organic layer was separated. After extraction with AcOEt thoroughly, the combined organic extracts were dried over $MgSO_4$. Concentration of the dried solvent afforded an oily residue, which was purified by silica gel column chromatography (40/1 → 40/2 ether/methanol) to give pure PGD_2 (1) (45.5 mg) as a colorless solid in 85% yield: IR (KBr) 3450, 1730, 1720 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (3 H, t, J = 6 Hz), 2.65–2.90 (1 H, dd, J = 7, 12 Hz), 4.00–4.30 (1 H, m), 4.45 (1 H, m), 5.30–5.70 (4 H, m); mass spectrum, m/e 334, 316, 246, 245, 191, 190, 161, 55; mass spectrum, m/e calcd for 1 ($C_{20}H_{30}O_4$, M^+–18) 334.2142, found 334.2159; $[\alpha]^{20}_D$ +9° (c 2.11, THF); mp 58–59 °C (recrystallized from AcOEt–n-hexane).

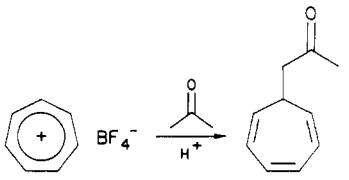
A New Preparation of α-Cycloheptatrienyl Ketones

I. D. Reingold,* H. A. Trujillo, and B. E. Kahr

Department of Chemistry, Middlebury College, Middlebury, Vermont 05753

Received September 18, 1985

In the course of an investigation into the synthesis of tropyl alcohol, we have discovered a new, efficient synthesis of α-cycloheptatrienyl ketones. Tropyl acetate appeared to be a reasonable precursor to tropyl alcohol, but our initial attempts to prepare it by the method of Hoffmann[1] (tropylium fluoroborate, potassium acetate, and acetic anhydride in acetone) led instead to tropyl acetone 1.



1

Reasoning that our tropylium fluoroborate might have been wet[2] and that the acetic anhydride had been hydrolyzed to acetic acid, we speculated that the reaction of acetone with tropylium salts might be acid catalyzed. Indeed, when tropylium fluoroborate is stirred in acetone with a few drops of acetic acid, a 97% yield of tropyl acetone is rapidly obtained. Previous preparations of tropyl acetone are quite laborious and provide product in significantly lower yields.[4]

The reaction presumably involves the enol of acetone reacting with tropylium salt, and thus the method should be quite general for enolizable ketones. Accordingly, a number of other substrates were examined to determine the scope and limitations of this reaction. Our most productive experiments were done in methanol or acetonitrile, using approximately a 1:1 ratio of tropylium salt and ketone; a slight excess of tropylium salt is preferable to an excess of ketone since the tropylium salt is easily removed. The results are presented in Table I.

Several comments are in order. First, the yields are good to excellent. Many of these compounds have been made before, but this is the first direct addition that produces product in high yields. The most general published method involves the treatment of tropylium salt with the enamines of ketones.[5] While excellent, the yields reported apply only to the alkylation step; when the preparation of the enamine is considered, yields reported here are uniformly better than or equal to those possible with the enamine procedure. Furthermore, several of the entries in Table I are not available from the enamine method, due to the unavailability of the appropriate enamines. On the other hand, much better control over regioselectivity is possible by using the earlier procedure. For example, 2-methylcyclohexanone affords a 3:2 mixture of the possible isomers with the present procedure, while a 20:1 ratio favoring the 6-substituted product is obtained with the enamine method. This latter ratio nearly corresponds to the ratio of the starting enamines isomers.

Second, no ditropyl adducts were observed with this procedure. To add a second tropyl group, the original adduct would have to enolize with loss of a proton. However, as Conrow has pointed out,[4a] it seems likely that enolization in these compounds always proceeds by loss of tropylium ion instead of proton, thus precluding multiple adducts. The results presented herein support this conclusion.

The third entry in Table I, the reaction of 2-butanone with tropylium salt, merits comment. As shown, when worked up after 5 h the product was almost entirely 3-tropyl-2-butanone (3). Shorter reaction times lead to a much higher percentage of 1-tropyl-2-butanone (2): after a reaction time of only 1 h, the ratio is closer to 2:1 favoring 3, as measured by gas chromatography, and a gradual increase in the ratio is observed, leveling off at about 4.5 h. It appears that production of 2 is kinetically controlled and that 3 is the thermodynamic product; thus the same equilibrium mixture should be obtained from a pure sample of the minor isomer 2 placed under the reaction conditions. However, a sample of nearly pure 2 in methanol containing acetic acid remained unchanged after 2 weeks.

Several possible explanations for this lack of equilibration have been considered. Adduct 2 does not actually revert directly to starting material, but rather to tropylium ion and the kinetic enol, the less substituted one. This enol may react again in the forward direction, unless there is something else present to scavenge the tropylium ion. Addition of excess 2-butanone (which would be present under the reaction conditions) had no effect, however. A second possible explanation is that the actual reaction conditions are more acidic than the ones we simulated, because the reaction generates fluoroboric acid. Addition of a few drops of 48% fluoroboric acid solution did cause the amount of "thermodynamic" isomer present to grow: the ratio of 2–3 changed from 40:1 to 10:1 in the course of a week. Although 3 may eventually have become the predominant isomer, the rate of isomerization was much too slow to account for the results observed during the reaction. At present, a suitable explanation for the observed results is not apparent.

Note should also be made of a few substrates that do not undergo this reaction. Acetaldehyde, propionaldehyde, ethyl acetate, and acetonitrile all failed to afford the desired adducts. The aldehydes decomposed under the reaction conditions to the same unidentified products which were obtained when they were stirred in methanol con-

(1) Hoffmann, R. W.; Loof, I. H.; Wentrup, C. *Liebigs Ann. Chem.* **1980**, 1198.

(2) Freshly prepared tropylium fluoroborate successfully provided tropyl acetate, identical with that reported in the literature.[1,3]

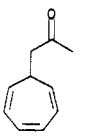
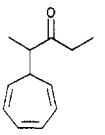
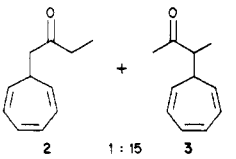
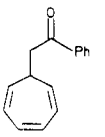
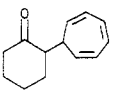
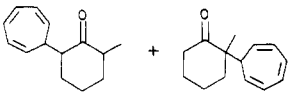
(3) Orlando, C. M., Jr.; Weiss, K. *J. Org. Chem.* **1962**, *27*, 4714. The NMR spectrum reported by these authors is displaced by about 0.5 ppm. The correct values are δ 2.0, 5.0, 5.5, 6.3, and 6.7. Our spectrum agrees with that obtained by Hoffmann: personal communication.

(4) (a) Conrow, K. *J. Am. Chem. Soc.* **1959**, *81*, 5461. (b) Vol'pin, M. E.; Akhrem, I. S.; Kursanov, D. N. *Zh. Obshch. Khim.* **1960**, *30*, 1187. (c) Conrow, K.; Naik, D. N. *J. Med. Chem.* **1963**, *6*, 69.

(5) Watanabe, T.; Soma, N. *Chem. Pharm. Bull.* **1970**, *18*, 1595.

0022-3263/86/1951-1627$01.50/0

Table I. Reaction of Ketones with Tropylium Salt

substrate	equiv tropylium salt	time, h	products	yield, %
	*a*	2		97
	0.33	1		95
	*a*	2[b]		97
	1.16	5	 2 1 : 15 3	75
	1.2	3		65
	0.9	2		75
	1.11	1.5	 3 : 2	89

[a] Ketone used as solvent. [b] At reflux.

taining acetic acid but no tropylium salt. The ester and the nitrile seemed inert, probably due to lack of significant enol concentration.[6] All four adducts are available by other methods. The acetaldehyde adduct has been prepared by using ethyl vinyl ether as a preformed enol;[8] the same procedure has been used (this time with the enamine)[5] to prepare the propionaldehyde adduct.[9] The ethyl acetate adduct was made in a multistep procedure starting with malonic acid;[4a] similarly, tropylacetonitrile was made by allowing cyanoacetic acid to react with tropylium salt followed by decarboxylation of the product.[4a] In addition, both aldehyde adducts have been prepared simply by stirring the aldehydes with the tropylium salt in aqueous ethanol.[10]

The reaction reported here is noteworthy for being acid catalyzed. Although there is nothing remarkable about the reaction per se, most chemists contemplating the alkylation of a ketone with a cation would suggest using basic conditions to generate the enol or the enolate, yet in those cases which have been tried, with the exception of active methylene compounds, basic catalysis is inefficient.[4a] An exception to this generalization is nitromethane, which does not react with tropylium fluoroborate under acid catalysis, but in the presence of triethylamine it smoothly affords 7-(nitromethyl)cycloheptatriene.

Experimental Section

NMR spectra were recorded with a Varian CFT-20 80-MHz NMR spectrometer, using deuterochloroform as solvent. Mass spectra were recorded with a JEOL MS-07 mass spectrometer. Infrared spectra were recorded using a Perkin-Elmer 727 IR spectrophotometer over the range of 4000–600 cm^{-1}. Melting points and boiling points are uncorrected. Elemental analyses were performed by Micanal, Tucson, AZ 85717. Solutions were dried over anhydrous magnesium sulfate.

Tropylacetone (1). (a) Tropylium fluoroborate[11] (0.57 g, 3.2 mmol) in 25 mL of acetone containing three drops of acetic acid was stirred for 2 h at room temperature. Water (5 mL) was added, and the product was extracted with four 15-mL portions of chloroform. The combined organic layers were dried, concentrated, and passed through a short column of silica gel by using chloroform as the eluant. Concentration afforded 0.46 g (97%) of a reddish oil: bp 44–48 °C (0.1 torr) [lit.[4c] bp 54–56 °C (0.1–0.3 torr)]; ^1H NMR δ 6.60 (2 H, m), 6.25 (2 H, m), 5.10 (2 H, m), 2.75 (2 H, d, J = 6 Hz), 2.2 (1 H, m), 2.11 (3 H, s); IR 3000, 1700, 1610, 1360, 1160, 700 cm^{-1}; mass spectrum, m/e 148.

(b) A solution of tropylium fluoroborate (5.16 g, 0.0290 mol) and acetone (5.17 g, 0.0891 mol) in 10 mL of methanol containing 5 drops of acetic acid was stirred for 1 h at room temperature. Water (10 mL) was added, and the mixture was extracted with three 20-mL portions of ether. The combined organic layers were washed thoroughly with water, dried, and concentrated to provide 4.09 g (95%) of a thin purple oil, identical in all respects with that obtained above.

2-Tropyl-3-pentanone. To 40 mL of 3-pentanone were added 0.55 g (3.09 mmol) of tropylium fluoroborate and 10 drops of acetic acid. The mixture was heated at reflux until all of the salt dissolved, about 2 h. The solution was washed with water, the

(6) Under conditions where the enol was scavenged by a reactive electrophile, ethyl acetate has been shown to have an undetectably small enol content.[7] No data is available on acetonitrile, but it should be similar to ethyl acetate.

(7) Gero, A. *J. Org. Chem.* **1954**, *19*, 469. Gero, A. *J. Org. Chem.* **1954**, *19*, 1960.

(8) Vol'pin, M. E.; Akhrem, I. S.; Kursanov, D. N. *Zh. Obshch. Khim.* **1960**, *30*, 159.

(9) Presumably enol silyl ethers would work just as well. We have not investigated this possibility.

(10) Vol'pin, M. E.; Akhrem, I. S.; Kursanov, D. N. *Zh. Obshch. Khim.* **1959**, *29*, 2855.

(11) Conrow, K. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol V, p 1138.

aqueous layer was extracted with chloroform, and the combined organic layers were dried and concentrated to give 0.53 g (97%) of an oil: NMR as reported.[5]

1- and 3-Tropyl-2-butanone (2 and 3). A solution of tropylium fluoroborate (1.0 g, 5.6 mmol) and 2-butanone (0.35 g, 4.9 mmol) in 4 mL of methanol containing 15 drops of acetic acid was stirred for 4.5 h at room temperature. Water (15 mL) was added, and the aqueous layer was extracted with three 15-mL portions of ether. The combined organic layers were washed with three 15-mL portions of water, dried, concentrated, and passed through a short silica gel column with methylene chloride as the eluant. Evaporation of the solvent left 0.59 g (75%) of a mixture of the two products as a brownish orange oil: IR ($CHCl_3$) 1675, 1350, 685 cm^{-1}; mass spectrum, m/e 91 (no parent peak was observed). A portion of the mixture was distilled twice [bp 60–65 °C (0.8 torr)] to provide a pale yellow oil. Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 80.95; H, 8.75.

A sample was separated on a Chromatotron to provide samples of the separated isomers, which were characterized by the following NMR spectra. **2**: δ 6.60 (2 H, t, J = 3 Hz), 6.15 (2 H, dt, J = 9, 3 Hz), 5.12 (2 H, dd, J = 9, 6 Hz), 2.73 (2 H, d, J = 7 Hz), 2.5–2.1 (3 H, m), 1.04 (3 H, t, J = 7 Hz). **3**: δ 6.58 (2 H, m), 6.15 (2 H, m), 5.13 (2 H, m), 2.83 (1 H, dq, J = 7, 10 Hz), 2.07 (3 H, s), 2.2–1.8 (1 H, m), 1.24 (3 H, d, J = 7 Hz).

Tropylacetophenone. A solution of tropylium fluoroborate (0.62 g, 3.5 mmol) and acetophenone (0.35 g, 2.9 mmol) in 5 mL of methanol containing 5 drops of acetic acid was stirred for 3 h at room temperature. Water (10 mL) was added, and the mixture was extracted with three 25-mL portions of ether. The combined organic layers were washed with two 25-mL portions of water, dried, and concentrated. The resulting oil was passed through a short silica gel column by using methylene chloride as the eluant. Evaporation of the solvent left 0.57 g of an oil, which by NMR analysis contained 70% tropylacetophenone[5] and 30% unchanged acetophenone.

2-Tropylcyclohexanone. A solution of tropylium fluoroborate (0.50 g, 2.8 mmol) and cyclohexanone (0.30 g, 3.1 mmol) in 5 mL of methanol containing 5 drops of acetic acid was stirred for 2 h at room temperature. Chloroform and water were added, and each layer was washed five times with 20 mL of the other solvent. The combined organic layers were dried, concentrated, and passed through a short silica gel column with methylene chloride as the eluant. Evaporation of the solvent left 0.40 g (77%) of an oil. The proton NMR spectrum is identical with that previously reported for 2-tropylcyclohexanone,[5] but all attempts to crystallize the material failed until a sample was distilled. The distillate formed yellow plates, mp 59–60 °C (lit.[5] mp 60 °C).

2- and 6-Tropyl-2-methylcyclohexanone. A solution of tropylium fluoroborate (1.02 g, 5.73 mmol) and 2-methylcyclohexanone (0.58 g, 5.2 mmol) in 7 mL of methanol containing 10 drops of acetic acid was stirred for 1.5 h at room temperature. Water (20 mL) was added, and the mixture was extracted with three 10-mL portions of ether. The combined organic layers were washed with three 20-mL portions of water, dried, and concentrated. The residue was passed through a short silica gel column using methylene chloride as the eluant. Evaporation of the solvent left 0.90 g (91%) of a mixture of the two products as an amber oil. Analysis of the mixture by proton NMR spectroscopy revealed the two products[5] to be present, in this case, in a 1:1 ratio.

7-(Nitromethyl)cycloheptatriene. Tropylium fluoroborate (0.45 g, 2.5 mmol) was dissolved in 10 mL of nitromethane containing 1 mL of triethylamine. The solution was heated to 60 °C for 15 min, then allowed to cool, and added to 15 mL of water. The mixture was extracted twice with 10 mL of ether, and the combined organic layers were washed with 10 mL of 10% aqueous sulfuric acid solution, dried, and concentrated. The residue was passed through a short silica gel column by using chloroform as the eluant; evaporation of the solvent left 0.31 g (82% of a yellow oil. The proton NMR of this material is identical with that previously reported.[12]

Acknowledgment. We thank the Research Corporation for financial support of this research.

(12) Hoskinson, R. M. *Aust. J. Chem.* **1970**, *23*, 399.

Registry No. 1, 16000-59-2; 2, 101198-70-3; 3, 101198-69-0; tropylium fluoroborate, 27081-10-3; acetone, 67-64-1; 3-pentanone, 96-22-0; 2-butanone, 78-93-3; acetophenone, 98-86-2; cyclohexanone, 108-94-1; 2-methyl cyclohexanone, 583-60-8; nitromethane, 75-52-5; 2-tropyl-3-pentanone, 29647-94-7; tropylacetophenone, 29647-95-8; 2-tropylcyclohexanone, 29647-89-0; 6-tropyl-2-methylcyclohexanone, 29647-91-4; 2-tropyl-2-methylcyclohexanone, 29647-92-5; 7-(nitromethyl)cycloheptatriene, 25928-20-5.

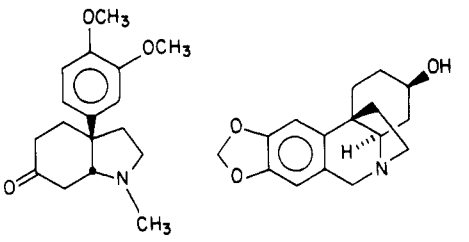
An Efficient Formal Synthesis of *d,l*-Mesembrine via a β-(Methoxy(phenylthio)methylidene) Enolate Robinson Annulation Sequence

Steven Hackett and Tom Livinghouse*

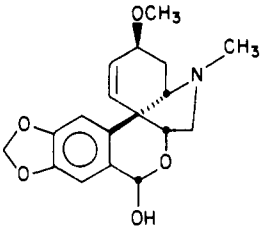
Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455

Received October 2, 1985

Alkaloids derived from various plants belonging to the family Aizoaceae[1] have remained attractive molecular targets for total synthesis.[2-7] The sceletium alkaloid mesembrine (**1**) can be regarded as a structural prototype for the more complex *cis*-3a-aryloctahydroindole alkaloids epielwesine (**2**)[8] and pretazettine (**3**). We envisaged the



1 **2**



3

azabicyclic skeleton of mesembrine (**1**) as arising from the cyclocondensation of the keto ester **5** with methylamine. The keto ester **5**, in turn, was expected to be available from the ketene *O,S*-acetal **6** via selective hydrolysis (H^+, THF–H_2O). We have previously reported that the alkylation of β-(methoxy(phenylthio)methylidene) enolates (e.g., **7**) provide products derived from α-substitution.[9] In

(1) Capps, T. M.; Hargrave, K. D.; Jeffs, P. W.; and McPhail, A. T., *J. Chem. Soc., Perkin Trans. 2* **1977**, 1098 and references therein.
(2) An asymmetric synthesis of (+)-mesembrine has appeared recently: Meyers, A. I.; Hanreich, R.; Wanner, K. T. *J. Am. Chem. Soc.* **1985**, *107*, 7776.
(3) Keck, G. E.; Webb, R. R., II. *J. Org. Chem.* **1982**, *47*, 1302.
(4) Oh-ishi, T.; Kugita, H., *Chem. Pharm. Bull.* **1970**, *18*, 299.
(5) Jeffs, P. W.; Cortese, N. A.; Wolfram, J. *J. Org. Chem.* **1982**, *47*, 3881.
(6) Martin, S. F.; Puckett, T. A.; Colapret, J. A. *J. Org. Chem.* **1979**, *44*, 3391.
(7) Stevens, R. V.; Lesko, P. M.; LaPalme, R. *J. Org. Chem.* **1975**, *40*, 3495.
(8) Overman, L. E.; Burk, R. M. *Tetrahedron Lett.* **1984**, *25*, 5739.
(9) Hackett, S.; Livinghouse, T. *J. Chem. Soc., Chem. Commun.* **1986**, 75.

0022-3263/86/1951-1629$01.50/0