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A SIMPLE SYNTHESIS OF DIHYDROJASMONE+

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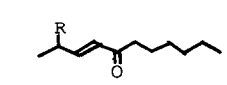
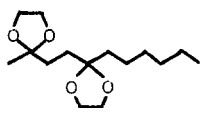
Abstract: Acetalization of a γ-substituted α,β-unsaturated ketone, followed by acid hydrolysis gave a cyclopentenone.

It is well-known that acid-catalyzed acetalization of alicyclic α,β-unsaturated ketones proceeds with concomitant migration of the double bond[1]. If acyclic γ-alkoxy enones undergo double bond isomerization during acetalization, the product should be 1,4-diacetals, valuable precursors to 1,4-diketones and cyclopentenones. This communication reports the utility of such an acetalization process in a synthesis of dihydrojasmone 8[2].

Bromination[3] (1 equiv. NBS, CCl_4 reflux, 1.5 h) of 3-undecen-5-one 1[4] gave the bromo enone 2[5] (95% yield). Addition of 2 to a mixture of anhydrous cupric bromide[6] (2 equiv.) and pyridine (5 equiv.) in MeOH[7] at -30° resulted in a green mixture which was then stored at room temperature (14 h) to give γ-methoxy enone 3[5] in 80% yield. Acetalization (ethylene glycol, toluene or benzene, TsOH, 20 h) of 3 afforded 1,4-diacetal 4[5], as expected. However, the product was contaminated with another acetal (20-50%) which was difficult to separate. The by-product was eventually identified as 5 through its hydrolysis product 6[5]. Thus, the mixture of acetals was hydrolyzed (0.5 N HCl, EtOH, rt) and the resulting ketones containing the well-known undecan-2,5-dione 7[2] were treated with alkali to give rise to a separable mixture of dihydrojasmone 8 and dioxane ketone 6[5]. We anticipated that the formation of 6 could be made reversible, and indeed 6 was converted into dione 7 in 75% yield when refluxed with conc. HCl in benzene for 18 h.



1 R=H
2 R=Br
3 R=OCH_3



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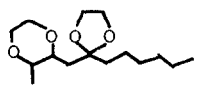

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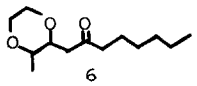

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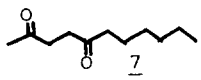

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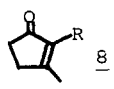

8 R=n-C_5H_{11}
9 R=n-C_4H_9

+ Dedicated to Professor Yau-Tang Lin on the occasion of his 70th birthday.

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Acetalization of the bromo enone 2 afforded exclusively the dioxane acetal 5 which arose presumably from displacement of bromide by ethylene glycol, followed by a Michael-type reaction and acetalization of the intermediate ketone 6. Acetal 5 was refluxed in a solution of acetic acid and conc. hydrochloric acid (1:1) to give dihydrojasmone 8 in 45% overall yield from enone 1. Dione 7 was shown to be the initial product by GC analysis and was isolable. The acid-catalyzed aldol condensation of dione 7 yielding dihydrojasmone 8 is rarely documented.

Similarly, dihydrocinerone 9[8] was prepared from 3-decen-5-one in 40% overall yield.

The facile formation of 2,3-disubstituted dioxane derivatives in the enone → diketone transformation may find use in the syntheses of heterocyclic systems.

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References and Notes

1. See, for example, J. A. Marshall, M. T. Pike and R. D. Carroll, J. Org. Chem., 31, 2933 (1966).

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3. cf. C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann and J. Pataki, J. Amer. Chem. Soc., 72, 4534 (1950).

4. I. G. Tishchenko, V. N. Sytin and I. F. Revinskii, Zh. Org. Khim., 13, 1154 (1977); C. A. 87, 102095y (1977). Enone 1 was also conveniently prepared from propionaldehyde and dimethyl (2-oxooctyl)phosphonate (NaH, THF, 20°, 2h) in 87% yield, bp 70°/1 mmHg.

5. Bromo enone 2, IR (film) 1680,1635 cm^{-1}, NMR ($CDCl_3$) δ 1.8 (3H, d,J=6 Hz), 4.73 (1H,m), 6.17 (1H,d,J=16 Hz), 6.9 (1H,dd,J=16,8 Hz); γ-methoxy enone 3, bp 80-33°/0.6 mmHg, IR (film) 1685,1640 cm^{-1}, NMR ($CDCl_3$) δ 1.27 (3H,d,J=6.5 Hz), 3.3 (3H,s), 3.93 (1H,m), 6.2 (1H,d,J=16 Hz), 6.72 (1H,dd,J=16,6 Hz); diacetal 4, NMR ($CDCl_3$) δ 1.68 (4H,s),3.82 (8H,s); dioxane ketone 6, bp 89-90°/0.1 mmHg, IR(film) 1710, 1110 (strong) cm^{-1}, NMR ($CDCl_3$) δ 1.08 (3H,d,J=6 Hz),3.67 (4H,s), 3.2-4.2 (2H,m), HRMS m/z calc. for $C_{13}H_{24}O_3$: 228.1725; found 228.1700.

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