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Direct Observation of an Antihomoaromatic Bicyclooctadienyl Cation

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The question of the bicyclohomoaromatic stabilization and destabilization is examined. The chemistry of bicyclo (3. 2. 1.) octa-3, 6–dienide anion has been studied on order to test these concepts. The bicyclooctadienide anion is shown to be stable delocalized ion which undergoes a facile proton-deuterium exchange reaction. The solvolysis of bicyclo (3.2.1) octa-3,6 –dienyl p–nitrobenzoate is much slower than the monoene analog. We have made direct observation of the bicycloocatadienyl and octenyl cations by ^{19}F–nmr spectroscopy, and were able to demonstrate that the bicyclooctadienyl cation was bishomoantiaromatic.

Introduction

The stabilization of carbonium ions and carbanions by means of cyclic charge delocalization or aromaticity is well documented and universally accepted.

The cyclopropyl cation **1**[1] and the cyclopentadienyl anion **2**[2] are just two examples of a large number of the wellknown carbonium ions and carbanions whose unusual stability is thought to be due to this effect.
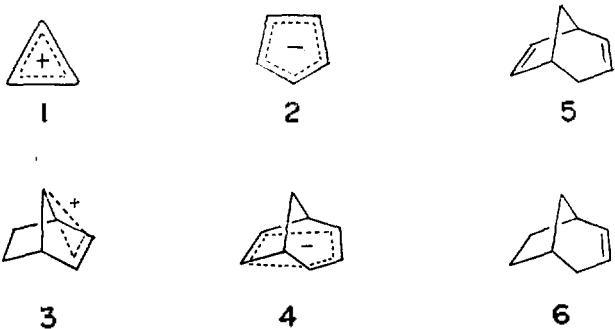
Recently many evidences have been presented in support of a new stabilization mechanism for carbonium ions and carbanions, generally known as homoaromaticity[3].

The 7-norbornenyl cation **3** and the bicyclooctadienyl anion **4** are considered to be homologs of **1** and **2**, respectively, and their unusual stability has been attributed to homoaromaticity.

Since the early work on the solvolysis of the cholestryl chloride[4], Winstein and his coworkers have been concerned about the long-range stabilization of ionic centers by remote carbons. One of the most fascinating concepts to develop from this interest was the theory of homoaromaticity[5]. Goldstein[6] used MO symmetry arguments to extend the concept of the homoaromatic ions to bicycloaromatic species.

Bicyclo(3.2.1)octa–3,6–diene(5), previously reported by Brown and Occolowitz[7], is more reactive compared with the monoene analog **6** in allylic proton–deuterium exchange in DMSO–*t*–BuOK. Molecular orbital symmetry arguments have suggested that anion **4** should also have enhanced stability. The ^{1}H–nmr spectrum of the bicyclohomopentadienide anion **4** has been reported by Winstein[8], and all of the features are in accordance with the delocalized six–π–electron bishomoaromatic species with appreciable ring currents. The rates of the solvolysis of the p–nitrobenzoates of bycyclo[3.2.1]octa–3,6–dienyl(7) and bicyclo[3.2.1] octenyl (8) in aqueous acetone have been studied by Diaz and his coworkers[9].

Here, the 6,7–double bond in **7** makes the intermediate cation a four–π–electron antiaromatic species and, therefore, retards the reaction in contrast with monoene analog **8**.

It occured to us that a study of the ^{19}F–nmr and ^{13}C–nmr spectra of the p–fluorophenyl bicyclooctadienyl cation **9** and especially comparison of these spectra with those of the p–fluorophenyl bicyclooctenyl cation **10** would be ideally suited in providing the information about long-

7   8

9   10

Results and Discussion
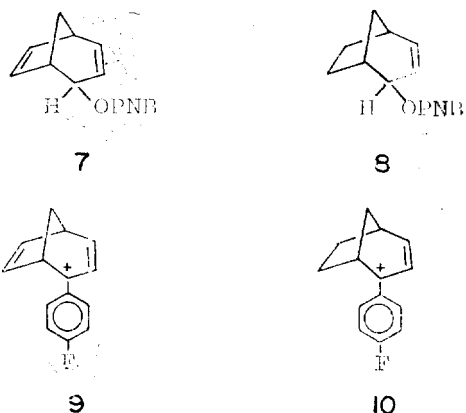
range–π–interactions and homoantiaromaticity in the octadienyl cation. The paraproton nuclear magnetic resonance chemical shift of the tertiary phenyl carbonium ions (11a) could serve as a measure of the π–electron demand of the carbonium ion center[10].

11a. R=H

11b. R=F
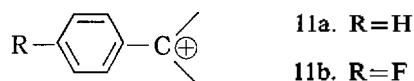
Although a linear correlation of the chemical shift value with the log of the calculated delocalization energies was observed over a range of carbonium ion stabilities, the ^{1}H–nmr chemical shift was too insensitive for energy differences to be useful (in the neighborhood of 1 ppm/100 kcal).

The ^{19}F–nmr spectroscopy is advantageous in view of its order of magnitude greater sensitivity to electron demands (1 ppm/0.75 kcal) of the cation center (11b), and comparative insensitivity to magnetic anisotropies of the solvent and molecule.

We are now able to calculate the homoantiaromatic destabilization energy by comparing the ^{19}F–nmr chemical shifts of the octenyl and octadienyl cations.

The carbinols were prepared from the Grignard reagent and the corresponding ketones in dry ether. Preparation and properties of the carbinols are described in the Experimental Section.

Assignment of resonance signals in the ^{1}H–nmr spectra of the carbinols achieved by decoupling experiments and by preparation of Eu (DPM)$_3$ complexes, and that in the ^{13}Cnmr spectra was confirmed by double–resonance experiments. Solution of carbonium ions were prepared as follows. To a stirred mixture of fluorosulfonic acid and sulfuryl chloride, a solution of each carbinol in CD$_2$Cl$_2$ was added dropwise at $-120°$C in a special reaction apparatus. The spectra of the carbonium ions were unchanged from $-120°$C to $-30°$C and hence, recorded at $-50°$C. At $-20°$C the carbonium ions rearranged producing unknown species. In the nmr spectra of the carbonium ions, the absorption signals usually shifted downfield compared with the carbionols. The chemical shift differences of the bicyclooctadienyl (I), bicyclooctenyl(II) and bicycloheptadienyl (III) cation relative to those of the corresponding precursors are summarized in Table 1.

The olefinic protons (H$_6$, H$_7$) in I appeared at δ7.27 and δ6.84 as a triplets, both protons shifting downfield by 0.63 and 0.83 ppm relative to H 6,7 in the corresponding carbinols. These shifts are appreciably more downfield in contrast with these for H 6,7 of III.

On the other band, the signal for H8 of I shifted downfield by 1.1 ppm relative to H8 in the corresponding carbinol. This value is about two times greater than that (0.5 ppm) for H 8 of II.

This may be attributed to a small ring current effect, which is also manifested by bicyclo (3.2.1) octa–3,6–dienide anion. Upfield shifts of the H8 protons in the octadienide anion relative to corresponding diene by 1.1 ppm are attributed at least partly to a ring–current effects[11]. This can be explained in term of the appreciable long range π–interactions between

TABLE 1.
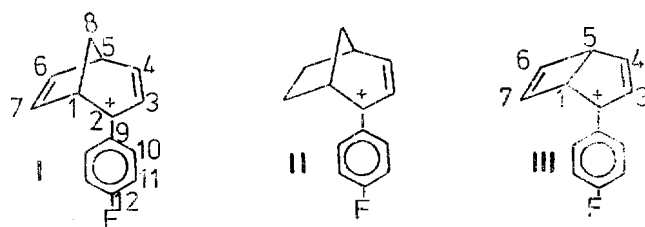
		1	2	3	4	5	6	7	8	9	10	11	12	^{19}F–nmr (δ, ppm)
I	a.	−1.8		−2.4	−2.9	−1.45	−0.63	−0.83	−1.1		−1.18	−0.67		−39.51
	b.	+0.65	−134.9	+0.938	−55.18	−11.2	−0.23 exo.	−3.5 endo.	−19.7	+11.29	−12.2	−5.6	−13.5	
II	a.	−2.2		−2.62	−2.98	−1.5	−1.03	−0.35	−0.5		−1.3	−0.62		−35.13
	b.	+0.5	−131.7	+7.7	−5-.18	−9.6	+3.8	−4.05	−7.0	+13.28	−12.6	−5.46	−12.2	
III	a.	−1.78		−2.9	−3.23	−1.38	−0.26	−0.47						

a. ^{1}H–nmr (δ, ppm); b. ^{13}C–nmr (δ, ppm)

the vacant *p*-orbital of the cationic center and the 6,7–double bond in I, which leads to a bishomocyclopentadienyl species.

Strikingly, the upfield shift (+7.7 ppm) of C3 in II is much greater than that(+0.938ppm) in I, while the shifts in unfield shift of C3 in I is the result of the inefficient allylic conjugation due to the unfavorable electrostatic interaction with the adjacent positive center, while the allylic conjugation is well facilitated.

The greater positive charge on C2 of I compared with C2 of II is also seen in the downfield shifts (–134.9 and –137.7 ppm) of the carbons relative to the corresponding carbinols. The ^{13}C–nmr spectra, therefore, indicate that the additional double bond (6,7) in I exerts negative effects on the charge delocalization.

Solvolysis of bicyclo (3.2.1)octa–3,6–dienyl and bicyclo (3.2.1) octa–3–enyl *p*–nitrobenzoates (OPNB) reported by Diaz[9] revealed that the bicyclooctadienyl-OPNB is about 150 times less reactive than the monoene analog, since the 6,7–olefinic group in the diene makes an antiaromatic homocyclopentadienyl carbonium ion intermediate.

An important evidence for the antiaromaticity of I can be obtained from ^{19}F–chemical shifts. The fluorine atom in the *p*–fluorophenyl bicyclooctadienyl cation (I) appeared at δ–75.63 and that in the *p*–fluorophenyl bicyclooctenyl species (II) at δ–80.53. The fluorine atom in I shifted downfield by about 4.38 ppm than that of II, when compared with corresponding the carbinols. Therefore, the additional 6,7–olefinic group destabilizes the carbonium ion intermediate, which contains a homoantiaromatic character. From the value of 4.38 ppm, the homoantiaromatic destabilization energy is estimated as about 3.28 kcal/mole by the Taft and Mckeeve's method[10].

In conclusion, the result of ^{1}H– ^{13}C–, and ^{19}F–nmr studies demonstrate that carbonium ion (I) becomes bishomoanantiaromatic and, hence, destabilized by the electronic effects of the 6,7–olefinic bond.

Experimental Section

General Procedures. All carbonium ion precursors were characterized by their melting points, ir, ^{1}H– ^{19}F– and ^{13}C–nmr, and mass spectra. Spectroscopic data were determined on a perkin–Elermer 283 infrared spectrophotometer, and a Schimadz GC–MS LKB 9000 mass spectrometer. Nmr spectra were recorded on a Varian EM–360 (60 MHz) or a XL–100 (100 MHz) spectrometer, tetramethylsilane being used as internal standard and in CDCl$_3$ as lock. Chemical shifts are reported and δ from Me$_4$Si and CFCl$_3$, with multiplicities: s=singlet, d=doubledt, t=triplet, q=quartet, dt=doublet of triplet, and m=multiplet. Melting point are uncorrected.

Crude reaction mixture was always checked with thin layer chromatography (TLC). Carbinols were purified by column chromatography with the aid of Merck 7734 Kieselgel. Carbonium ion solutions were made up to approximately 10 % concentration by addition of soulutions of the carbinols in CD$_2$Cl$_2$ to stirred fluorosulfonic acid and SO$_2$ClF at–120°C

in a special apparatus. The chemical shifts in ^{1}H–, and ^{13}C–nmr spectra of carbonium ions were determined from referenced internal CD$_2$Cl$_2$(δ5.4, 53.6). The ^{19}F–chemical shifts of the carbonium ions were taken up from computer analyzed data.

1. Synthesis of Carbinols

(1) *p–Fluorophenyl bicyclo(3.2.1)octa–3,6–dien–2–ol.*

Bicyclo(3.2.0)hex–2–en–6–endo–Carboxaldehyde(I). To a rapidly stirred suspension of 110g (1.12 mole) of anhydrous sodium carbonate in the solution of 83.7 g (0.9 mole) of bicyclo(2.2.1) heptadiene in 730 m*l* of methylene chloride was added 75 g 42 % peracetic acid (0.405 mole). The reaction temperature was maintained at 20 °C during the addition, which required 50 min After 2 h the mixture was filtered, and the filter cake washed with methylene chloride. The methylene chloride was distilled off and residue fractionated to yield 26.0 g (I) (70 %), bp 84–85 °C (75 mmHg) with infrared absorption spectrum in agreement with expectation[12].

Bicyclo(3.2.0)hex–2–en–6–endo–carboxylic Acid(II). The carboxaldehyde (I) (33.0 g, 0.31 mole) mixed with 162 g (0.96 mole) of silver nitrate, 375 m*l* of water and 150 m*l* of 95 % ethanol, was stirred vigorously, and to it was added during 3 hr. 57 g sodium hydroxide in 750 m*l* of water. The mixture was allowed to stand overnight. The filtered solution was washed with ether, acidified with 5 *N* hydrochloric acid and thoroughly extracted with ether dried over magnesium sulfate and evaporated to give 20.0 g (52 %) of crude product. This material was crystallized from *n*-hexane, mp 85°C; ^{1}H-nmr (CDCl$_3$): 1.83 (*m*, 2H), 2.62 (*m*, 3H), 5.68 (*m*, 2H), 11.4 (s, 1H).

Bicyclo(3.2.1)octa–3,6–dien–2–on(III). The carboxylic acid (II) 20 g (0.16 mole) was dissolved in 150 m*l* of ether plus 10 drops of pyridine in a 250 m*l* flask fitted with a drying tube, and thionyl chloride (27.1 g, 0.23 mole) in 10 m*l* of absolute ether was added in one lot and the solution stirred for 1 h until gas evolution ceased. The reaction mixture was refluxed for 3 hr The solvent was removed and residue fractionated to gave 19.0 g (84%) as brown oil: ^{1}H-nmr (CDCl$_3$):δ 2.35 (*m*, 2H), 2.66 (*t*, 2H), 2.88 (*m*, 1H), 5.06 (*m*, 1H), 5.86 (*m*, 1H). To a stirred solution of diazomethane, which was prepared from Diazald (70 g, Aldrich, D 2.800–0) and potassium hydroxide in diglyme, in absolute ether was added 19 g of acid chloride in 20 m*l* of dry ether. The solution was chilled in an ice–bath prior to and during the addition of the acid chloride. The reaction mixture was stirred for 4 hr and allowed to stand overnight in a refrigerator. The solvent was removed, and residue oil was dissolved in THF (dried over LiAlH$_4$). The crude diazoketone was photolysed directly under nitrogen with a 450 watt Hanovia medium pressure mercury lamp as a 5 % solution in tetrahyrofuran. Removal of the THF on a rotary evaporator gave 9.2 g (57 %) of brown oil; ir (CCl$_4$) (cm^{-1}): 1580. The pure ketone was obtained by column chromatography (SiO$_2$/CH$_2$Cl$_2$). ^{1}H-nmr (CDCl$_3$): δ 2.53 (*t*, 2H), 3.31 (*m*, 2H), 5.41 (*q*, 1H), 6.15 (*q*, 1H), 6.7 (*q*, 1H), 7.35 (*q*, 1H).

p–Fluorophenyl bicyclo(3.2.1)octa–3,6–dien–2–ol(IV). To a stirred solution of the Grignard reagent prepared from 4–

bromofluorobenzene (6.5 g, 0.038 mole) and magnesium turning (1.5 g, 0.05 mole) in dry ether was added dropwise the solution of the ketone (III). (3 g, 0.025 mole) in absolute ether. During the addition of the ketone the reaction temperature was maintained by gentle reflux. After addition of the ketone, the reaction mixture was heated to reflux with stirring for 1 h. After cooling the mixture was poured into a saturated ammonium choloride solution and extracted with ether (3×100 ml). The extract was washed once with water and dried over magnesium sulfate and evaporated. The crude product gave 2.4 g (44.4 %) of the alcohol as a brown oil. The carbinol was purified by column chromatography on silica gel using methylene chloride as eluent. $Ir(CCl_4)$ (cm^{-1}): 3560, 3420, 3050, 2940, 2860, 1600, 1500, 1220, 1160, 1040, 1010, 920, 830, 740. ^1H-nmr(CDCl$_3$): δ 1.94 (t,2H), 2.3 (s, 2H), 2.3 (s, 1H), 2.68 (quin, 1H), 3.03 (quin. 1H), 5.27 (Dd. 1H), 6.01 (q, 1H), 6.48 (q, 1H), 6.64 (q, 1H), 7.0 (t, 2H), 7.7 (q, 2H). $^{13}C-nmr$ (CDCl$_3$): 39.26, 43.34, 59.82, 74.08, 114.67, 120.13, 129.04, 137.76,, 137, 26 143.34, 145.74, 162.01. $^{19}F-nmr$ (CDCl$_3$): -115.4. mass: m/e 216 (M$^+$).

(2) *p–Fluorophenyl Bicyclo(3.2.1)octa–3–en–2–ol.*

Bicyclo(2.2.2)octa–5–en–2–ethylester(I). A mixture of 37.0 g (0.46 mole) of 1,3-cyclohexadiene and 59.2 g (0.59 mole) of acrylic acid ethyl ester was sealed in a glass tube and heated in a metal bomb at 160 °C for 12 hr. The mixture was fractionally distilled and gave 73.6 g (69.7 %) of I: ^1H-nmr (CDCl$_3$): δ 1.13-1.179m, 9H), 2.55(m, 2H), 2.91(n, 1H), 4.06(q, 2H), 6.2 (m, 2H).

Bicyclo(2.2.2)octa–5–en–2–hydrazide(II). A solution of 57.4 g of the ester (I) and 63.7 g of 98 % hydrazine hydrate in 79.7 ml of absolute ethanol was heated to reflux for 48 h. The yield of solid was 55 g, mp 97-103 °C.

Endo–2–N–carbethoxyaminobicyclo(2.2.2)octa–5–ene(III). A solution of 55 g (0.33 mole) of the hydrazide(II) in 50 ml of water and 30.8 ml of concentrated hydrochloric acid was covered with 360 ml of ether and cooled to 0 °C in an ice–salt–bath. A solution of 25.3 g (0.36 mole) of sodium nitrate in 55 ml of water was added, to the stirred, colled reaction mixture. The yellow ether layer was separated, and the aqueous layer was extracted with ether (3×100 ml). The ether extract was washed with cold saturated aqueous sodium carbonate, dried over calcium chloride. The ether extract was diluted with 157 ml of absolute ethanol. The ether was distilled by a short vigreux column, and the remaining solution was heated to reflux for 3 h. After removal of the ethanol by distillation, the mixture was fractionally distilled and gave 13.5 g (21 %) of (III): mp 295-300 °C: ^1H-nmr (CDCl$_3$): δ 1.1-2.2 (m, 7H), 2.62 (m, 2H), 3.66 (s, 2H), 6.33 (m, 2H), 7.0 (s, 1H).

Bicyclo(3.2.1)octa–3–en–2–ol.(IV). A solution of 44.3 g (0.23 mole) of the urethane (III) and 22.8 g of potassium hydroxide in 662 ml of water was heated to reflux for 15 hr. The crude product (amine) was obtained by steam distillation. The distillate was acidified with concentrated hydrochloric acid, and the mixture dried in a steam bath. The alcohol(IV) was obtained in 69 % yield when an aqueous solution of the hydrochloride of endo–2–amino bicyclo(2.2.2) octa–3–

ene was treated with sodium nitrate according to the method of Wildman and Saunder[13]. The carbinol (IV) was purified by column chromatography on silica gel. mp 102.5°C; $^1H-$ nmr (CDCl$_3$): δ 1.26-1.91 (m, 6H), 2.44 (m, 2H), 3.77 (t, 1H), 5.48 (q, 1H), 61.11 (t, 1H).

Bicyclo(3.2.1)octa–3–en–2–one(V). Manganess dioxide; Concentrated aqueous potassium permanganate was added to a stirred aqueous manganess sulphate solution kept at 90 °C, until a slight excess was present. Stirring at 90 °C was continued for a further 25 min. The oxide was collected by filteration, washed well with hot water, then with methanol and ether, and dried at 120-130 °C. The mixture of 3 g of the carbinol (IV) and 33.6 g of manganese dioxide in absolute n–hexane was stirred at 25 °C for 72 hr. in a dark room. The reaction mixture was filtered, and removal of n–hexane on a rotary evaporator gave 1.9 g (64.8 %) of (V): ir (CCl$_4$) (cm^{-1}); 1450 $^1H-$mnmr (CDCl$_3$): δ 1.6 (m, 3H), 2.04 (m, 3H), 2.91 (q, 2H), 5.82 (q, 1H), 7.26 (t, 1H).

p–Fluorophenyl Bicyclo(3.2.1)octa–3–en–ol(VI). The carbinol was prepared from the Grignard reagent and 1.5g (0.012 mole) of the ketone (V) in dry ether according to the method of the previous section. The carbinol (VI) was purified by column chromatography on silica gel using methylene chloride as eluent, and gave 1.4 g (45 %) as a viscous oil: $Ir(CCl_4)$ (cm^{-1}): 3600(m), 3420(s), 3010(m), 2950(s), 2870(s), 1600(s), 1500(s), 1450(m), 1300(s), 1220(s), 1150(s), 1080 (s), 1050(s), 980(s), 940(m), 880(m), 830(s) 750(s). $^1H-$ nmr (CDCl$_3$): δ1.13-2.2 (m, 7H), 2.44 (m, 2H), 5.37 (q, 1H), 6.16 (qd, 1H), 7.01 (t, 2H), 7.34 (q, 2H). $^{13}C-nmr$ (CDCl$_3$) δ 22.75, 31.55, 47.08, 114.47, 128.23, 136.16, 143. 18, 161.86. $^{19}F-nmr$ (CDCl$_3$): δ-115.69. mass: m/e 218 (M$^+$).

2. Sythesis of Cations

p–Fluorophenyl Bicyclo(3.2.1)octa–3,6–dienyl Cation. The cation solutions were prepared by a described method according to the general procedure in the experimental section. The nmr spectra were recorded at -50 °C: ^1H-nmr (CD$_2$Cl$_2$): δ 3.05 (m, 2H), 4.13 (m, 1H), 4.9 (s, 1H), 6.84 (t, 2H), 7.27 (t, 1H), 7.67 (td. 2H), 8.73 (m, 2H), 9.35 (q, 1H). $^{13}C-nmr$ (CD$_2$Cl$_2$): δ 50.49, 53.34, 60.05, 120.30, 120.49, 128.10, 132.05, 135.28, 149.33, 142.28, 145.97, 175.58, 192.44, 209.01. $^{19}F-nmr$ (CD$_2$Cl$_2$): δ-75.63 ppm.

p–Fluorophenyl Bicyclo(3.2.1)octa–3–enyl Cation. The spectra were recorded at -50°C; ^1H-nmr (CD$_2$Cl$_2$) (ppm): 1.28-1.91 (m, 2H), 2.06 (q, 2H), 2.91(d, 2H), 3.83(sext. 1H), 4.06 (q, 1H), 7.63(t, 2H), 8.02(q, 1H), 8.67 (q, 2H), 9.14(t, 1H). $^{13}C-nmr$ (CD$_2$Cl$_2$): δ26.86, 27.77, 43.11, 45.18, 47.25, 119.94, 120.46, 129.91, 140.92, 193,. 37, 174.06, 210.44. $^{19}F-nmr$ (CD$_2$Cl$_2$): δ-80.56 ppm.

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Novel Synthetic Reactions Using 1-Fluoro-2,4,6-trinitrobenzene. An Efficient Direct Esterification Method

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Synthetic utility of 1-fluoro-2,4,6-trinitrobenzene (FTNB) as a condensing agent was investigated. The use of FTNB and DMAP was found to be very effective for direct esterification of carboxylic acids with alcohols or thiols. However, this system was not very effective for macrolactonization. Reaction of 2,4,6-trinitrophenyl esters with several nucleophiles was investigated briefly. Plausible reaction mechanisms of esterification are presented. It seems that the reaction proceeds via the intermediacy of 2,4,6-trinitrophenyl esters by initial formation of 2', 4', 6'-trinitrophenyl-4-dimethylaminopyridinium salt from which the trinitrophenyl group is transferred to the carboxylic acid.

Introduction

Esterification of carboxylic acids to the corresponding esters plays an important role in organic synthesis. In synthetic applications such conversions often must be accomplished in complex molecules containing other functional groups. Consequently, it is important that esterification proceeds under mild conditions in high yields.

As part of our continuous efforts directed toward the development of new condensing agents, we recently outlined in a preliminary account[1] a convenient method for direct esterification of carboxylic acids using 1-fluoro-2,4,6-trinitrobenzene (FTNB)[2] as a condensing agent under mild conditions. Recent efforts in our laboratory have centered around mechanistic insights of esterification reaction and synthetic usefulness of FTNB in the related reactions. This paper describes a detailed account of our results.

Results and Discussion

Preparation of Carboxylic Esters. It has been previously demonstrated that treatment of equimolar amounts of carboxylic acids and FTNB with 1 equiv of triethylamine in acetonitrile at room temperature for 2 hrs, followed by the addition of equimolar amounts of an alcohol and triethylamine results in the formation of the corresponding esters.[3] The reported procedure was found to be effective only for

simple carboxylic acids and alcohols. Esterification of hindered carboxylic acids like pivalic acid gave low yields of esters even under forcing conditions.

Direct esterification using equimolar amounts of benzoic acid, cyclohexanol and FTNB in the presence of 2 equiv of triethylamine at room temperature for 12 hrs was attempted. As the reaction proceeded, it turned to dark brown and cyclohexyl benzoate was obtained in poor yield (24%). Presumably, low yield is due, in part, to the fact that an alcohol also reacts with FTNB in the presence of triethylamine to form its 2,4,6-trinitrophenyl ether. It is known that the reaction of 2,4-dinitrofluorobenzene with alcohols in the presence of triethylamine affords the corresponding 2,4-dinitrophenyl ethers, which are suitable in many instances for the characterization of alcohols.[4] We have indeed observed that treatment of equimolar amounts of FTNB and methanol with excess of triethylamine readily afforded methyl 2,4,6-trinitrophenyl ether. The use of various amine bases such as diisopropylethylamine, imidazole, and pyridine was also found to be ineffective.

$$RCOOH + R'OH \xrightarrow[\text{FTNB}]{\text{DMAP}} RCOOR' \tag{1}$$

$$\tag{2}$$
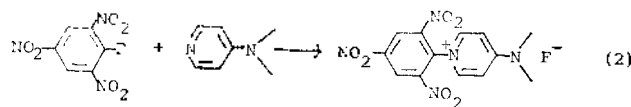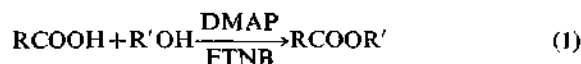
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