Tetrahedron Letters No. 27, pp. 2575-2578, 1971. Pergamon Press. Printed in Great Britain.

A NEW SYNTHESIS OF 1,4-DIKETONES: APPLICATION TO THE SYNTHESIS OF CIS-JASMONE[1]

John E. Mc Murry[2] and Thomas E. Glass

Division of Natural Sciences, University of California

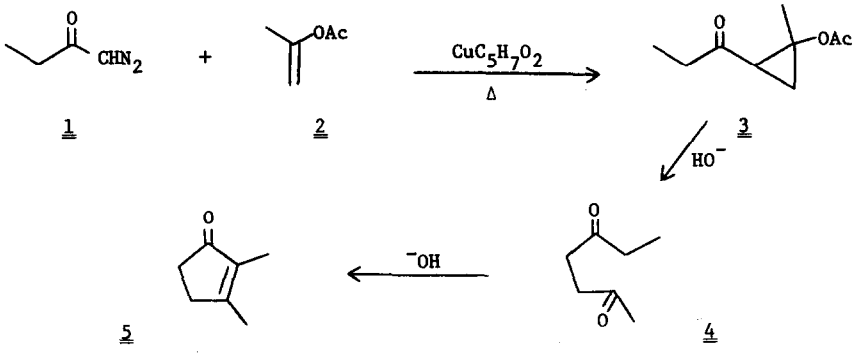
Santa Cruz. California 95060

(Received in JSA 28 April 1971; received in UK for publication 9 June 1971)

1,4-Diketones are useful intermediates for further transformation into cyclopentenones and furans, and, although a considerable amount of quite ingenious effort has been directed toward finding a general route to their synthesis[3], there remains room for improvement. We wish to report one new route to 1,4-diketones and to illustrate its utility in a synthesis of cis-jasmone[4].

In 1957, Sorm and his colleagues[5] demonstrated the feasibility, albeit in low yield, of intermolecular insertion of an α-ketocarbene into the carbon-carbon double bond of various olefinic substrates[6]. In particular, Sorm reported that the copper sulfate catalyzed decomposition of diazoacetone in the presence of isopropenyl acetate gave a 27% yield of 2-acetyl-1-methyl-cyclopropyl acetate. It occurred to us that treatment of the acetoxy-cyclopropyl ketone product with base should cleave it to a 1,4-diketone which, on further base treatment, might then be cyclized to a cyclopentenone[7]. In fact, when the product 3 (26%) resulting from copper sulfate catalyzed insertion of 1-diazo-2-butanone into isopropenyl acetate was refluxed for 1 hr with 4% methanolic NaOH, an 85% yield of 2,3-dimethylcyclo-pentenone was obtained (2,4-DNP, m 226-227°; lit[8] 226-227). Clearly, the critical step in this sequence is the α-ketocarbene insertion, and our initial effort was therefore directed at finding a catalyst which would improve the yield of this step. After an examination of a

large number of possible catalysts, we found that cuprous acetylacetonate[9] was by far the most effective tried and gave, in our model system, a 55% yield of insertion product 3 - a yield improvement of greater than 100% over Sorm's original work. We found cuprous acetylacetonate to be much more effective than any of the other copper catalysts normally used for these insertion reactions, and it would thus seem to be the catalyst of choice for α-ketocarbene + olefin insertions.

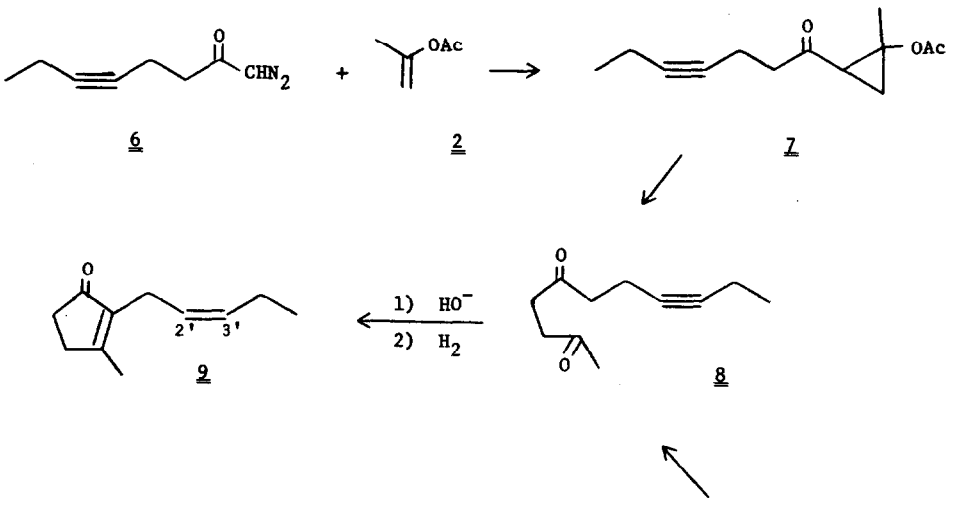


1 2 3 4 5

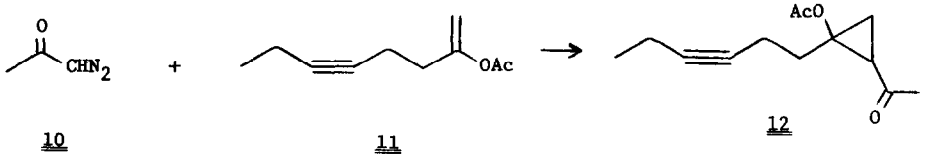
One interesting feature of this synthesis is that the functionality (enol acetate + α-ketocarbene) is interchangeable between the two reactants; i.e. there are always two possible routes to any given 1,4-diketone, and one can choose the easier. For example, in a synthesis of cis-jasmone we need the diketone 8. The two possible syntheses of 8 are given in Scheme 1. Clearly, Path A is the better route since diazoketone 6 can be easily prepared from the known corresponding acid, and since isopropenyl acetate is readily available. In fact, the known[10] 4-heptynoic acid was transformed with oxalyl chloride into its acid chloride and thence, by treatment with diazomethane into diazoketone 6 (90% overall) [ir (film) 2120, 1645 cm^{-1}; nmr (CCl_4) τ 4.30 (s, 1H), 7.54 (broad singlet, 4H), 7.86 (q, 2H, J=7 Hz), 8.91 (t, 3H, J=7 Hz)]. When diazoketone 6 was slowly added to excess isopropenyl acetate at 75° in the presence of cuprous acetylacetonate, insertion occurred and 7 was isolated by chromatography in 35% yield as a mixture of epimers [ir (film) 1750, 1705 cm^{-1}; mass spectrum (80 ev) m/e (rel intensity), 207 (1), 179 (30), 165 (60), 137 (100), 109 (60)]. Refluxing for 2 hr with 4% methanolic NaOH converted 7 into the known[4e] 2'3'-dehydrojasmone (90%) (2,4-DNP, m 165°; lit[4e] 166°). Selective reduction of the triple bond over the Lindlar catalyst[11] then

Path A

Scheme 1



Path B



gave pure cis-jasmone 9 in 95% yield [ir (CCl_4) 1705, 1650 cm^{-1}; nmr (CCl_4) τ 4.78 (m, 2H), 7.16 (d, 2H, J=5 Hz), 7.98 (s, 3H), 9.03 (t, 3H, J=7 Hz); mass spectrum (70 ev) m/e (rel intensity), 164 (M^+, 70), 149 (80), 135 (70), 95 (70), 81 (100)] (2,4-DNP, m 116°, lit[4a] 117.5°).

Although further work needs to be done on the insertion step, we feel that, considering the magnitude of the transformation involved, a 24% overall yield from 4-heptynoic acid to cis-jasmone is certainly acceptable and clearly demonstrates the potential of this new synthesis. We are continuing our exploration of the scope of this method.

Acknowledgement: We thank the Alfred P. Sloan Foundation and the National Cancer Institute of The National Institutes of Health for their support of this work.

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1. This material was presented at the first annual Workshop on Organic Synthesis in Natural Products Chemistry, Santa Cruz, California, August 24-26, 1970.

2. Author to whom inquiries should be addressed.

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