

$[\alpha]_D -162^\circ$ (*c* 0.1 in pyridine)²⁷ the melting point of which was unchanged by admixture of an authentic sample of the anilide⁹ of 2,4-di-*O*-methyl-D-galactose, m.p. 215.5–216°,

(27) An error of at least 15% may have been involved in measuring this rotation and, consequently, its divergence from that reported for the compound is not surprising. The rotation serves to show, however, that the acetolysis of VI did not yield 2,4-di-*O*-methyl-DL-galactose as may have been anticipated from the results obtained by T. L. Cottrell and E. G. V. Percival [*J. Chem. Soc.*, 749 (1942)] on the acetolysis of methyl 3,6-anhydro- β -D-galactopyranoside.

$[\alpha]_D -183^\circ$ (pyridine). The infrared spectra (Nujol mulls) of the two anilides were identical.

The component, *R_f* 0.61, 15 mg. yield, undoubtedly was 2,4-di-*O*-methyl-3,6-anhydro-D-galactose which survived the acetolysis since the compound was converted to 2,4-di-*O*-methyl-D-galactose (identified by paper chromatography) by the procedure described above for the acetolysis of VI and deacetylation of the product.

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Derivatives of Fluorene. III. Stereoisomerism and Polymorphism of N-Aryl Azomethines¹

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A pair of azomethine stereoisomers and a pair of enantiotropic polymorphs in the 9-phenyliminofluorene series have been prepared, isolated and characterized.

Introduction

During the preparation of a series of azomethine derivatives of fluorene, it was found that 2-nitrofluorenone condensed with *p*-toluidine in the presence of a Lewis acid catalyst to give a product isomeric with the product obtained from the condensation of 2-nitrofluorene with *p*-nitrosotoluene in the presence of a base. The melting points of the two compounds differed by 26°. Analogous reactions substituting *p*-nitrosoethylbenzene and *p*-aminoethylbenzene for *p*-nitrosotoluene and *p*-toluidine, respectively, yielded the nitrone in one case and the anil in the other.

In a similar series, the condensation of 2,5-dinitrofluorenone with *p*-fluoroaniline in the presence of a Lewis acid yielded two products,² large hexagonal red-colored plates and fine yellow needles. Both had the same elemental analysis and molecular weight. The melting points differed by about 2°. When the catalyst was zinc chloride the main product was the red solid. With aluminum chloride the product was an equal mixture of both forms. A mixture melting point was not depressed. These substances undoubtedly are polymorphs.

While several reports of the isolation of stereoisomeric azomethines have appeared in the literature, they are in question or have been proved polymorphs rather than isomers.^{3–6} On the basis of dipole moment measurements, it has been suggested that phenylimino Schiff bases can exist in the *trans* form only,⁴ and, in the case of benzyldeneaniline, a linear arrangement for the N-phenyl group has been suggested.⁷ Thus it was of interest to investigate the compounds we obtained because of the question concerning the ability of

an azomethine to exist in two stereoisomeric forms.

Experimental^{8,9}

N-(2-Nitrofluorenylidene)-*p*-toluidine. Method—A. A mixture of 5.6 g. (0.025 mole) of 2-nitrofluorenone (m.p. 224.5–225.0°), 4.3 g. (0.040 mole) of *p*-toluidine and 0.25 g. of freshly fused zinc chloride was heated at 160–170° for 45 min.; a melt quickly formed. The cooled reaction mixture was dissolved in hot chloroform and the solution was filtered. The insoluble toluidine-zinc chloride compound was removed by filtration. A mixture of amorphous yellow unreacted 2-nitrofluorenone and crystalline orange-colored product totaling 7.4 g. was obtained by crystallization from the chloroform. The density of the product was much greater than that of the 2-nitrofluorenone; thus the latter was removed by stirring the mixture in ether and decanting. The procedure was repeated until a nearly pure product remained. It then was recrystallized from chloroform, heated under vacuum at 184° until a sublimate was no longer evident and recrystallized twice from benzene; yield 5.6 g. of large, orange-colored rods, m.p. 192–193°. Crystallization from acetone gave m.p. 192–193°.

Anal. Calcd. for C₂₀H₁₄N₂O₂: C, 76.42; H, 4.49; N, 8.91; mol. wt., 314. Found: C, 76.22; H, 4.31; N, 8.83; mol. wt. (Rast method), 311.

Method B.—Five drops of 1% sodium ethoxide in ethanol was added to a refluxing solution of 4.2 g. (0.020 mole) of 2-nitrofluorene (m.p. 159.0–159.5°) and 3.4 g. (0.028 mole) of *p*-nitrosotoluene (m.p. 47–48°)¹⁰ in 450 ml. of absolute ethanol. The solution was refluxed 3 hours. The product crystallized from the cooled solution and was collected on the filter. Further crops were obtained by concentrating the mother liquors: yield 6.08 g., m.p. 210–215°. Crystallization from benzene raised the m.p. to 214.5–215.5°. Crystallization from acetone produced orange-colored rods, m.p. 217.5–218.5°. A series of mixture melting points of 20%, 40%, 50%, 60% and 80% of the product from A in that from B were 193–207°, 192–202°, 189–203°, 190–202° and 190–197°, respectively.

Anal. Calcd. for C₂₀H₁₄N₂O₂: C, 76.42; H, 4.49; N, 8.91; mol. wt., 314. Found: C, 76.27; H, 4.46; N, 8.96; mol. wt. (Rast method), 307.

Inoculation of a supersaturated solution of the product from method A in benzene with a crystal of the product from method B produced no crystallization at room temperature for three days, although the crystal used as seed did not

(8) All melting points are corrected.

(9) Analyses were performed by Drs. Weiler and Strauss, Oxford, England, and Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

(10) Prepared by method of R. Lutz and M. Lytton, *J. Org. Chem.*, **2**, 73 (1937).

(1) This work was supported in part by a research grant (C-1744) from the National Cancer Institute of the National Institutes of Health, Public Health Service. For the preceding paper in this series see footnote 2.

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(3) O. Anselmino, *Ber.*, **40**, 3465 (1907).

(4) V. De Gaouck and R. J. W. Le Fèvre, *J. Chem. Soc.*, 741 (1938).

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(6) V. De Gaouck and R. J. W. Le Fèvre, *J. Chem. Soc.*, 1392 (1939).

(7) C. Wiegand and E. Merkel, *Ann.*, **550**, 175 (1942).

dissolve. Large crystals formed slowly after the third day. They were collected on a filter the eighth day, m.p. 191.5–193°.

Hydrolysis of N-(2-Nitrofluorenylidene)-*p*-toluidine. Product from Method A.—Azomethine (m.p. 192–193°, 0.5 g.) was dissolved in 50 ml. of glacial acetic acid, and at reflux 5 ml. of concentrated hydrochloric acid was added. The solution was refluxed 1 min.; an equal amount of water was added and the solution cooled. Long, yellow needles crystallized and were collected on the filter; yield 0.35 g., m.p. 222.5–223.0°. A mixture melting point with authentic 2-nitrofluorenone gave no depression.

Product from Method B.—Azomethine (m.p. 217.5–218.5°, 0.30 g.) in 25 ml. of glacial acetic acid was treated as above, yielding 0.19 g. of yellow needles, m.p. 223.0–223.5°, giving no depression of the melting point with 2-nitrofluorenone.

N-(2-Nitrofluorenylidene)-*p*-ethylaniline.—A mixture of 11.2 g. (0.05 mole) of 2-nitrofluorenone, 9.7 g. (0.08 mole) of *p*-aminoethylbenzene¹¹ and 1 ml. of boron fluoride ethyl ether was heated for 20 min. at 130–135°. Crystallization from chloroform yielded 5.4 g. of unreacted 2-nitrofluorenone and 8.0 g. of fine orange-colored needles, m.p. 167.5–168.0°.

Anal. Calcd. for C₂₁H₁₈N₂O₂: C, 76.81; H, 4.91; N, 8.53. Found: C, 76.62; H, 4.86; N, 8.69.

N-(2-Nitrofluorenylidene)-*p*-ethylaniline-N-oxide.—A solution of 4.7 g. of *p*-nitrosoethylbenzene¹⁰ in 20 ml. of absolute ethanol was added to a refluxing solution of 4.2 g. (0.02 mole) of 2-nitrofluorenone in 380 ml. of absolute alcohol. Then 5 drops of 0.5% sodium ethoxide solution was added and reflux was continued for three hours. Ethanol (100 ml.) was removed by distillation and the solution was cooled yielding 2.7 g. of transparent yellow plates, m.p. 185–195° dec. Recrystallization from benzene raised the m.p. to 217–218° dec.

Anal. Calcd. for C₂₁H₁₈N₂O₃: C, 73.23; H, 4.58; N, 8.14. Found: C, 73.49; H, 4.68; N, 8.09.

N-(2,5-Dinitrofluorenylidene)-*p*-fluoraniline was prepared with aluminum chloride catalyst.² A chloroform solution of the product yielded red plates and yellow needles. A mixture of absolute ethanol and benzene (4:1) dissolved the yellow crystals. The red compound was pulverized and heated at 176° for 3 hr. Recrystallization from carbon tetrachloride yielded 5.7 g. of red plates, m.p. 182–183.5°.

Anal. Calcd. for C₁₉H₁₀FN₃O₄: C, 62.81; H, 2.78; N, 11.57; mol. wt., 363. Found: C, 62.88; H, 2.77; N, 11.50; mol. wt. (Rast method), 370.

Concentration of the alcohol–benzene extract produced yellow crystals. Fractional crystallization from acetone removed 4.5 g. of unreacted 2,5-dinitrofluorenone, m.p. 244–245° (subl.), and 5.6 g. of long yellow needles were recovered, m.p. 183–184.5°.

Anal. Calcd. for C₁₉H₁₀N₃O₄F: N, 11.57; mol. wt., 363. Found: N, 11.59; mol. wt. (Rast method), 361.

The two forms were easily interconverted. When an alcoholic solution of the yellow product was allowed to stand at room temperature, the red form crystallized in about three hours. The red form crystallized from benzene or tetrachloroethylene as yellow needles. A portion of the yellow product covered with tetrachloroethylene reverted to the red form in about three hours. A mixture of the red and yellow forms melted at 181–183°.

Hydrolysis of N-(2,5-Dinitrofluorenylidene)-*p*-fluoroaniline.—Each form was hydrolyzed in the manner described above. In each case, long yellow crystals resulted, m.p. 245.5–246.5° (subl.) and gave no melting point depression with authentic 2,5-dinitrofluorenone.

Physical Measurements.—The infrared absorption spectra were obtained with a Perkin–Elmer model 21 spectrophotometer equipped with a sodium chloride prism. The KBr disks were made by grinding the compound in a mortar, thoroughly mixing it with Harshaw Chemical Co. infrared grade potassium bromide, vibrating the mixture in a Wig L Bug amalgamator manufactured by the Crescent Dental Mfg. Co., for 3 min. and pressing at 20,000 lb. total load.

The ultraviolet absorption spectra were obtained with a Beckman DU spectrophotometer.

(11) Prepared by the method of D. Balcom and A. Furst, *THIS JOURNAL*, **75**, 4334 (1953).

The refractive index increments were obtained with a Phoenix Precision Instrument Co. B-S differential refractometer.¹² The constant, relating change of position of slit image with change of cell to change in refraction, was 9.17×10^{-4} for the green Hg line at 5461 Å. Stock solutions of the compounds in chloroform, 10 mg. of compound/1 ml. of solvent, were diluted for the measurements by taking aliquots and adding solvent to give 0.50% and 0.25% solutions. The specific refractive increment $\Delta n/c$ is apparently independent of the concentration at these dilutions. The temperature at which the measurements were made was $22 \pm 0.3^\circ$.

X-Ray diffraction determination of molecular weights as well as the comparison of intensities of the N-(2-nitrofluorenylidene)-*p*-toluidine compounds were obtained by means of Weissberg and oscillation photographs about the *b*-axis (CuK α = 1.5418 Å.). Measurement of the diffraction patterns gave the following unit cell parameters: compound m.p. 217.5–218.5°; $a_0 \sin \beta = 43.68$ Å., $b_0 = 31.28$ Å., $c_0 = 9.46$ Å.; compound m.p. 191–192°; $a_0 \sin \beta = 42.50$ Å., $b_0 = 30.80$ Å., $c_0 = 9.61$ Å.

Densities of N-(2-nitrofluorenylidene)-*p*-toluidine as determined by the flotation method¹³ using carbon tetrachloride and alcohol at 24–25° were 1.311 g./cc. for the compound melting at 217.5–218.5°, and 1.308 g./cc. for the compound melting at 191–192°.

Results and Discussion

Figure 1 shows the molar extinction coefficient as a function of wave length in the ultraviolet region for the two N-(2-nitrofluorenylidene)-*p*-toluidine products. It is noteworthy that although the spectra are very similar in shape and general regions of absorption, ϵ_{\max} of the higher-melting compound is the larger and appears at a shorter wave length, whereas the secondary absorption band is found at a longer wave length and is less intense than the corresponding band of the lower-melting compound.

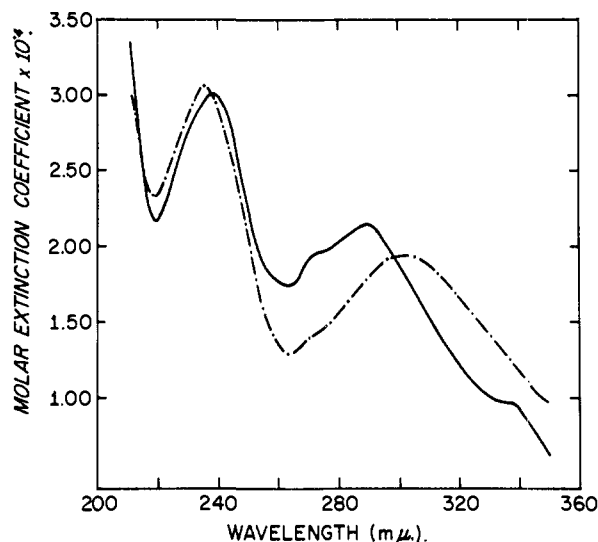


Fig. 1.—Ultraviolet absorption spectra of N-(2-nitrofluorenylidene)-*p*-toluidine compounds in 95% ethanol: —, acid-catalyzed condensation product of ketone and amine; - - -, base-catalyzed condensation product of methylene and nitroso compounds.

These differences could be expected by analogy both with isomeric azobenzenes and stilbenes. In these series it has been found generally that *trans*

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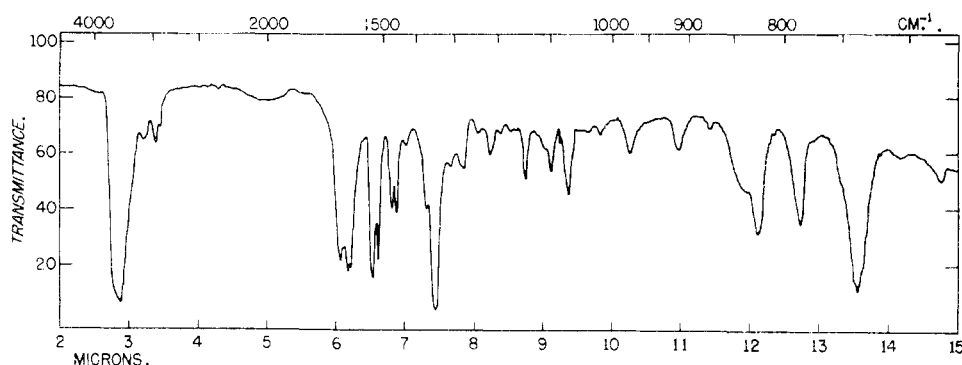


Fig. 2.—Infrared absorption spectrum of *N*-(2-nitrofluorenylidene)-*p*-toluidine, m.p. 192–193°, in KBr disk.

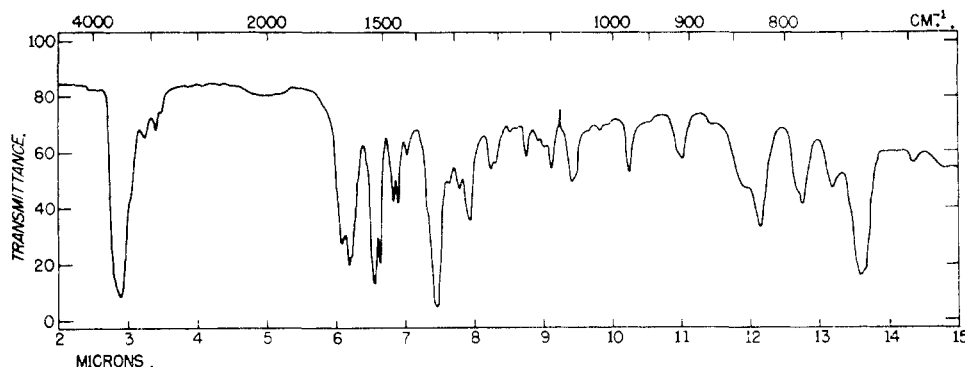


Fig. 3.—Infrared absorption spectrum of *N*-(2-nitrofluorenylidene)-*p*-toluidine, m.p. 217.5–218.5°, in KBr disk.

isomers have a greater absorption at the maximum near 3000 Å.¹⁴ Theoretical deduction¹⁵ indicates that the more elongated of two isomers absorbs the more strongly and on this basis it is possible that the compound melting at 191–192° (see Fig. 1) is the more elongated; that is, the phenyl group attached to the nitrogen atom is oriented away from the benzene ring of the fluorene nucleus bearing the nitro group.

A change of solvent from hexane to absolute ethanol to 50% aqueous ethanol produces a shift in absorption of 1 to 3 $m\mu$ in the 237 $m\mu$ region while the absorption band at 285–286 $m\mu$ undergoes a bathochromic shift of about 10 $m\mu$, indicating that the latter absorption probably is due to K-bands.¹⁶

The infrared absorption spectra of the two *N*-(2-nitrofluorenylidene)-*p*-toluidine isomers in potassium bromide pellets are reproduced (Figs. 2 and 3). The absorption in the 6.1–6.2 $m\mu$ region, tentatively assigned to the $>C=N-$ band, shows a change from 1650 to 1640 cm^{-1} from the lower to higher melting compound. The absorption of the low melting isomer at 1370 cm^{-1} is evidenced only as a shoulder for the other isomer, whereas the bands at 1260 and 759 cm^{-1} in the spectrum of the high melting isomer are absent in the spectrum of the low melting isomer.

Infrared spectra of the two *N*-(2-nitrofluorenylidene)-*p*-toluidine isomers also were obtained in chloroform solution. The spectra were similar as

to general regions of absorption, but the following differences were noted. The higher-melting isomer showed a single absorption at 918 cm^{-1} whereas the lower-melting isomer showed a double absorption in that region, one at 918 and another at 907 cm^{-1} . The first-mentioned compound absorbed at 1265, 1287, 1315 and 1370 cm^{-1} . The latter absorbed at 1275 cm^{-1} , very weakly at 1282 and at 1305 cm^{-1} but it did not absorb in the 1370 cm^{-1} region. It is also interesting to note that both compounds absorbed at 1610 and 1620 cm^{-1} but the intensities were reversed. Although the spectra, both in potassium bromide pellets and in chloroform solution, indicated that the substituents of each molecule are the same, there are small differences which would be expected for isomers.

The specific refractive index increments, $\Delta n/c$, where c is the concentration in g./ml., as determined for the low melting compound were 0.240, 0.242 and 0.243 for the 1.00, 0.500 and 0.250% solutions, respectively, average 0.242. The values for the higher melting compound were 0.252, 0.250 and 0.251 for similar solutions, average 0.251. This also indicates that the compounds were dissimilar in solution.

X-Ray analyses were undertaken, and it was found that the unit cell was composed of 32 molecules which precluded structural analysis. However, molecular weights were determined and intensities compared. The size of the unit cell for the low melting compound was 12,600 Å.³; the density of the crystal was 1.308 g./cc., mol. wt. 310. The unit cell volume of the higher melting compound was 12,932 Å.³; the density was 1.314 g./cc., mol. wt. 319.6.

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Intensities of the $h0l$ reflections from crystals of the most pure preparation of each compound were slightly different. It was thought that the difference might be due to impurities. Diffraction patterns of the products in various stages of purification showed that impurities did indeed affect the intensities, but that the difference between the patterns of the most pure preparations could not be explained in terms of impurities present during preparation.

The condensations of 2-nitrofluorenone and 2-nitrofluorene with *p*-aminoethylbenzene and *p*-nitrosoethylbenzene, respectively, were undertaken because the products, if *N*-arylazomethines, would be the closest analogs of the *p*-methyl derivatives. However, in this case the nitroso condensation yielded a nitron instead of an anil.

Both differently colored *N*-(2,5-dinitrofluorenylidene)-*p*-fluoroaniline products absorbed at 227 $m\mu$ ($\epsilon_{\max} 33.2 \times 10^3$) and at 279 $m\mu$ ($\epsilon_{\max} 26.1 \times 10^3$). Shoulders occurred at 315 $m\mu$ ($\epsilon_{\max} 10.7 \times 10^3$) and at 337 $m\mu$ ($\epsilon_{\max} 9.47 \times 10^3$).

The specific refractive index increments for the yellow form were 0.216, 0.213 and 0.223 (av. 0.217) for the 1.00% 0.50% and 0.25% solutions, respectively, and for the red form they were 0.215, 0.213 and 0.213 (av. 0.214).

A comparison of the infrared spectra of the two compounds in Nujol mulls showed bands at 1556 and 1369 cm^{-1} in the spectrum of the yellow compound which were absent in the other spectrum.

Bands in the yellow spectrum at 1219 and 1228 cm^{-1} are replaced by one band at 1223 cm^{-1} in the spectrum of the red compound. The greater number of absorption bands in the spectrum of the yellow compound indicates a lesser degree of crystalline order and a lower stability. It is noteworthy that both forms of this substance exhibit identical spectra in potassium bromide disks. Apparently one or both forms changed when subjected to the pressure necessary to form the disk. It would appear that one cannot always distinguish between polymorphs by the potassium bromide pellet method.

Although the two *N*-(2,5-dinitrofluorenylidene)-*p*-fluoroaniline compounds are markedly different in color and gross crystalline structure, the two forms are identical in solution. The infrared spectra of their Nujol mulls are dissimilar, indicating that these forms are polymorphs rather than isomers.

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Plant Polyphenols. III. The Isolation of a New Ellagitannin from the Pellicle of the Walnut

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The major constituent of the tannin from the walnut pellicle has been isolated. Analyses of numerous derivatives of the compound, for which the name *juglanin* is proposed, show that its molecular formula is $\text{C}_{27}\text{H}_{22}\text{O}_{18}$ and that it contains eleven hydroxyl groups. Acid and alkaline hydrolyses of juglanin give ellagic acid (I), gallic acid and glucose. The yields of these hydrolysis products and the analytical data indicate that juglanin is a polyphenol formed by the esterification of three hydroxyl groups of glucose with a molecule of gallic acid and a molecule of hexahydroxydiphenic acid (II). It is therefore isomeric with corilagin, but differs in the position of attachment of the galloyl and/or hexahydroxydiphenoyl units to glucose.

The isolation of ellagic acid, gallic acid, methyl gallate and a mixture of ellagitannins from the pellicle (skin) of the walnut has been previously reported.² Complex mixtures of ellagitannins frequently occur in plants. However, much of the earlier work on the structures of these substances is of doubtful value because of the difficulties encountered in the separation of individual constituents from the tannin mixtures and the lack of reliable methods for determining the purity of the isolated compounds. Thus little progress in the structural chemistry of ellagitannins was made until the recent work of Schmidt and his co-workers on the isolation and chemistry of corilagin³⁻⁵ and che-

bulagic acid^{6,7} from commercial myrobalans and divi-divi.

Two-dimensional chromatograms of the crude walnut tannin show that it contains at least ten polyphenols. Visual examination of the intensity of the spots in the developed chromatograms indicates that the polyphenol mixture consists chiefly of one major constituent (Table I, A) and smaller quantities of three other components (B,D,E). The high R_f value of A in water and the somewhat higher R_f values of B, C and D in organic solvents suggested the possibility of the selective removal of the latter components from aqueous solutions of

(1) Financial support for this work was provided by the Diamond Walnut Growers, Inc.

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