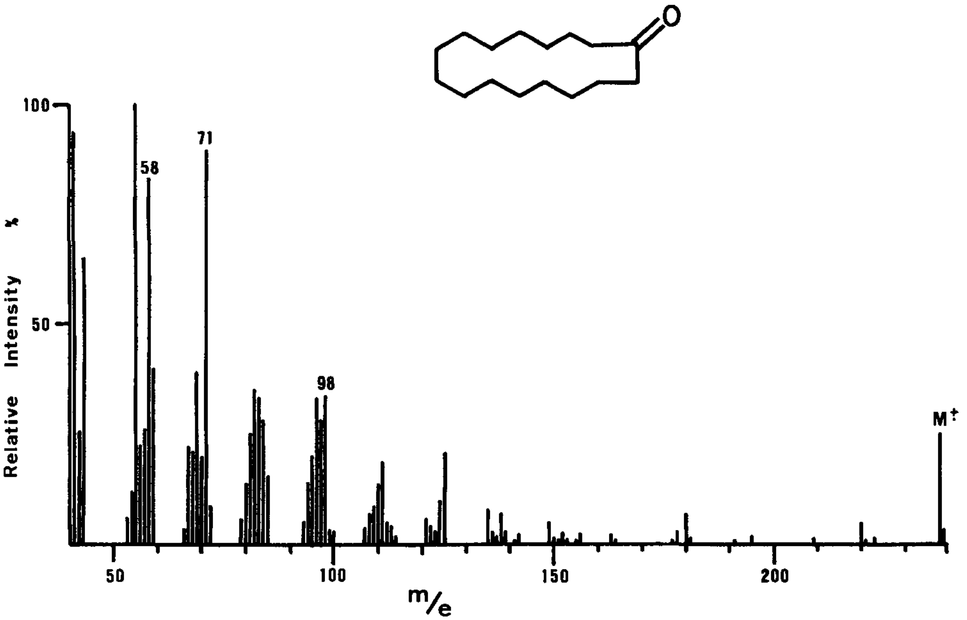


Fig. 3. *Relative intensities of* m/e *for cyclohexdecanone*

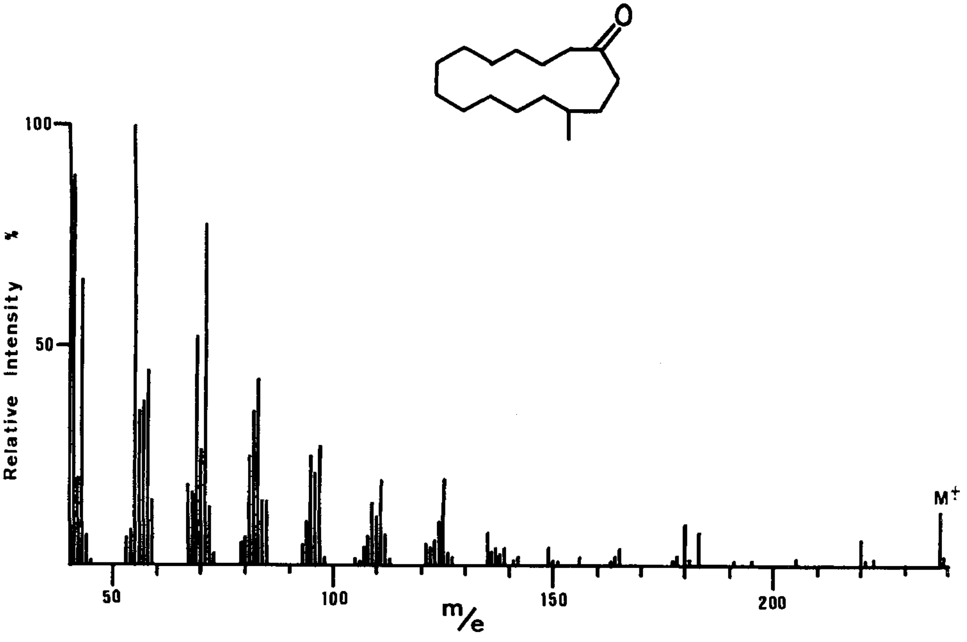
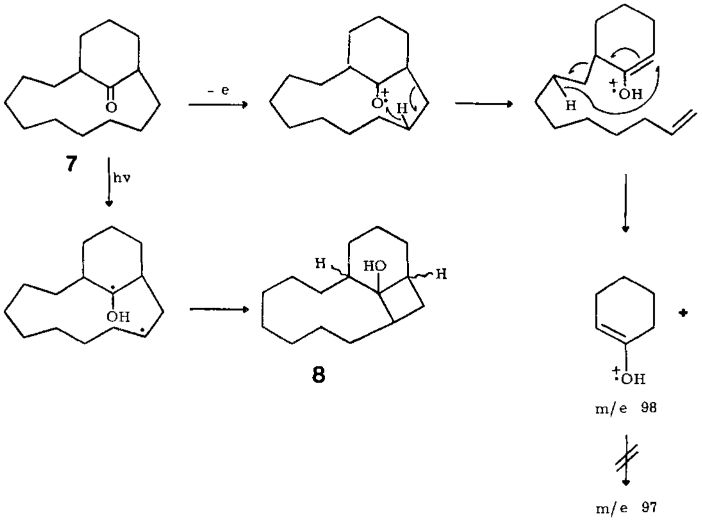


Fig. 4. *Relative intensities of* m/e *for 4-methylcyclopentadecanone*

Many years ago, *Prelog* suggested [14] that macrocyclic ketones could conceivably exist in two conformations with respect to the carbonyl group, where it is either oriented towards the exterior, 'outside', or towards the interior of the ring, 'inside'. Later, *Brown* showed [15] how most of the effects involved could be explained by changes in the co-ordination number of the carbonyl carbon atom. More recently, *Ledaal*, on the basis of dipole moment measurements and NMR. spectra, has revived the idea that with increasing ring size, the conformation of the carbonyl group changes from 100% 'outside' in C_5, to true 'inside' conformation at C_{11} and C_{12} [16].

Scheme 3



At first sight, the data presented here might seem to support the last idea, but increasing conformational mobility of the rings would equally account for the observations. Indeed, a comparison of the mass spectra of cyclohexadecanone (Fig. 3) and of 4-methylcyclopentadecanone (Fig. 4) shows that in presence of the methyl group a significant lowering of the *m/e* 58 fragment takes place, a fact that is very difficult to explain using the 'inside-outside' conformational argument, since if the carbonyl group is 'inside', the hydrogen atom on the carbon carrying the methyl group should be more, not less easily, transferred than a hydrogen from a methylene group. On the other hand, if the effect of the methyl group is to render that side of the molecule more rigid, it can be argued that the hydrogen to be transferred is not normally in the neighbourhood of the carbonyl group, but becomes so by conformational movement.

Because of the possibility to predict by mass spectrometry the likelihood of a γ-hydrogen transfer, we examined the bicyclic ketone **7**[8] to see whether it would behave like a cyclododecanone, molecular models implying that the carbonyl group is fixed in a favourable position for hydrogen transfer to occur. In fact this compound exhibited by far the highest amount of double γ-hydrogen transfer of any substance

---

[8] Prepared from δ-ethoxycarbonyl-cyclododecanone [17] with trimethylene dibromide in the presence of sodium hydride and subsequent decarboxylation. We thank Mr. *M. Pawlak* for assistance in this preparation.

examined. The fragment at *m/e* 98 amounted to 14.4% of the total ionization, and we may safely assume that it is best represented by the ion radical of cyclohexanone enol (Scheme 3). This is in accord with the fact that on irradiation in cyclohexane **7** is converted (> 60% yield) to a new tricyclic alcohol **8** (m.p. 64°) for which the analytical and spectral data are in agreement with the structure assigned.

BIBLIOGRAPHY

[1] *A. F. Thomas, B. Willhalm & R. Müller*, Organic Mass Spectr. *2*, 223 (1969).

[2] *K. H. Schulte-Elte & G. Ohloff*, Chimia *18*, 183 (1964); *B. Camerino & B. Patelli*, Experientia *20*, 260 (1964).

[3] *T. Mori, K. Matsui & H. Nozaki*, Tetrahedron Letters *1970*, 1175.

[4] *M. Barnard & N. C. Yang*, Proc. chem. Soc. *1958*, 302.

[5] *N. C. Yang*, 13th Solvay Conference on Chemistry, John Wiley, New York 1967, p. 1.

[6] *H. Budzikiewicz, C. Djerassi & D. H. Williams*, 'Mass Spectrometry of Organic Compounds', Holden-Day, San Francisco, 1967, p. 155.

[7] *C. H. Bamford & R. G. W. Norrish*, J. chem. Soc. *1938*, 1544.

[8] *W. G. Leighton & G. S. Forbes*, J. Amer. chem. Soc. *52*, 3139 (1930).

[9] *S. Meyerson, C. Fenselau, J. L. Young, W. R. Landis, E. Selke & L. C. Leitch*, Organic Mass Spectr. *3*, 689 (1970).

[10] *A. F. Gerrard, R. L. Hale, R. Liedtke, W. H. Faul & C. A. Brown*, Organic Mass Spectr. *3*, 683 (1970).

[11] *H. Budzikiewicz, C. Fenselau & C. Djerassi*, Tetrahedron *22*, 1391 (1966).

[12] *J. H. Beynon, R. A. Saunders & A. E. Williams*, Applied Spectroscopy *14*, 95 (1960).

[13] *J. Seibl & T. Gäumann*, Z. anal. Chem. *197*, 33 (1963); *D. H. Williams, H. Budzikiewicz & C. Djerassi*, Mh. Chem. *95*, 166 (1964).

[14] *V. Prelog*, J. chem. Soc. *1950*, 420.

[15] *H. C. Brown, R. S. Fletcher & R. B. Johannesen*, J. Amer. chem. Soc. *73*, 212 (1951).

[16] *T. Ledaal*, Tetrahedron Letters *1967*, 4397; *idem.*, *ibid. 1968*, 651.

[17] *S. J. Rhoads, J. C. Gilbert, A. W. Decora, T. R. Garland, R. J. Spengler & M. J. Urbigkit*, Tetrahedron *19*, 1625 (1963).

---

189. Synthetic Studies on Damascenones

by **G. Büchi** and **H. Wüest**

Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts, USA

Dedicated to Dr. *Roger Firmenich* on the occasion of his 65th birthday

(12. VII. 71)

Summary. The odor principle β-damascenone and its isomer α-damascenone have been prepared by treatment of the corresponding ethyl safranates with excess allyl lithium followed by alkoxide catalyzed isomerization of the resulting products with β,γ-unsaturated ketonic side-chains. Addition of allyltriphenylphosphorane (preferably prepared from allyltriphenylphosphonium chloride) rather than the propenyl isomer to ethyl α-isopropylidene-acetoacetate produced ethyl α-safranate. This represents a new, potentially general method for the synthesis of functionalized cyclohexadienes.

Damascenone (**1**)[1], a trace constituent of Bulgarian rose oil (*Rosa damascena Mill.*) has an exceptionally powerful, as well as pleasing, odor and promises to become a key

---

[1] Doricenone (trade mark applied for by *Firmenich & Co.*, Geneva).