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RADICAL CHEMISTRY BASED ON (+)-CIS-PINONIC ACID

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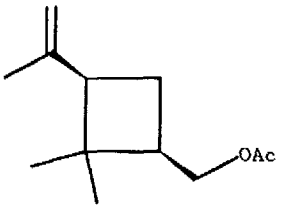
Summary. The capture of the radical from decarboxylation of (+)-cis-pinonic acid has been investigated. Efficient trapping agents give good yields of desired products. Less efficient trapping conditions permit undesired opening of the four-membered ring.

Recently Wolk, Goldschmidt and Dunkelbaum[1] reported an elegant synthesis of the sex pheromone of the citrus mealybug. This compound, the acetate 1, was obtained from (+)-cis-pinonic acid 2, itself readily available from (+)-α-pinene. The final stage was methylenation of the ketone function with the Wittig reagent.

A key step in this synthesis was the conversion of the acid 2 into the nor-bromide 3. Now we have recently shown[2] that the acyl derivatives of thiohydroxamic acids are an excellent source of carbon radicals. Typical thiohydroxamic acids for this purpose are N-hydroxy-2-thiopyridone 4 and the thiazoline derivative[3] 5. Acyl derivatives of these reagents are efficiently converted into, say, the corresponding nor-bromides in the presence of $BrCCl_3$ or CBr_4, or nor-chlorides with CCl_4.

Dr. J. L. Wolk (Bar-Ilan University) kindly informed us that the cis-pinonic acid derivative of 5 did not undergo the desired reaction on irradiation in CCl_4 under reflux. With the encouragement of Dr. Wolk and his colleagues, we have investigated the reason for this failure. For convenience, we worked with the cis-pinonic acid derivative of 4. Preparation through the acid chloride provoked epimerisation of the ketone, but using D.C.C. the derivative 6 was readily obtained (72%) (yellow crystals from CH_2Cl_2, m.p. 107-108°). Irradiation of a solution of 6 in $BrCCl_3$ at room temperature with a tungsten lamp afforded the desired bromide[1] 3 (84%).



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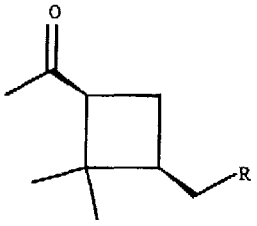
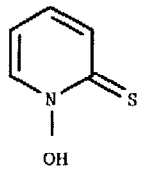


2 R=COOH
3 R=Br
6 R=CO-O-N
7 R=SePh
8 R=S-2-Pyridyl
11 R=OH
12 R=OAc



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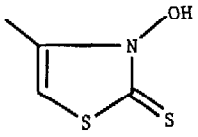

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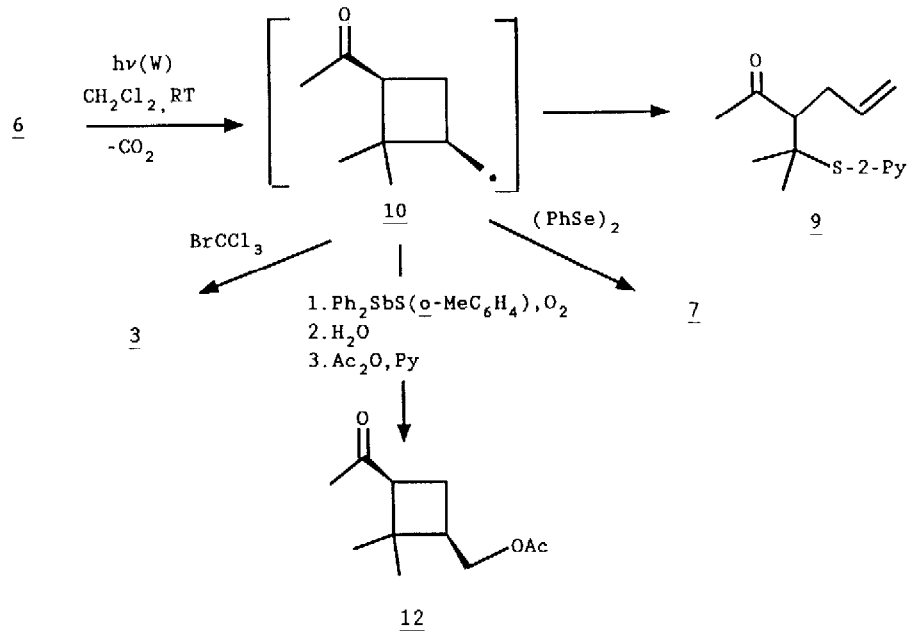
Diphenyldiselenide is an excellent trap for radicals.[4] Photolysis of 6 (0.38 mmol) in CH_2Cl_2 in presence of $(PhSe)_2$ (0.38 mmol) gave the phenylselenide 7 (98%)

The acyl derivatives of 4, in the absence of a radical trap, undergo decarboxylative rearrangement to give 2-pyridylsulfides. When derivative 6 in CH_2Cl_2 was photolyzed alone at room temperature, it afforded some (8%) of the expected pyridyl sulfide 8, but the major product was the vinyl derivative 9. This came from the ring opening of radical 10 and not from rearrangement of 8. When the photolysis was carried out at -20° to -30°, the yield of 8 increased (45%) and that of 9 decreased (19%). Similar results were observed with $(PhSe)_2$ trapping experiments at low concentrations of the trap.

We recently reported that the acyl derivatives of 4 and 5 react with $Sb(SPh)_3$ in the presence of oxygen to furnish in high yield the corresponding nor-alcohol ($R\text{-}CO_2H$ —> R-OH).[5] This is an interesting reaction involving an organoantimony intermediate. It should shorten the synthesis of acetate 1.

Using $Sb(SPh)_3$ on a small scale gave alcohol 11 (70%). Since $Sb(SPh)_3$ is hydroscopic (yielding PhSH which traps competitively the radicals), we examined instead $Ph_2SbS(o\text{-}MeOC_6H_4)$. Ph_3Sb was heated with p-toluenesulfonic



acid hydrate in benzene to give Ph_2SbOTs (78%), m.p. 175-178° . In tetrahydrofuran at -30° to -20° with a two-fold excess of o-methoxythiophenol, this gave the known[6] $Ph_2SbS(o\text{-}MeOC_6H_4)$ (82%, m.p. 102-104°). With this reagent, there was a fast reaction (5-10 mins) to give the nor-alcohol derivative. Addition of sufficient water to hydrolyze the antimony-oxygen bond followed by acetylation with acetic anhydride and pyridine gave directly the desired acetate 12 (75%) characterized as $[\alpha]_D$ +102±3° (C=10, in $CHCl_3$) (lit.[1] + 103° in $CHCl_3$). This procedure was extended to dihydrocinnamic acid (91% of β-phenylethyl acetate) and to cyclododecanecarboxylic acid (81% of cyclododecyl acetate).

We have thus been able to improve the synthesis of acetate 12, the direct precursor of the pheromone 1. We have also been able to explain the reasons for the earlier difficulties based on derivatives of 5 (ring opening[7] of the radical 10 at the higher temperature.)

In our earlier work[2] on the Hunsdiecker-Borodin reaction, we prepared acyl derivatives of 4 in situ and decomposed them thermally. Although the results were satisfactory, the present room temperature photolysis procedure is milder and we recommend it. In a recently accepted paper[8] Curran,

Newcomb and their collaborators have demonstrated the superiority of the room temperature photolysis of the acyl derivatives of 4 for the preparation of bromides and especially iodides.

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