Electrophilic Substitution of 4a-Methyl-1,3,9-triphenyl-4a*H*-fluorene[1]

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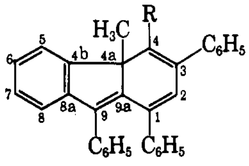
Electrophilic substitution reactions of the strongly basic hydrocarbon (Ia) are described. The new substitutions are chlorination with either thionyl chloride or phosphorus oxychloride in dimethyl sulfoxide, the Vilsmeier formylation with dimethylformamide and phosphorus oxychloride, and nitration with cupric nitrate in acetic anhydride. In each reaction substitution occurs in the 4-position. The intermediate iminium salt can be isolated easily in the Vilsmeier synthesis, and the salt is readily reduced to the tertiary amine. The 4-nitro compound is identical with a product obtained earlier from the hydrocarbon and nitrous acid in hot acetic acid.

In earlier papers of this series[2-4] it was shown that the lower melting hydrocarbon obtained from the polyphosphoric acid-catalyzed condensation of acetophenone is 4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ia). It was shown also that protonation of this hydrocarbon occurs stereospecifically as position 4 to give a new stable carbonium ion which can be isolated as the perchlorate, fluoroborate, or bromide.[4] It has been shown[4] that hydrocarbon Ia is readily brominated when treated with dimethyl sulfoxide and ethyl bromide according to the method of Fletcher and Pan,[5] and the location taken by the entering bromine atom was deduced as position 4 (structure Ib). Part of the argument for this assignment rested on the fact that the deuterio compound (Ic), obtained from the bromide by conversion to the lithium compound and reaction of the latter with deuterium oxide, lost deuterium when subjected to rearrangement by hydrobromic acid in acetic acid, yielding 4-methyl-1,3,9-triphenylfluorene (II).

The facile protonation and mild bromination of Ia have prompted an investigation of other electrophilic substitutions of the hydrocarbon. One of the most interesting processes discovered is the essentially quantitative reaction of the hydrocarbon with either thionyl chloride or phosphorus oxychloride and dimethyl sulfoxide in benzene. The reaction presumably proceeds through the intermediate III previously proposed[6] as the precursor of the α-chlorosulfide formed from the sulfoxide and thionyl chloride.



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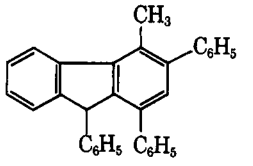


II

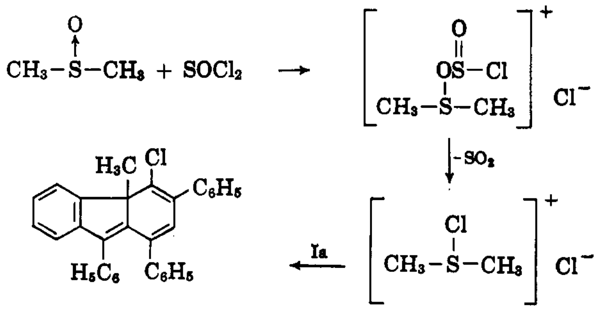
a, R = H e, R = CHO

b, R = Br f, R = $CH{=}\overset{+}{N}(CH_3)_2$

c, R = D g, R = $CH_2{-}N(CH_3)_2$

d, R = Cl h, R = NO_2

The infrared spectrum of the chloro compound (Id) was nearly identical with that of 4-bromo-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ib). The n.m.r. spectrum of the chloro compound showed, in addition to aromatic and methyl proton absorption, one vinyl proton absorption as a singlet at 3.60 τ. These spectral data show that the position of the chlorine atom in Id is the same as that of the bromine atom in Ib.



III

When the hydrocarbon (Ia) was treated with an equimolar amount of phosphorus oxychloride in dimethylformamide and the reaction mixture was worked up by the addition of water, an 86% yield of 4-formyl-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ie) was realized. The infrared spectrum of Ie showed strong absorption at 1655 cm.$^{-1}$ indicting a conjugated carbonyl group. The n.m.r. spectrum of Ie showed the absorption of a sharp singlet in the vinyl proton region at 3.52 τ. The aldehyde proton absorbed at 0.35 τ. Unambiguous proof that formylation had taken place in the 4-position was obtained by formylation of 4a-methyl-1,3,9-triphenyl-4a*H*-fluorene-4*d* (Ic). Since formylation of the deuterated hydrocarbon (Ic) in the 4-position would eliminate the deuterium from the compound, the n.m.r. spectrum of the product should be identical with the spectrum of the aldehyde obtained from the undeuterated hydrocarbon, *i. e.*, singlet vinyl absorption at 3.52 τ. The expected identity of the n.m.r. spectra of the two samples of the aldehyde was indeed observed.

The intermediate iminium salt (If) could be isolated when the hydrocarbon (Ia) was treated with equimolar amounts of dimethylformamide and phosphorus oxychloride in benzene. After vigorous stirring at room temperature for five minutes the reaction mixture became blood red and a beautiful red crystalline solid precipitated. This material was shown to be the dimethylimine salt (If). The infrared spectrum of If shows strong C=N absorption at 1640 cm.$^{-1}$. The n.m.r. spectrum of If shows that there is a great deal of double bond character to the carbon–nitrogen bond. The two methyl groups attached to the nitrogen are nonequivalent. These methyl group protons appear as singlets at 7.49 and 6.30 τ. The proton α to the nitrogen absorbs at -0.33 τ. The methyl group at the

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[1] Grateful acknowledgment is made of partial support of this work by a grant from the National Science Foundation (G-6223) and of a Fellowship (1960–1962) to H. W. M. provided by the Phillips Petroleum Co.

[2] H. W. Moore and H. R. Snyder, *J. Org. Chem.*, **28**, 535 (1963).

[3] R. W. Roeske, D. B. Bright, R. L. Johnson, W. J. DeJarlais, R. W. Bush, and H. R. Snyder, *J. Am. Chem. Soc.*, **82**, 3128 (1960).

[4] H. W. Moore and H. R. Snyder, *J. Org. Chem.*, **28**, 297 (1963).

[5] T. L. Fletcher and H. L. Pan, *J. Am. Chem. Soc.*, **78**, 4812 (1956); *Chem. Ind.* (London), 660 (1957).

[6] F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, **77**, 575 (1955).

4a-position absorbs at 7.85 and the vinyl proton at the 2-position gives a singlet at 3.45 τ.

Smith[7] showed that lithium aluminum hydride reduction of the iminium salt obtained as an intermediate in the Vilsmeier formylation of indole gave the known compound gramine. Lithium aluminum hydride reduction of the iminium salt (If) proceeded instantaneously to give 4-dimethylaminomethyl-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ig). The n.m.r. spectrum of Ig is in strict agreement with the proposed structure. The methyl groups attached to the nitrogen are now equivalent and show absorption as a singlet at 7.82 τ. The methyl at the 4a-position comes at 8.02 τ. Methylene absorption appears as a singlet at 6.37 and the one vinyl proton at the 2-position appears as a singlet at 3.52 τ.

An earlier attempt[8] to effect the nitration of the hydrocarbon Ia with fuming nitric acid at room temperature did not lead to a pure product. However, reaction with nitrous acid in hot acetic acid gave a pure substance having the composition of a mononitro derivative and believed to be an α,β-unsaturated nitro compound.[3] It is now found that nitration of the hydrocarbon Ia with cupric nitrate in acetic anhydride at 0°, according to the method of Anderson, Nelson, and Tazuma,[9] gives 4-nitro-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ih) in good yield. The infrared spectrum of the nitro compound (Ih) showed strong nitro group absorption at 1520 and 1345 cm.$^{-1}$. The n.m.r. spectrum showed methyl group absorption at 7.92 and the vinyl proton at the 2-position appeared as a singlet at 3.65 τ. The sample of the nitro compound prepared in this experiment was found to be identical with that prepared earlier[3] from nitrous acid by comparison of the infrared spectra and by mixture melting point determination.

It was of interest to determine the fate of substituents in the 4-position when compounds Ib and Ie containing them are subjected to the action of 48% hydrobromic acid in refluxing acetic acid, the conditions causing rearrangement of Ia to the fluorene (II). In a variation[2] of this rearrangement of the hydrocarbon (Ia) in which dimethyl sulfoxide was employed as the solvent, bromination at the 9-position evidently occurred, since the product obtained after treatment of the reaction mixture with water was the fluorenol having the structure of II but with a hydroxyl group in place of the hydrogen atom at position 9. A similar reaction occurred when the bromo compound (Ib) was heated with hydrobromic acid in acetic acid under conditions of moderate concentration (3 g. of Ia and 4 ml. of hydrobromic acid in 75 ml. of acetic acid); the principal substance isolated after recrystallization of the crude product from a mixture of ethanol and chloroform was 9-ethoxy-4-methyl-1,3,9-triphenylfluorene (38%). Only a little (7%) of hydrocarbon II was isolated, although it may have formed in considerably larger amounts, its separation from the mixture being rather difficult. Free bromine was detected as a product of the reaction. In a similar experiment in which the relative amounts of the bromo compound and hydrobromic acid were about the same (0.8 g. and 1 ml.) but the relative amount of acetic acid (150 ml.) was increased severalfold, only hydrocarbon II was isolated. Evidently the bromo compound (Ib) in acid solution is a source of positive bromine, perhaps through the elimination of a positive bromine ion from the protonated species to yield the parent hydrocarbon (Ia) which then protonates and rearranges to II, with the liberated bromine ion attacking either II or the hydrogen bromide in the solution.

A similar treatment of the aldehyde (Ie) gave only the rearranged hydrocarbon (II). Presumably the protonated form of the aldehyde expels carbon monoxide to generate the carbonium ion related to Ia, which then rearranges.

Experimental[10]

Preparation of 4-Chloro-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Id).—Two grams (0.005 mole) of 4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ia) was dissolved in 100 ml. of benzene and 20 ml. of dry dimethyl sulfoxide in a 250-ml. three-necked round-bottomed flask equipped with an automatic stirrer, $CaCl_2$-protected condenser, and a dropping funnel. To this yellow solution was added 1.18 g. (0.010 mole) of thionyl chloride over a period of 15 min. Immediately upon addition of the thionyl chloride the solution became dark blue-green, and the odor of dimethyl sulfide was very prevalent. The color faded to yellow after about 5 min. The addition of thionyl chloride caused an increase in temperature to 35°. The reaction solution was stirred for 3 hr. without any application of heat. The solvent was then removed by distillation at reduced pressure leaving 2.1 g. (94%) of 4-chloro-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene, m.p. 206–208°.

Anal. Calcd. for $C_{32}H_{23}Cl$: C, 86.68; H, 5.19. Found: C, 86.42; H, 5.40.

Preparation of 4-Formyl-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ie).—Two grams (0.005 mole) of Ia was dissolved in 100 ml. of dry dimethylformamide in a 250-ml. three-necked round-bottomed flask equipped with a $CaCl_2$-protected condenser, automatic stirrer, and a dropping funnel. The solution was vigorously stirred at room temperature while 1.2 g. (0.007 mole) of $POCl_3$ was added slowly. Immediately upon addition of the $POCl_3$ the reaction solution turned a deep orange-red. This solution was heated on the steam bath for 1 hr. Water (50 ml.) was added to the hot solution, causing the precipitation of an orange-red solid. This aqueous mixture was heated on the steam bath for 1.5 hr. At the end of this time the solid was a brilliant orange in color. Recrystallization three times from absolute ethanol gave 1.9 g. (86%) of 4-formyl-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene, m.p. 175–176°.

Anal. Calcd. for $C_{33}H_{24}O$: C, 90.82; H, 5.50. Found: C, 90.63; H, 5.80.

Repetition of the experiment on a smaller scale (1/20) but with the deuterio compound 4a-methyl-1,3,9-triphenyl-4a*H*-fluorene-4*d*[4] gave about 70% of a product identical with that just described in melting point, mixture melting point, and n.m.r. spectrum.

Preparation of the Iminium Salt (If).—Five grams (0.012 mole) of 4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ia) and 1 g. (0.015 mole) of dimethylformamide was dissolved in 100 ml. of dry benzene in a 250-ml. three-necked round-bottomed flask equipped with an automatic stirrer and a $CaCl_2$-protected condenser. The yellow solution was vigorously stirred while 1.4 g. (0.015 mole) of $POCl_3$ was added in one portion. Immediately upon addition of the $POCl_3$ there was a flash of blue color; this blue color lasted only a few seconds and then the solution became yellow.

About 5 min. later the solution was blood red. This red solution was stirred at room temperature for 4 hr. At the end of this time a beautiful crystalline solid had precipitated. The solid was removed by filtration giving 5.3 g. (92%) of the salt If, m.p. 152–155° dec. Because of the instability of the salt in hot solutions, attempts to purify it for analysis were unsuccessful.

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(7) G. F. Smith, *J. Chem. Soc.*, 3842 (1954).

(8) Richard L. Johnson, Ph.D. thesis, University of Illinois, 1955.

(9) A. G. Anderson, J. A. Nelson, and J. J. Tazuma, *J. Am. Chem. Soc.*, **75**, 4980 (1953).

(10) Melting points are uncorrected. Microanalyses were carried out by Mr. J. Nemeth and his associates, University of Illinois.

Preparation of 4-Dimethylaminomethyl-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ig).—Two grams of the iminium salt was dissolved in 100 ml. of dry tetrahydrofuran in a 250-ml. round-bottomed three-necked flask equipped with an automatic stirrer and a $CaCl_2$-protected condenser. Lithium aluminum hydride was added in small portions over a period of 30 min. During this period of time, the color of the reaction solution changed from deep red to light yellow. The reaction mixture was stirred at room temperature for 2 hr. Fifty milliliters of wet ether was then slowly added to decompose the complex and any unchanged lithium aluminum hydride. The reaction mixture was filtered and the solvent was removed by distillation under reduced pressure. A yellow solid was obtained, which after recrystallization from a 1:1 mixture of ethanol and chloroform gave 1.5 g. (74%) of 4-dimethylaminomethyl-4a-methyl-4a*H*-fluorene, m.p. 192–193°.

Anal. Calcd. for $C_{35}H_{32}N$: C, 90.32; H, 6.66; N, 3.02. Found: C, 89.85; H, 6.83; N, 2.97.

Preparation of 4-Nitro-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene (Ih).—One and one-half grams (0.0037 mole) of Ia was added to 100 ml. of freshly distilled acetic anhydride in a 250-ml. three-necked round-bottomed flask equipped with an automatic stirrer, a thermometer, and a $CaCl_2$-protected reflux condenser. The reaction solution was cooled to 5° by means of an ice–water bath and stirred vigorously while 0.5 g. (0.0045 mole) of cupric nitrate in 20 ml. of acetic anhydride was added over a period of 15 min. The solution immediately became dark blue-green upon addition of the cupric nitrate. The ice–water bath was removed and the dark blue-green reaction solution was allowed to warm to room temperature. The solution was then vigorously stirred at room temperature for 4 hr. At the end of this time the reaction mixture was still blue-green, but it was more like the color of cupric nitrate than it had been earlier in the reaction. Water (100 ml.) was added and the resulting mixture was stirred, with cooling, for 30 min. During this time the acetic anhydride hydrolyzed and a brilliant orange solid precipitated. This material was collected by filtration and recrystallized from a 1:1 mixture of ethanol and chloroform giving 1.1 g. (65%) of 4-nitro-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene, m.p. 196–198°.

Anal. Calcd. for $C_{32}H_{23}NO_2$: C, 84.76; H, 5.07; N, 3.09. Found: C, 84.38; H, 5.15; N, 3.14.

Reaction of 4-Bromo-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene with 48% Hydrobromic Acid in Glacial Acetic Acid Followed by Reaction with Ethanol.—Three grams of 4-bromo-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene[4] was added to 75 ml. of glacial acetic acid in a flask equipped with a stirrer and a reflux condenser connected to a trap containing chloroform. Four milliliters of 48% hydrobromic acid was added and the mixture was stirred and heated. A deep blue-green color soon developed and then slowly faded to yellow after 3 hr. of reflux. The chloroform solution in the trap had a pale color (bromine) and it gave a definite iodine color when shaken with aqueous sodium iodide. The grey solid that separated when the reaction solution was cooled to about 0° was recrystallized four times from 1:1 chloroform–ethanol to give 1.2 g. (38%) of 9-ethoxy-4-methyl-1,3,9-triphenylfluorene, m.p. 150–152°, identical in melting point, infrared spectrum, and n.m.r. spectrum with the sample prepared from the 9-hydroxy compound as described subsequently.

Dilution of the acetic acid solution from which the foregoing crude product had been separated with about 100 ml. of water caused the separation of a solid. Four recrystallizations of this material from 1:1 ethanol–chloroform gave 0.2 g. (7.2%) of 4-methyl-1,3,9-triphenylfluorene[3] (II), m.p. 163–164°, identified by mixture melting point.

In a reaction in which 0.8 g. of the bromo compound (Id) was heated with 150 ml. of acetic acid and 1 ml. of 48% hydrobromic acid, only 4-methyl-1,3,9-triphenylfluorene (II, 0.4 g., 62%) was isolated.

Preparation of 9-Ethoxy-4-methyl-1,3,9-triphenylfluorene from 9-Hydroxy-4-methyl-1,3,9-fluorene.—A mixture of 0.20 g. of 4-methyl-1,3,9-triphenyl-9-fluorenol[2] and 50 ml. of concentrated hydrochloric acid was refluxed for 15 min. and then allowed to stand at room temperature for 12 hr. Filtration gave 180 mg. (90%) of white crystalline 9-chloro-4-methyl-1,3,9-triphenylfluorene, m.p. 192–195°. The material was very sensitive to moisture. Accordingly, a sample prepared in this way (4.3 g.) was heated under reflux for 1 hr. with 100 ml. of ethanol–chloroform and the solid remaining after removal of the solvent mixture under reduced pressure was recrystallized four times from 1:1 ethanol–chloroform to give 4.3 g. (95%) of the ethoxy compound, m.p. 150–152°. The n.m.r. spectrum showed the characteristic absorption of the ethyl group (triplet at 8.99 and a quartet at 6.82 τ with a coupling constant, $J = 7$ c.p.s., with the relative intensity of the quartet to the triplet being 2:3).

Anal. Calcd. for $C_{34}H_{28}O$: C, 90.26; H, 6.19. Found: C, 90.24; H, 5.98.

Reaction of 4-Formyl-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene with 48% Hydrobromic Acid in Acetic Acid.—Four grams of 4-formyl-4a-methyl-1,3,9-triphenyl-4a*H*-fluorene was dissolved in 150 ml. of glacial acetic acid in a flask equipped with a stirrer and a reflux condenser. Two milliliters of 48% hydrobromic acid was added, giving a deep brown-yellow solution. The color changed as the solution was heated and stirred, becoming an intense blue-green as the boiling point was reached and then slowly fading to brown-yellow after 4 hr. at reflux. Dilution of the cooled solution with water gave a grey solid. After five recrystallizations from 1:1 ethanol–chloroform there remained 2.0 g. (52%) of 4-methyl-1,3,9-triphenylfluorene, m.p. 162–164°, identified by mixture melting point with an authentic sample.[3]

N.m.r. Spectroscopy.—The n.m.r. spectra were recorded by Mr. D. Johnson and his associates with a Varian Associates high resolution spectrometer (A-60) at a frequency of 60 Mc. per second. Spectra were obtained in 30% solutions with tetramethylsilane as an internal standard. Chemical shifts are expressed as shielding values (τ) as defined by G. V. D. Tiers.[11]

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(11) G. V. D. Tiers, *J. Phys. Chem.*, **62**, 1151 (1958).