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ACETOLYSIS OF THE EPIMERIC 3,3-DIMETHYL-7-TOSYLOXYBICYCLO[2.2.1]HEPTAN-2-ONES

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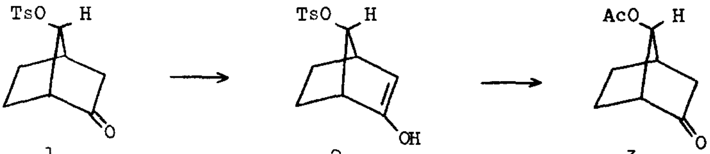
Recently we reported that the rate determining step in the unusually rapid solvolysis of anti-7-tosyloxybicyclo[2.2.1]heptan-2-one (1) was the conversion of 1 into its enol, 2. The enol then ionized in a fast step to give an intermediate which collapsed to give 3 with complete retention of stereochemistry in the 7-position.[1] In contrast 4 solvolyzed at a relatively slow rate to give a mixture of 5 and 6 with 95% of inversion of stereochemistry at C-7.[2] Although this complete difference in solvolytic behavior was instructive insofar as it illustrated the role of enolization in carbonyl participation, it failed to provide an insight into the chemical consequences of the stereochemical relationship between a nonenolized carbonyl group and a leaving tosylate function. We now wish to report on the acetolysis of 3,3-dimethyl-anti-7-tosyloxybicyclo[2.2.1]heptan-2-one (7) and 3,3-dimethyl-syn-7-tosyloxybicyclo[2.2.1]heptan-2-one (8), an epimeric pair, which have nonenolizable carbonyl groups.



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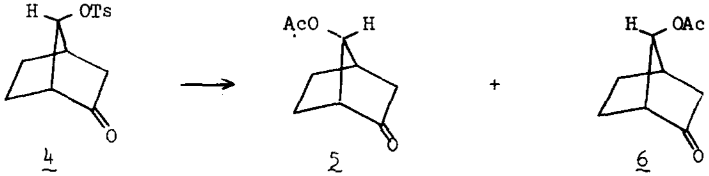

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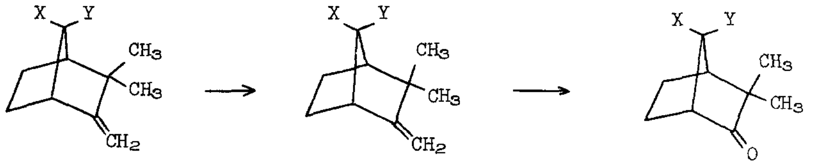
The epimeric alcohols, 9 and 10, as prepared from d,l-camphor,[3,4] were converted into the corresponding acetates and tosylates.[4] Ozonolysis of the epimeric pairs 11 and 12, and 13 and 14 gave 7, 8, 15, and 16, respectively, in 57, 25, 87, and 79% yields, respectively.[5]



9, X = OH, Y = H
10, X = H, Y = OH

11, X = OTs, Y = H
12, X = H, Y = OTs
13, X = OAc, Y = H
14, X = H, Y = OAc

7, X = OTs, Y = H
8, X = H, Y = OTs
15, X = OAc, Y = H
16, X = H, Y = OAc

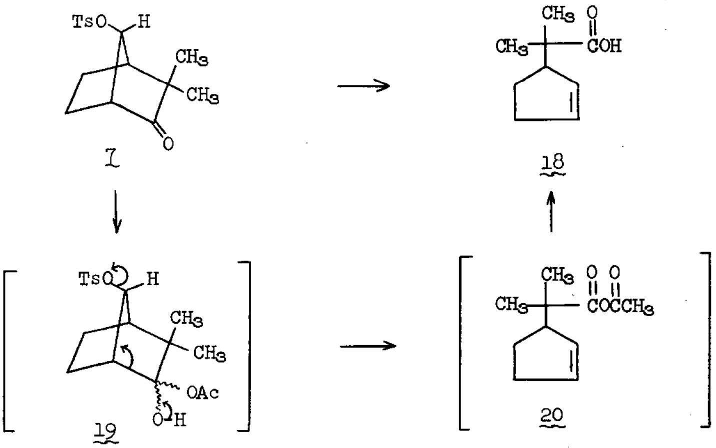
Table I lists the rates of acetolysis of 7, 8, 4, and 7-norbornyl tosylate (17). As noted 7 solvolyzes ca. twenty times faster than 8. Both 4 and 8 solvolyze slower than 17, as would be expected since the inductive effect of the carbonyl function should have a rate retarding influence. The only unusual feature of the rate comparison was that of the four compounds compared, 7 had the fastest rate, even though the presence of the carbonyl function might have been expected to exhibit a rate decreasing effect. It remained for the product studies to show whether 7 was five times faster than 17 and twenty times faster than 8 due

Table I. Acetolysis Rates of 7-Norbornyl Tosylates

Compound	Ref.	Temp. (°C)	Rate (sec^{-1})	$k_{rel}^{@}$ 200°	$\Delta H^{\ddagger}$ (kcal/mole)	$\Delta S^{\ddagger}$ e.u.
7		210.0 ± 0.1	$(7.12 \pm 0.09) \times 10^{-4}$			
		200.0 ± 0.1	$(3.03 \pm 0.03) \times 10^{-4}$	56	34.6	-2.4
		190.0 ± 0.1	$(1.43 \pm 0.01) \times 10^{-4}$			
8		220.0 ± 0.1	$(7.02 \pm 0.08) \times 10^{-5}$			
		210.0 ± 0.1	$(3.24 \pm 0.03) \times 10^{-5}$		34.4	-8.8
		200.0 ± 0.1	$(1.52 \pm 0.02) \times 10^{-5}$	3		
4	6	200.0 ± 0.1	$(5.45 \pm 0.19) \times 10^{-6}$	1	34.9	-9.8
7-Tosyloxynorbornane (17)	7	200.0	5.49×10^{-5}	10	35.7	-3.5

to dipole-dipole interactions or due to the intermediacy of an alternate mechanistic route.

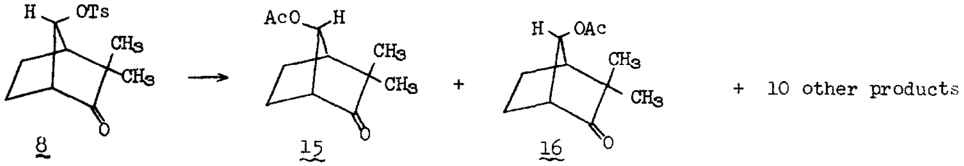
When 7 was solvolyzed in acetic acid buffered with sodium acetate at 200° only one product could be isolated. Infrared spectroscopy demonstrated that this product was an acid.



Mechanistic considerations suggested that this acid was probably (Δ-2-cyclopentenyl)-2,2-dimethylacetic acid (18). This assignment was verified by the nmr spectrum of 18 which showed the two methyls adjacent to the asymmetric center[8] as three proton singlets at τ 8.83 and 8.88, a broad one proton multiplet centered at τ 6.90 due to the tertiary allylic hydrogen, a broad two proton multiplet at τ 8.19 due to the non-allylic methylene protons, and a multiplet at τ 7.60 (two protons) due to the allylic methylene protons. The vinyl protons appeared as multiplets at τ 4.12 and 4.32 (one proton each). When either the multiplet at τ 6.90 or 7.60 was irradiated the multiplets due to the vinyl protons were simplified, and when both multiplets (τ 6.90 and 7.60) were irradiated simultaneously, the vinyl proton multiplets collapsed to an AB quartet with a coupling constant of 6 cps. In general the vinyl hydrogen pattern was the same as that which has been established as being characteristic of 3-substituted cyclopentenes.[9]

The formation of 18, as the sole isolable product (67% yield), could occur *via* concerted ionization and bond breakage in 7 to yield an acylium ion, which, on reaction with the nucleophilic solvent would give 20. Under the work-up conditions 20 would be expected to hydrolyze to 18. A more likely mechanistic path would involve formation of 19 through the addition of acetic acid to 7 followed by concerted cleavage-ionization to give 20 directly.

The acetolysis of 8 in sodium acetate buffered acetic acid at 200° led to considerable decomposition. Even at very short reaction times the acetolysis of 8 led to a mixture of twelve products. Fortunately ca. 50% of the reaction mixture was 15 and ca. 20% was 16.



Since the reaction products were determined at less than 5% reaction for 8, little significance can be placed on the exact percentages of 15 and 16. However it is safe to say that the acetolysis of 8 occurred with predominant inversion of stereochemistry.

The dramatic difference in the products formed from 7 and 8 clearly demonstrated that the stereochemical relationship between the carbonyl group and the ionizing function can have an overwhelming effect on the reaction path. The relatively small rate difference between the acetolysis of 7 and 8 indicated that the energetics of the two different reaction routes were surprisingly similar.

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