

FREE RADICAL FRAGMENTATION OF
DERIVATIVES OF [2 + 2] PHOTOADDUCTS

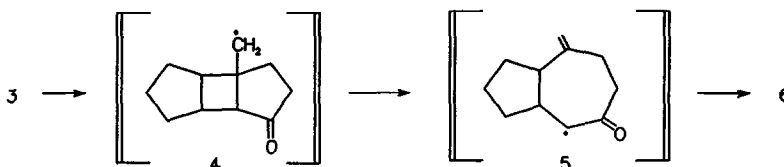
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ABSTRACT: Conversion of [2 + 2] photoadducts to iodoketone derivatives followed by free radical fragmentation of the cyclobutylcarbinyl moiety gives ring systems which are present in a variety of terpenoid natural products.

Adducts derived from mixed [2 + 2] photoadditions have been employed in a variety of ways for the synthesis of natural product carbon skeletons.¹ Normally the further transformation of the adducts involves ionic² or thermal reactions³ while free radical processes have received much less attention.^{4,5} In this letter we describe the free radical fragmentation of photoadduct derivatives which lead to carbon skeletons of particular interest in terpenoid synthesis.

The adducts derived from four different combinations of cycloalkenone and cycloalkene were examined in this study. First, photoaddition⁶ of enone ester 1 with cyclopentene gave the known adduct 2 as a 9:1 anti:syn mixture (cis ring fusions).² The adduct was then converted to the iodide 3 using methodology previously reported in our ionic studies of these substrates.² The sequence involved ketalization, reduction of the ester group, hydrolysis of the ketal and conversion of the neopentyl alcohol moiety using an improved, mild iodination procedure employing iodine, triphenylphosphine and imidazole in dichloromethane.⁷ In the crucial free radical step it was anticipated that the primary radical (4) formed initially from 3 would undergo fragmentation before reduction because of the strain of the cyclobutylcarbinyl system and because of the stability provided by the carbonyl group in the radical 5 formed after fragmentation. In the event, treatment of 3 with tributyltin hydride (TBTH) and a catalytic amount of AIBN in benzene for 1.5 hours gave in 90% yield the desired cis fused product



6.⁸ It should be noted that the 9:1 anti:syn mixture of adduct 2 is of no consequence as that stereochemistry is lost in the fragmentation reaction. Product 6 possesses the 5-7 ring system present in the guaiane (and pseudoguaiane) sesquiterpenoids and many of these natural products also have a methylene substituent at the 6-position.⁹ The carbonyl group at the 3-position in 6 is strategically situated for introduction of the isopropyl moiety present in guaianes and if the alkene component in the photoaddition is a cyclopentenone ketal then a protected carbonyl group ends up at the 10-position where an additional carbon is required to complete the sesquiterpenoid skeleton. In addition, if a homochiral ketal of cyclopentenone is employed in the irradiation then all the products in the sequence would be optically enriched.¹⁰

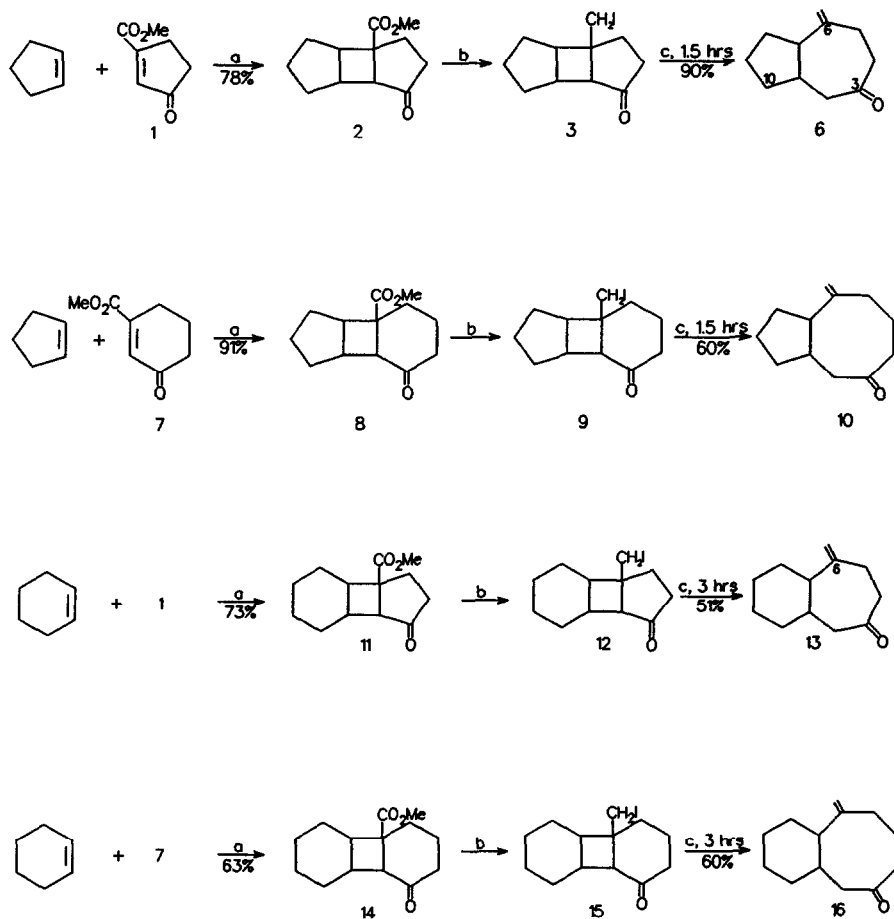
Next we investigated the adduct formed by photoaddition of enone 7 with cyclopentene. Adduct 8 was formed in high yield as an 87.13 anti:syn mixture (cis ring fusions) as reported previously.² 8 was converted as described above to iodide 9, which was then treated under the usual conditions with TBTH to give a 60% yield of cis fused product 10. Although 3 would be expected to be more strained than 9, in the latter iodide there is still a sufficient driving force to give the fragmentation product in reasonable yield. The 5-8 ring system in 10 is also present in the asteriscane sesquiterpenoids¹¹ and the ophiobolane sesterterpenoids.¹²

The third adduct, 11, was prepared in 73% yield by irradiation of enone 1 with cyclohexene. In the manner described above, 11 was converted to iodide 12 which upon treatment with tributyltin hydride gave cis fused 13 in 51% yield. The 6-7 ring system of 13 is present in the himachalane sesquiterpenoids and in particular, α -himachalene has a methylene substituent at the 6-position.¹³ With this system, employing a homochiral ketal of cyclohexenone (rather than cyclohexene) in the photoaddition step would again lead to optically enriched products.¹⁰

Finally, photoaddition of enone 7 and cyclohexene gave adduct 14 which was converted to iodide 15. This iodide would be expected to be the least strained of the four investigated, but upon treatment with tributyltin hydride it gave in 60% yield the fragmentation product 16 with a 6-8 cis fused ring system.

In conclusion, the free radical fragmentation methodology of cyclobutylcarbinyl systems outlined in this communication shows great promise for the synthesis of a number of terpenoid carbon skeletons either in racemic or optically enriched form. Approaches to the synthesis of several natural products which apply and extend this methodology are now under investigation.

Scheme: Conversion of Photoadducts to Fragmentation Products



Reagents: (a) hu, CH_2Cl_2 (b) (1) $\text{HOCH}_2\text{CH}_2\text{OH}$, H^+ (2) LiAlH_4 , ether
 (3) H_3O^+ (4) I_2 , Ph_3P , imidazole, CH_2Cl_2 , R.T.
 (c) $(n\text{-Bu})_3\text{SnH}$ (1.5 equiv.), AIBN (0.02 equiv.), benzene, reflux.

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