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FACILE SYNTHESIS OF 2-SUBSTITUTED CYCLOPENTENONES

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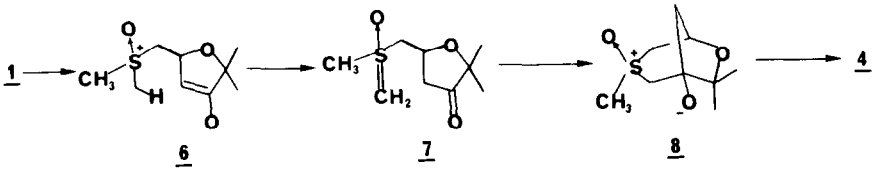
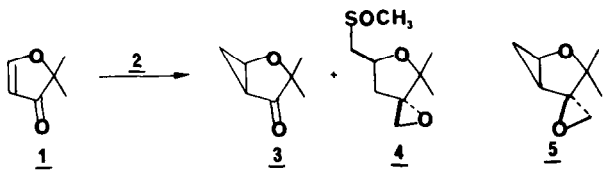
Summary An efficient synthesis of 2-substituted cyclopentenones is reported Key reactions are the cylopropanation of 2,2-dimethyl-3(2H)-furanone and subsequent conversion to the title compounds by oxidative fragmentation.

Recent disclosures from these laboratories have detailed the 2+2 photochemical cycloaddition reaction between various alkenes and 2,2-dimethyl-3(2H)-furanone (1), and the conversion of their photoproducts to substituted cyclohexenones [1a, 2] A reasonable extension of this process would be the formation of cyclopentenones from the corresponding cyclopropanes, compounds which should be available by standard cyclopropanation of 1 Considerable recent interest in synthetic routes to cyclopentenone derivatives is the result of their occurrance in such important classes of natural products as the jasmones, rethrolones, certain prostaglandins, and the methylenomycins (as the 2,3-epoxide), among others [3] Reported here are the results of our preliminary experiments which verify these expectations.

Exposure of furanone 1 to one equivalent of dimethyloxosulfonium methylid (2) in dimethyl sulfoxide followed by a non-aqueous workup afforded two major products, the desired cyclopropane 3 (47%) and sulfoxide 4 (43%) Sulfoxide 4, present as a mixture of sulfur diastereoisomers, was readily removed by washing with water [4] Treatment of 1 with two equivalents of 2 yielded sulfoxide 4 and epoxide 5 (45%), the latter presumably formed by reaction of 3 with excess ylid All attempts to improve the 3/4 ratio were ineffective. For instance, performing the cyclopropanation reaction under phase transfer conditions [5] afforded only trace amounts of 3, sulfoxide 4 being isolated in 87% yield Exposure of 1 to various sulfoximine anions was also unsuccessful [6], as were indirect routes involving methylene transfers to allylic alcohol derivatives However, the modest yield of 3 in the sulfur ylid reaction is offset by its ease of isolation, normal aqueous workup of the cyclopropanation reaction yielding 3 as the sole product

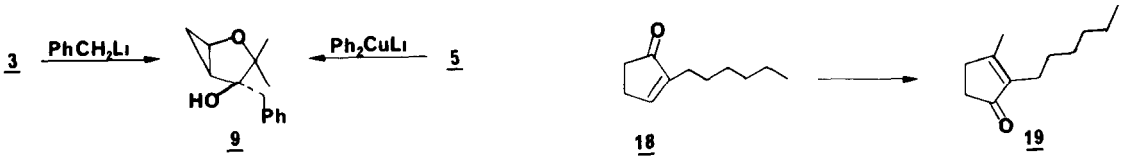


The origin of 4 is of some interest. Intramolecular proton abstraction in Michael adduct 6 would yield a new ylid 7 capable of attack at the carbonyl carbon to give the bicyclic intermediate 8. Collapse of 8 by intramolecular alkylation on oxygen would then afford 4. This general process has been previously noted in the reaction of 2 with acrylates [7]



The conversion of cyclopropane 3 to the desired cyclopentenones could be effected in a manner analogous to that recently reported for the corresponding cyclobutane photoadducts [1a] Addition of a variety of alkyl lithium reagents to the carbonyl of 3 led in good yield to the expected tertiary alcohols 9, which were predominantly the endo alcohol isomers. For those alkyl lithium reagents not commercially available, it was convenient to employ the in situ method for their generation as described by Pearce [8] The tertiary alcohols 9 could also be prepared from the cyclopropane epoxide 5 by direct reaction with a lithium dialkyl cuprate [9] For instance, alcohol 9 was formed either by reaction of 3 with benzyl lithium [10] or by treatment of 5 with lithium diphenyl cuprate. This dual route to the tertiary alcohols offers considerable flexibility in the choice of the organometallic reagent which might be required for a particular synthetic application. Nitrosation of the alcohol mixtures in the usual manner (NOCl, -20°, pyridine) followed by irradiation of the crude pentane extracts (450 watt lamp, pyrex) and concentration led to the 1,4-keto aldehydes 16 which were directly cyclized by one of several procedures [11] to give the 2-substituted cyclopentenones 17 in good yield (Table I). This Barton fragmentation [12] procedure has been previously applied to several furanone/alkene photoadducts [1a] It is likely that the reaction proceeds by fragmentation of the initially formed alkoxy radical 12 to give nitroso ether 13 followed by a retroaldol cyclopropane cleavage to give the observed products The exact details remain to be elucidated.

It is worth noting that cyclopentenone 18 (entry 4) can be converted to dihydrojasmone (19) in two steps as has been previously reported by Buchi [13] Thus, the five step conversion of 2 to 19 can be accomplished in 52% overall yield, making the process competitive with the best procedures currently in the literature



In conclusion, the chemistry reported herein offers a general solution to the synthesis of variously substituted cyclopentenones. The ready accessibility of differently substituted 3(2H)-furanones [14] and the possibility that substituted sulfur ylids can be employed in the cyclopropanation step suggests that a wide spectrum of cyclopentenone derivatives can be secured by this general procedure [15, 16].

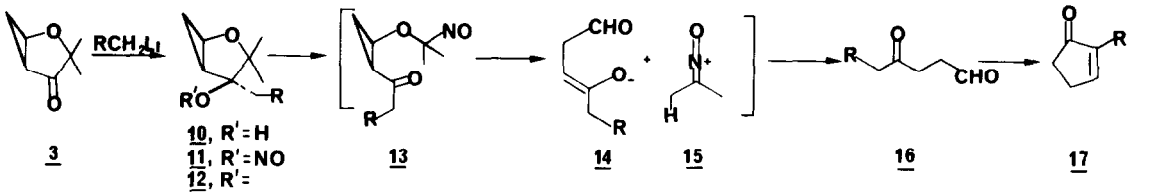


TABLE I. Formation of 2-Substituted Cyclopentenones

entry	RCH_2		alcohol (%)	cyclopentenone (%)
1	n-C_4H_9	(A)	87	70[d]
2	i-C_4H_9	(B)	85	89[e]
3	n-C_8H_{17}	(B)	75	60[f]
4	n-C_6H_{13}	(B)	72	80[g]
5	$CH_2C_6H_5$ [h]		79	85[i]
6	C_6H_5	(A)	61	--[j]

a) Organolithium reagents were either commercially purchased (A) or prepared *in situ* (B), reference 7 b) *Endo/exo* alcohol ratio ranged from 95/5-67/33. c) Combined yield for nitrosation, irradiation, and cyclodehydration (1% NaOH/ether biphase, reference 11a) d) Reference 17. e) Reference 18 f) Reference 19. g) Reference 20 h) Reference 10 i) Reference 21 j) Yield of keto aldehyde was 98%, reference 22

References and Notes

1. (a) Paper No. XI in the series. For X see S. W Baldwin and H R Blomquist, Jr , *J. Am. Chem Soc* , in press, (1982), (b) financial support from the National Institutes of Health (GM 26266) is acknowledged with appreciation.

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4. All new compounds gave satisfactory elemental analyses and spectral data in accord with the assigned structures The isomeric sulfoxides 4 were converted to a single sulfone on oxidation with hydrogen peroxide/acetic acid

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