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CYCLOHEXENONES BY THE PHOTOANNELATION OF ALKENES WITH 2,2-DIMETHYL-3(2H)-FURANONE

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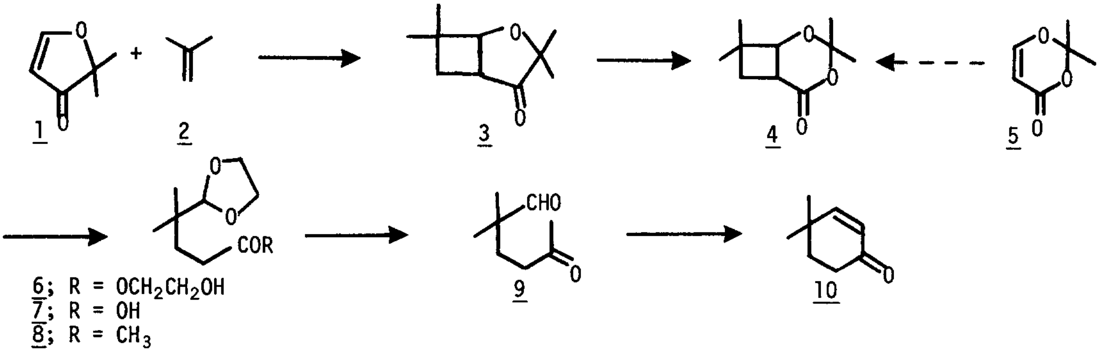
The photoaddition of alkenes to 2,2-dimethyl-3(2H)-furanone affords products which can be efficiently elaborated to cyclohexenones by two different methods.

During the past several years we have been exploring the utility of acyclic α-formyl ketones, particularly formyl acetone, as partners in the photochemical annelation of alkenes. [1-3] Although our results have been encouraging, problems were frequently encountered when a synthetic goal required that either addend in the photocyloaddition reaction contain an additional heteroatom suitable for future elaboration. Specifically these problems consisted of increased reaction times and decreased yields, a general deterioration of chemical efficiency. [4]

It occurred to us that an attractive solution to this problem would be at hand if the formyl ketone partner, or a suitable equivalent, could be maintained in a specific enol configuration by an actual covalent bond. One candidate for such an addend would be a 1,3-dioxolen-4-one, which after photoaddition to an alkene would be suitably arranged for further elaboration. Dioxolenone candidates for photochemical equivalents of formyl acetone are necessarily unsubstituted at the 5 and 6 positions (*eg*. 5) but unfortunately no examples of such compounds can be found in the literature. To date our attempts to prepare pure samples of such compounds have been unsuccessful, although work is continuing.

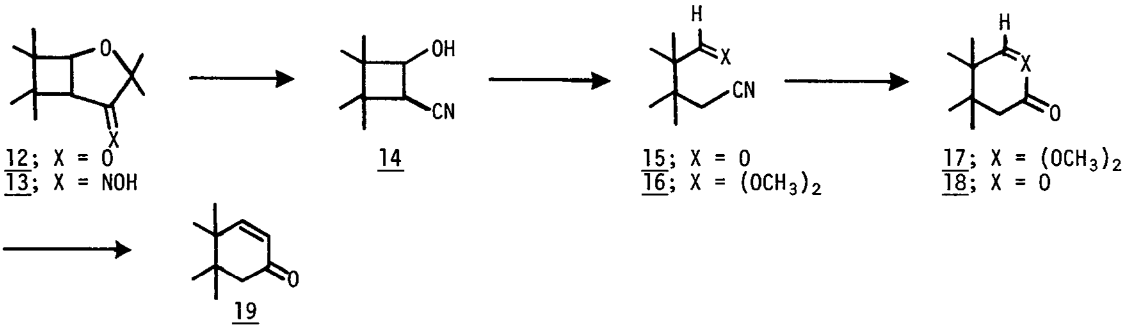
A viable alternative to the 5,6-unsubstituted dioxolenones has been found in 2,2-dimethyl-3(2H)-furanone (1), a compound whose photochemistry with several cyclic and acyclic alkenes has been recently studied by Margaretha. [5] For example 1 reacts with isobutylene to afford an essentially quantitative yield of adduct 3 as a single regiochemical isomer (head-tail). [6,7] Elaboration of photoproduct 3 could then be realized by one of two different reactions sequences. For instance Baeyer-Villiger oxidation of (3) with *m*-chloroperbenzoic acid afforded oxalactone 4 in excellent yield. It is worth noting that lactone 4 is identical to the product which would have arisen by the direct photochemical addition of 2,2-dimethyl-1,3-dioxolenone (5) to isobutylene, thus making the preparation of compounds such as 5 previously mentioned less compelling. Treatment of 4 with ethylene glycol (*p*-TsOH) gave acetal ester 6, the carboxylic acid 7 of which smoothly added methyl lithium to afford methyl ketone 8. [8] Hydrolysis of the acetal group followed by aldol cyclization of 9 yielded 4,4-dimethylcyclohexenone (10) in good yield, the same product obtained as the major regioisomer in the reaction between formyl acetone and isobutlylene followed by aldol cyclization. [1]


1 2 3 4 5

6; R = OCH_2CH_2OH
7; R = OH
8; R = CH_3

9 10

In certain instances the photoproducts from 1 and other alkenes were resistant to Baeyer-Villiger oxidation under a variety of prolonged and forcing conditions. In these cases it proved advantageous to expose the oxime of the photoproduct to Beckmann fragmentation [9] conditions. Thus reaction of oxime 13, derived from the photolysis of furanone 1 and tetramethylethylene (11), with thionyl chloride (CCl_4/0°) smoothly afforded hydroxynitrile 14, which was then ring opened to the cyano aldehyde 15 by exposure to base (NaH/-ether). Treatment of acetal nitrile 16 with methyl lithium [10] followed by a neutral aqueous workup afforded methyl ketone 17 which was then hydrolyzed and cyclized as before to give a good yield of 4,4,5,5-tetramethylcyclohexenone (19), identical with an authentic sample. [1] These and related results for the photoannelation of several alkenes are presented in Table I. With alkenes such as 2, 20, 23, and 26, which can give two regioisomers, the regioselectivity of the photoaddition reaction is always in the same sense as with formyl acetone (eventual aldehyde attached to the more highly substituted alkene carbon, head-tail) but the regiochemical preference is significantly enhanced in the present case, making the method more synthetically viable. In addition the reaction with alkenes containing a variety of functional groups has been shown to occur efficiently, overcoming the major limitation of the formyl acetone photoadditions as mentioned previously.


12; X = O
13; X = NOH

14

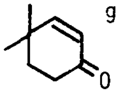
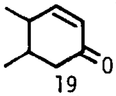
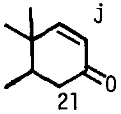
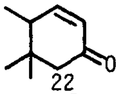
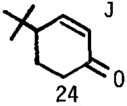
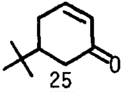
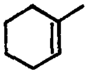
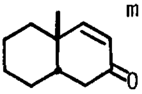
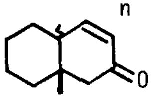
15; X = O
16; X = $(OCH_3)_2$

17; X = $(OCH_3)_2$
18; X = O

19

In summary photoaddition of furanone 1 to a variety of alkenes provides regioselective photoproducts which can be efficiently elaborated to cyclohexenone derivatives by two methods. [11] The application of the reaction sequence to the synthesis of several natural products is underway.

TABLE I. Cyclohexenones from 2,2-Dimethyl-3(2H)-furanone[a]

Alkene	hν, %[b] (ratio)[c]	Acetal, %, from[b]		Cyclohexenone(s)	%, from[b]	
		Baeyer-Villiger[d]	Beckmann[e]		acetal acid	acetal nitrile
 2	95[f]	87	32	 [g] 10	60	74
 11	99[f]	....[h]	60	 [i] 19	....	76
 20	99[f] (3:1)	....[h]	59	 [j] 21 +  22	....	64
 23	68	67	67	 [j] 24 +  [l] 25	60	61
 26	99 (4:1)	....[h]	54	 [m] 27 +  [n] 28	....	71

[a]Footnote 12. [b]Yields are of purified products and have not been optimized. [c]Footnote 13. [d]Combined yield for the four step conversion of photoproduct to acetal acid, eg., 3 → 6. [e]Combined yield for the four step conversion of photoproduct to acetal nitrile, eg., 12 → 16. [f]Footnote 5. [g]Footnote 14. [h]Photoproduct inert to Baeyer-Villiger conditions. [i]Footnote 1. [j]Footnote 15. [k]Footnote 16. [l]Footnote 17. [m]Footnote 18. [n]Footnote 20.

References and Notes

1. S. W. Baldwin, R. E. Gawley, R. J. Doll, and K. H. Leung, J. Org. Chem., 40, 1865 (1975).
2. S. W. Baldwin and R. E. Gawley, Tetradedron Lett., 3969 (1975).
3. S. W. Baldwin, R. E. Gawley, J. M. Wilkinson, K. H. Leung, S. A. Haut, and R. J. Doll, manuscript in preparation.
4. It is likely that the decreased photochemical efficiency in the presence of heteroatoms is associated with a weakening of the intramolecular hdydrogen bond in the formyl ketones by the additional basic and polar heteroatoms, thus permiting energy wasting cis-trans isomerization in the excited state.
5. (a) P. Margaretha, Chimia, 29, 203 (1975); (b) P. Margaretha, Tetrahedron, 29, 1317 (1973); (c) P. Margaretha, ibid., 27, 6209 (1971); (d) P. Margaretha, Tetrahedron Lett., 4891 (1971)
6. The complete regiospecificity (head-tail) of the photoreaction between furanone 1 and isobutylene is to be contrasted with 3/1 regioselectivity (head-tail) observed between formyl acetone and isobutylene. [3]
7. Two interesting reports of the photoaddition of other furanones have appeared. (a) T. Ogino, T. Kubota, and K. Manaka, Chem. Lett., 323 (1976), (b) T. Ogino, K. Yamada, and K. Isogai, Tetrahedron Lett., 2445 (1977).
8. M. J. Jorgenson, Org. React., 18, 1 (1970).
9. R. K. Hill, J. Org. Chem., 27, 29 (1962).
10. A variety of alkyl lithium reagents have been added smoothly to the acetal nitriles to give, after hydrolysis and cyclodehydration, the same 2-substituted cyclohexones which would have arisen from the photoannelation of the corresponding 4-substituted formyl acetone. The procedure for the alkyl lithium addition is an adaptation of the procedure of Saucy. B. A. Pawson, H.-C. Cheung, S. Gurbaxani, and G. Saucy, J. Am. Chem. Soc., 92, 336 (1970).
11. In our hands photoproduct elaboration is generally more convenient by the nitrile route because it can be used in all cases and involves more easily handled intermediates.
12. New photoproducts and important isolated intermediates gave satisfactory elemental analyses (±0.3%). All intermediates and cyclohexenones yielded spectral data consistent with assigned structures.
13. The regiochemical ratios (head-tail/head-head) were determined by analysis of characteristic pmr absorptions of the photoproducts [5] and other intermediates as well as by gc and gc/ms analysis of the final cyclohexenones. The stereochemistry of the furanone cyclobutane ring fusion is cis, with additional but inconsequential stereoisomerism possible at other centers in some cases.
14. R. L. N. Harris, F. Komitsky, Jr., and C. Djerassi, J. Am. Chem. Soc., 89, 4765 (1967).
15. (a) K. L. Cook and A. J. Waring, J. Chem. Soc., Perkin Trans. I, 529 (1973); (b) reference 13.
16. E. W. Garbisch, Jr., J. Org. Chem., 30, 2109 (1965).
17. (a) J. J. Barieux and J. Gore, Bull. Soc. Chim. Fr., 1649 (1971); (b) J. J. Barieux, J. Gore, and J. C. Richer, ibid., 1020 (1974).
18. The structures of cis-octalone 27 and the corresponding trans isomer had been initially transposed [19a,b] because of some very unusual stereochemical results from normally well-behaved reactions. [19c] We thank Professor J. E. McMurry for disclosing details of this problem prior to publication.
19. (a) J. E. McMurry and L. C. Blaszczak, J. Org. Chem., 39, 2217 (1974); (b) D. L. Boger, Tetrahedron Lett., 17 (1968); (c) J. E. McMurry, L. C. Blaszczak, and M. A. Johnson, ibid., 1633 (1978).
20. J. A. Marshall and R. A. Ruden, J. Org. Chem., 37, 659 (1972). We thank Professor Marshall for providing a pmr spectrum of authentic cis-octalone 28.

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