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THE FLOW THERMOLYSES OF 1-ISOBUTENYL ALKYNYL- AND 2-METHYLPHENYl ALKYNYL KETONES. SYNTHESIS OF METHYLENOMYCIN B

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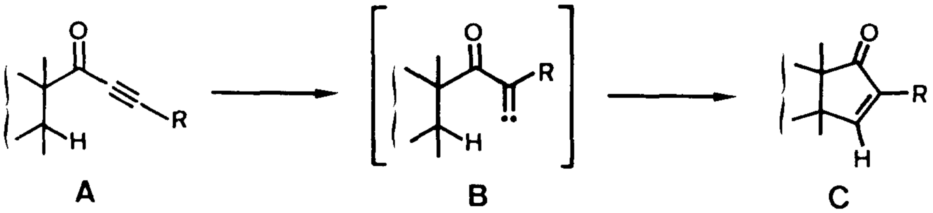
Abstract: The gas flow thermolyses of 1-isobutenyl alkynyl and 2-methylphenyl alkynyl ketones were found to lead to phenols and to cyclopentenones. The results are explained by a 5-ring carbene process (the known α-alkynone cyclization) and a 6-ring as well as a 5-ring addition process. The latter two (novel) processes are thought to be intramolecular "C-H to C≡C additions" in two directions. The 5-ring addition process was used in a short (but low yield) synthesis of methylenomycin B.

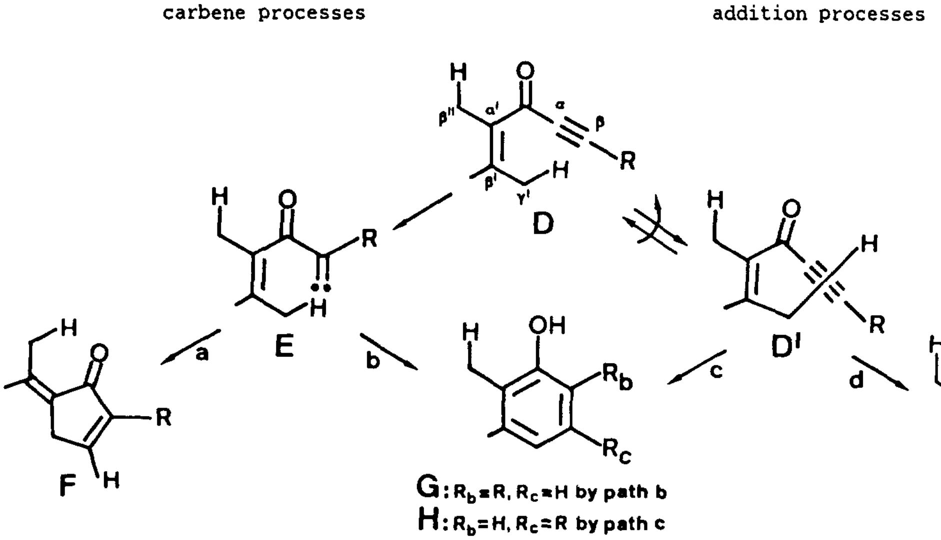
Our previous studies on the thermal cyclization[1] of alkyl alkynyl ketones A̲ showed that the intermediate alkylidene carbene B̲ always inserts into the H-C bond five bonds away, thus leading to 5-ring products C̲ (Scheme 1).

Scheme 1



In our attempts to find examples of a carbene process leading to 6-ring products, we subjected five alkenyl alkynyl or phenyl alkynyl ketones to gas flow thermolysis. These ketones are substituted on the alkenyl or phenyl group with methyl groups in such a way that they all provide H-atoms (vinylogously activated) in the γ'-position and three of them also H-atoms in the β''-position (Scheme 2, formula D̲).

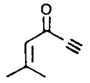
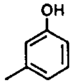
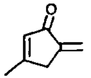
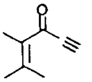
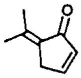
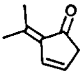
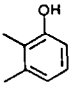
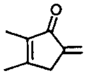
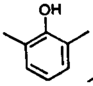
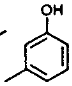
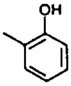
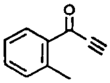
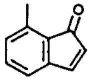
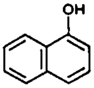
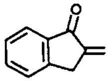
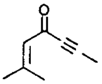
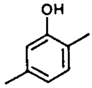
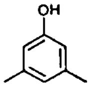
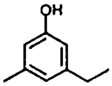
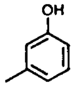
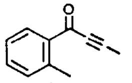
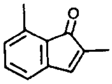
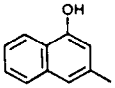
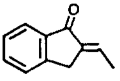
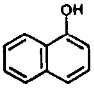
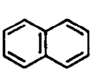
Scheme 2



One carbene process would convert D̲ (via E̲) into the 5-ring products F̲ by path a and the other carbene process would convert D̲ (via E̲ and then dienones) into the 6-ring products G̲ by path b (left side of Scheme 2). We were, however, unable to unequivocally demonstrate the occurrence of path b. Instead, an alternative thermal reaction of these alkynyl ketones D̲ was uncovered, which we call the "addition process": The activated C(γ'),H-bond formally adds across the C(α),C(β)-triple bond; this can occur in two ways, path c leading to 6-ring products H̲ (via dienones) and path d to 5-ring products I̲ (right side of Scheme 2). In most cases the yields were low since paths c and d competed with each other and also, when possible, with path a.

The Table shows in column 1 the starting materials, the propynones 1̲, 4̲ and 9̲ and the butynones 13̲ and 16̲[2], along with the thermolysis temperatures (600 - 800°). The products, all with a newly formed 5- or 6-ring, are listed in columns 2 - 6 according to their likely path of formation, namely path a, b, c, d (see Scheme 2) or "others". We note: 1) The 5-ring products 5̲ + 6̲ (traces), 10̲ (30%), and 17̲ (10%) must have been formed by path a (the α-alkynone cyclization[1]). This shows that path a is followed to some extent in all cases where it is possible. 2) The 5-ring products 3̲ (11%), 8̲ (20%), 12̲ (7%), and 19̲ (2%)[3] must have been formed by path d; i.e. path d is followed to some extent in all cases where it is

Table. Starting materials and products of thermolysis i)ii).

starting material (thermol. temp. °C)	product(s) by path a	b	c	d	others
 1 (660)	not possible	 2 (37%)	iii)	 3 (11%)	
 4 (610)	  5 6 traces	 7 (5%)	iii)	 8 (20%)	   traces (6%)
 9 (720)	 10 (30%)	 11 (24%)	iii)	 12 (7%)	
 13 (700)	not possible	 14 (3%)	 15 (33%)	not found	  (3%) (4%)
 16 (800)	 17 (10%) iv)	not present v)	 18 (7%) iv)	 19 (2%) iv)	  (3%) iv) (10%) iv)

i) The %-numbers in parentheses under the product formulae give the reaction yields, as determined by anal. GC with internal standard and relative response factor, except for the yields from <u>16</u>, for which see iv). ii) The spectral data of all compounds support the structures given here. iii) These products could have been formed by path b or c. iv) These reaction yields were determined by anal. GC without internal standard and response factor (preparative scale separation not possible). v) Proven by anal. GC comparison with an authentic sample of 2-methyl-1-naphthol.

possible, except one. 3) Among the 6-ring products from the butynones **13** and **16**, the phenols **15** (33%) and **18** (7%) must have been formed by path c. The significance of **14** (3%) as sole evidence for path b is not entirely convincing[4]. 4) The 6-ring products **2** (37%), **7** (5%) and **11** (24%), i.e. the phenols formed from the propynones **1**, **4** and **9**, might be the result of either path b or c. Our observation 3 would suggest that these phenols **2**, **7** and **11** are due to path c. However, if the carbene formation from the butynones **13** and **16** (methyl migration) is assumed to be impeded somewhat as compared to the one from the propynones **1**, **4** and **9** (H-migration), then these phenols **2**, **7** and **11** might nevertheless be due to path b. The latter hypothesis appears less likely since the thermolysis of **16** furnished the product **17** of path a, showing the carbene to have been formed[5]. 5) The "others" paths referred to in the last column of the Table may be of a radical disproportionation type.

The second example of the Table (thermolysis of **4**) represents a simple (albeit low yield) total synthesis of the cyclopentenoid antibiotic methylenomycin B (**8**), isolated[6] from a strain of *Streptomyces violaceoruber* and previously synthesized in several ways[7].

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REFERENCES AND NOTES

1. M. Karpf & A.S. Dreiding, Helv. Chim. Acta 1979, **62**, 852. J. Ackroyd, M. Karpf & A.S. Dreiding, Helv. Chim. Acta 1984, **67**, 1963 and references cited therein.
2. All the alkynyl ketones of this work were obtained by the method of L. Birkofer, A. Ritter & H. Uhlenbrauck, Chem. Ber. 1963, **96**, 3280, using the general procedures described in reference 1.
3. Recently, a report appeared on the photochemical transformation of **16** into **19** and its (Z)-stereoisomer; the mechanism proposed there does not follow path d: V.B. Rao, S. Wolff & W.C. Agosta, J. Am. Chem. Soc. 1985, **107**, 521.
4. This is because of the low yield of **14**, because of the proven absence of the corresponding product from the thermolysis of **16**, and because one of the "others" paths cannot be excluded as an explanation for the formation of **14**.
5. Alkylidene carbenes have never been proven to insert forming 6-rings and, to our knowledge, there are only two cases (R.F.C. Brown, F.W. Eastwood, K.J. Harrington & G.L. McMullen, Aust. J. Chem. 1974, **27**, 2393; R.F.C. Brown, F.W. Eastwood & G.P. Jackman, Aust. J. Chem. 1977, **30**, 1757) where a 6-ring carbene mechanism was not ruled out, but both of them allow alternative interpretations.
6. T. Haneishi, N. Kitahara, Y. Takiguchi & M. Arai, J. Antibiot. 1974, **27**, 386.
7. H. Stetter & W. Haese, Chem. Ber. 1984, **117**, 682; M. Mikolajczyk & P. Balczewski, Synthesis 1984, 691 and references cited therein.

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