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REACTIONS OF METHYL β-VINYLACRYLATE WITH β-DICARBONYL COMPOUNDS--A NEW ROUTE TO FUNCTIONALIZED BRIDGED RING SYSTEMS[1]

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The 1,6-addition of nucleophiles to activated butadienes was first demonstrated by Kohler and Butler (1) in the reaction of sodiomalonic ester with methyl β-vinylacrylate(I). The early literature has been reviewed by Ralls(2). The purpose of this communication is to report two new modes of reaction of I with nucleophiles, which involve subsequent intramolecular 1,4-addition of a prototropic derivative of the initial 1,6 addend, as the ring forming step(3).

Dimedone(II) is converted to its conjugate anion, III, through the action of the dimethylsulfinyl anion(4) in dimethylsulfoxide ($DMSO^-$ -DMSO). Reaction of the anion with the ester; I, for four days at 75-80°, gives a 95% yield(5) of a product $bp_{0.2mm}$ 118-119°, to which structure VI is assigned on the basis of its combustion analysis (Found: C,66.71; H, 8.08%) and spectral properties. Its infrared [$\lambda_{max}^{CCl_4}$ 5.75(ester C=O), 6.05, 6.15 (vinylogous ester, double bond)μ], ultraviolet [$\lambda_{max}^{95\%EtOH}$ 259(ϵ = 12,300)mμ] and mass(6) [m/e 252 (parent and base peak), 179($P-CH_2CO_2Me$)] spectra are all consistent with the above formulation. Particularly decisive is its 100 Mc nmr spectrum, which, in addition to demonstrating the absence of vinylic hydrogens, the presence of a methyl ester (τCCl_4 6.32, 3H, singlet) and non-equivalent methyl groups (τ8.92, 3H, singlet; τ8.97, 3H, singlet), contains a 1H multiplet (τ5.5-5.8) which is assigned to H_X and a 2H eight line pattern (τ7.27-7.62) which is assigned to $H_A(\tau_A 7.37)$ and $H_B(\tau_B 7.50)$ with $|J_{AB}|=16$ cps , J_{AX} = 8 cps and J_{BX} = 6 cps. An 8H multiplet from τ7.7-8.6 accounts for the remaining protons.

Similarly, dihydroresorcinol is converted under the same conditions to compound VII, mp 53-54°, in 54% yield(5). These data are summarized below, and a likely pathway for the formation of VI is indicated.

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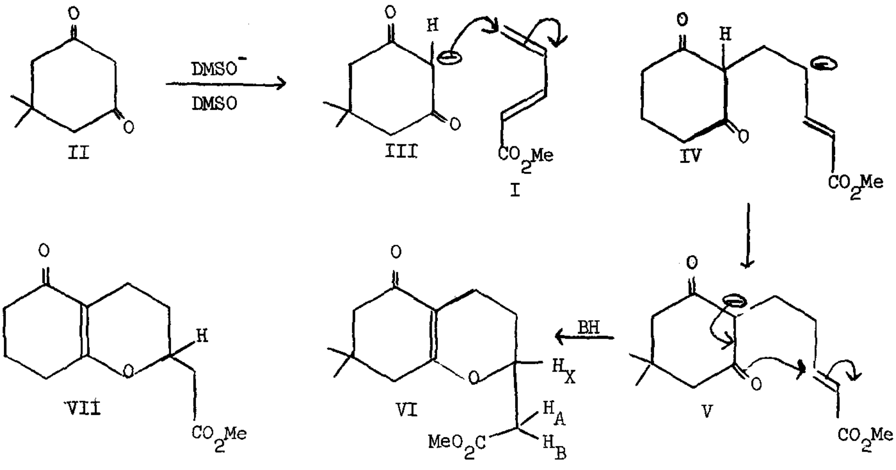
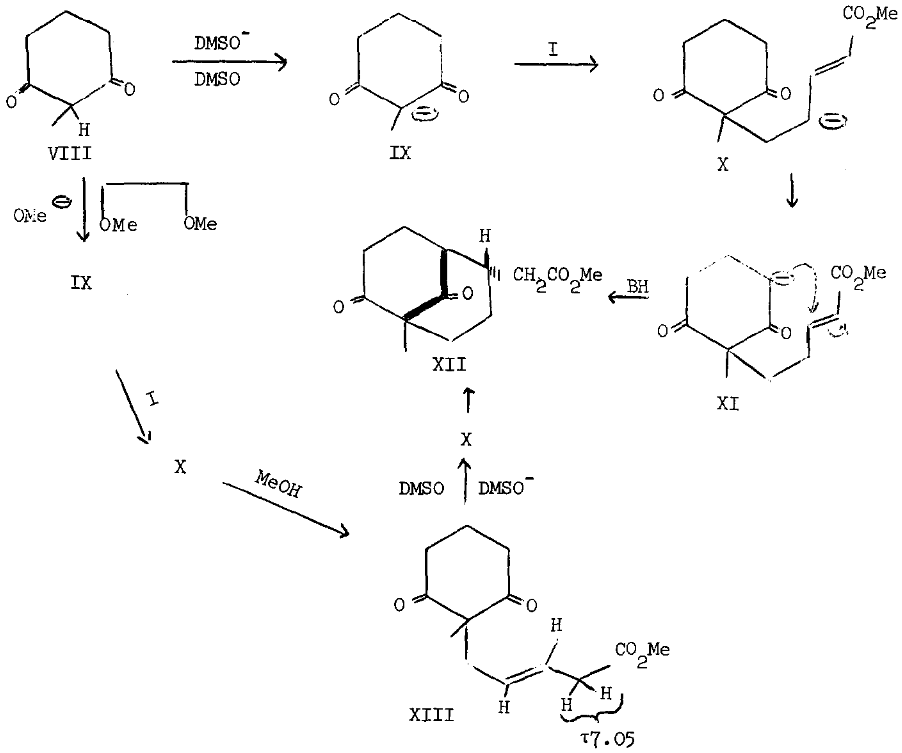
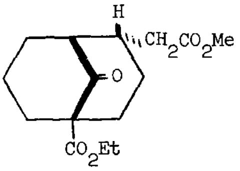


It was of interest to test the result in a system where interconversion of an extended enolate such as IV, with a β-dicarbonyl anion such as V, is structurally blocked. Reaction of methyldihydroresorcinol(VIII) with DMSO$^-$-DMSO gives the anion, IX, which upon reaction with compound I for 4 days at 75-80° gives a 42%(5) yield of an adduct, bp$_{0.18}^{mm}$ 117-119°, to which structure XII is assigned on the basis of its combustion analysis (Found: C, 75.40; H, 7.66%) and infrared (7,8,9) [$\lambda_{max}^{CCl_4}$ 5.75, 5.84μ], nmr [τ_{CCl_4}=6.40(3H, singlet) 7.1-8.8(12H, multiplet), 8.90(3H, singlet)] and mass(10) [m/e 238(parent), 165(P-CH$_2$-CO$_2$Me) and 109(base peak)] spectra. Confirmatory evidence for the assignment comes from the fact that this compound is formed from the reaction of XIII with DMSO$^-$-DMSO. Compound XIII, bp$_{0.2}^{mm}$ 124-125°, was itself obtained in 50%(5) yield from the reaction of the anion IX, formed from VIII, via sodium methoxide in monoglyme, with the ester,I. The structure assignment of XIII follows from its infrared (7,8) [$\lambda_{max}^{CHCl_3}$ 5.77, 5.88, 6.0(C=C) and 10.3 $({}_{H}{>}C{=}C{<}^{H})\mu$] nmr [$\tau_{CCl_4}$=4.2-5.0(2H, multiplet), 6.4(3H, singlet), 7.05(2H, doublet J=7 cps), 7.3-8.4(8H, multiplet), 8.9(3H, singlet)], and mass(11) [m/e 238(parent), 109(base peak)] spectra. The β-γ, rather than α-β, disposition of the double bond(12) in XIII follows from the overlap of the two vinylic absorptions and from the relatively low field doublet, τ7.05, which is the result of combined deshielding of the adjacent ester and double bond functions.

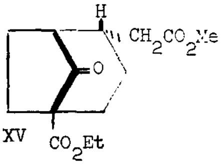
The stereochemistry of compound XII has not been determined with certainty, but we tentatively assign the configuration of the methylacetate chain to be cis to the three carbon bridge, thereby enabling it to assume an equatorial disposition in the chair-chair system(13). Since Michael reactions are generally reversible, the most stable product would be expected.

Reaction of carbethyoxycyclohexanone with DMSO$^-$-DMSO, followed by reaction with compound I gave a 76%(5) yield of the bridgehead β-ketoester, XIV, bp$_{0.4mm}$145-146°, (DNP: mp 126.5-127). Its combustion analysis (Found: C, 64.13; H, 8.03%), infrared [$\lambda_{max}^{CCl_4}$ 5.75(ester C=O) 5.83(ketone C=O)μ], nmr [τ6.02 (2H, quartet, J=7 cps), 6.5(3H, singlet), 7.2-8.9 (17H, multiplet, containing a triplet, J=7 cps, centered at τ8.8)], and mass [m/e 282(parent), 107(basic peak)] spectra are consistent with the assignment. Similarly, carbethoxycyclopentanone under the same conditions gives XV, bp$_{0.5mm}$122-123°, (DNP mp 135-136°) in 35%(5) yield. The stereochemistry of XIV and XV is postulated on similar grounds to that of XII. These results are summarized, and a plausible route to the bridged systems is suggested (14,15).





XIV



XV

This method appears to be very promising for the synthesis of multiply functionalized bridged ring systems. Studies designed to exploit this one step entry are in progress.[16]

References

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3. For previous examples of the formation of bridged ring systems via intramolecular Michael addition, see: (a) E. J. Corey, M. Ohno, R. B. Mitia, and P. A. Vatakancherry, J. Am. Chem. Soc., 86, 478 (1964) and (b) R. B. Woodward, F. I. Brutschy, and H. Bair, ibid., 70, 4216 (1948).

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5. The reactions were conducted with a 2:1:1 ratio of β-dicarbonyl cpd.: base: ester, I. Thus the dicarbonyl system serves as the proton donor (BH). The yields are based on compound I. The unreacted β-dicarbonyl compound is recovered through basic extraction;

6. The mass spectra were obtained from an LKB-9000 instrument by Mr. John Nawarol.

7. Since β-diketones generally(8) and of this type(9), are known to give rise to two carbonyl stretching absorptions, the peak at 5.74μ in structure XII is a composite arising from the ester and ketone functions, while the peak at 5.84μ is due only to the ketone. The relative intensities, 5.74>5.84 are in accord with this supposition. Similarly, the peak at 5.77μ in structure XIII is a composite peak.

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10. The structure of the base peak, 109 in XII and XIII, has not been established.

11. Of all the compounds in this series, only XIII fails to give a P-CH$_2$CO$_2$Me cleavage product in its mass spectrum. This is in accord with the difficulty associated with cleavage at a vinyl position.

12. The presence in the reaction mixture of ca. 12% of a corresponding α-β unsaturated isomer was indicated from examination of the spectral properties of a partially purified sample. This compound was not obtained in pure form.

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14. It is interesting to note that no products of cycloaddition similar to those obtained from the reaction of enamines(15) with compounds I, were encountered in these studies.

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16. For a recent example of a one-step entry to the bicyclo[3,3,1]nonane system, see reference 9.