J = 10.0 Hz and 5.5 Hz, C-3 H), 8.64, 8.71, 8.82 and 8.88 (each s, *ca.* 18, 6 CH_3).

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, C, 69.13; H, 10.21.

Photolysis of Chrysanthemol (1c) in *n*-Hexane.—A solution of 17.1 g (0.11 mol) of 1c[20] in 1.1 l. of *n*-hexane was irradiated with a 500-W high pressure mercury lamp for 28 hr. The crude product was distilled through a 10-cm spinning-band column after removal of the solvent through a 40-cm Widmer column. The first liquid fraction of bp 47–68° (19 mm) consisted of prenol **8**, 2.4 g (25%): ir (neat) 3400 (OH), 1670 and 830 (C=CH) cm^{-1}. Its phenylurethan derivative had mp 62–64° (lit.[10] mp 64°). The second oily fraction of bp 52–53° (1.5 mm) was characterized as lavandulol (**9**), 3.3 g (20%), by comparison with an authentic specimen[11] *via* vpc and ir. The residue, 4.6 g, was nondistillable.

Photolysis of Chrysanthemic Acid (1a) in *n*-Hexane.—A solution of **1a** (3.36 g, 0.02 mol) in 200 ml of *n*-hexane was irradiated with a 100-W lamp for 70 hr. After removal of the solvent, the oily residue was dissolved in 30 ml of *n*-hexane and the solution was extracted with 5% aqueous potassium hydroxide solution (three 20-ml portions). The orgnaic layer was dried (Na_2SO_4). Removal of the solvent left 0.55 g (16%) of an oil, which afforded colorless crystals of **5**, mp 46–49°, on cooling. The combined alkaline extracts were neutralized with 10% hydrochloric acid and the resultant oil was taken up with chloroform (three 30-ml portions). Work-up afforded 2.3 g (68% recovery) of a viscous oil, which was identified as recovered **1a** by comparison with an authentic sample *via* vpc and ir. No trace of senecioic acid **4** was detected by vpc analysis of the crude product. Furthermore, it was found that photodecarboxylation of **1a** had occurred during the photolysis to less than 3% as determined by titration of the evolved carbon dioxide with aqueous sodium hydroxide solution.

Photolysis of Chrysanthemamide (1d) in Ether.—A solution of 3.34 g (0.02 mol) of 1d[10] in 200 ml of ether was irradiated with a 100-W lamp for 90 hr. After removal of the solvent, the residual oil was purified on alumina (neutral, activity grade III), eluting with *n*-hexane, benzene, and ether, successively. The *n*-hexane fraction afforded 0.3 g of oily hydrocarbon which was discarded. The benzene and ether fractions gave a mixture (2 g) of **5** and recovered **1d** on vpc. Further purification of this mixture on a silica gel column (with dichloromethane) gave pure **1d** and **5** both in 10% yields.

Photolysis of Dihydrochrysanthemo-δ-lactone (2) in *n*-Hexane.—A solution of 3.36 g (0.02 mol) of 2[2] in 200 ml of *n*-hexane was irradiated with a 100-W lamp for 90 hr. The crude oily product obtained after removal of the solvent was purified on a silica gel column eluting with *n*-hexane and benzene, successively. The *n*-hexane fraction gave 0.44 g of an oily hydrocarbon which was discarded because of the absence of carbonyl bands in the ir spectrum. The first benzene fraction afforded 1.16 g of a compound, which was shown to be acidic by the presence of carboxyl absorption bands in the ir spectrum. It showed three large peaks on vpc and could not be identified because of difficulties in obtaining pure materials. Further elution with benzene gave 0.74 g (20%) of β-isopropenyl-δ,δ-dimethyl-δ-pentanolactone (**11**) after purification by preparative vpc: ir (neat) 1720 (δ-lactone), 1640 and 890 (C=CH) cm^{-1}; nmr ($CDCl_3$) τ 5.12 and 5.20 (partly overlapped s, 2, C=CH), 8.22 (broad s, 3, C=CCH_3), 8.52 and 8.55 [s, 6, $C(CH_3)_2$], and 7.00–8.20 (m, *ca.* 5, methine and methylene protons); mass spectrum (75 eV) *m/e* (rel intensity) 168 (5.1, M^+) and 68 (100, $C_5H_8^+$). Further elution with benzene gave 0.43 g (13% recovery) of recovered **2**.

Registry No.—**1a**, 10453-89-1; **1b**, 97-41-6; **1c**, 5617-92-5; **1d**, 22841-81-2; **2**, 22841-82-3; **7b**, 22841-83-4.

Acknowledgment.—We are very grateful to Dr. T. Nishida of the Nippon Electric Varian Ltd. and to Mr. K. Watanabe of JEOL Co. for running nmr spectra and vpc separations.

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Fragmentation without Rearrangement of the *p*-Fluoro Label in the Mass Spectra of Some Six-Membered Heterocycles

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Scrambling results by the *p*-fluoro-labeling technique are reported for a pentaarylpyridine, a tetraarylpyrazine, and a triaryl-*as*-triazine. There is little or no randomization of the label before each of the major fragmentations of the molecular ions. Such results are discordant with the statistical randomization of molecular ions of six-membered aromatic compounds found by deuterium-labeling studies. The discrepancy could suggest that the valence-isomer formation of six-membered rings postulated previously to occur on electron impact is not the mechanism of randomization; another mechanism, less likely but preserving this previous suggestion, is also proposed.

The degree of hydrogen scrambling before fragmentation of some six-membered aromatic ring compounds in the mass spectrometer is essentially complete, and mechanisms of scrambling have been suggested which resemble the photochemical transformation of benzene into valence tautomers.[2,3] In addition, there is scrambling of hydrogen in decomposing molecular ions of thiophene, but not in those of furan, in the mass spectrometer; the extent of scrambling is a function of the particular decomposition of the molecular ion.[4] These results are each the product of deuterium-labeling studies, and have therefore several explanations: they may indicate rearrangement of the carbon skeleton through intermediates similar to the photochemical intermediates,[2,3] but they might merely indicate that hydrogen atoms migrate about an essentially intact heavy-atom skeleton. Several examples have now been offered in support of the latter mechanism in special cases.[5,6]

We have recently suggested an inexpensive companion method to deuterium replacement of protium, the *p*-fluoro label.[7] In this method, the *p*-fluorophenyl substituent replaces an unsubstituted phenyl substituent; in typical examples the *p*-fluoro substituent

(1) Fellow of the Alfred P. Sloan Foundation, 1969–1971.
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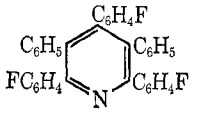
influences the intensities of unsubstituted[8] and substituted[9] ions only slightly, and in this way acts as an inert label. Since hydrogen migrations and the migrations of alkyl and aryl groups do not parallel each other in mass spectral decompositions,[10] parallelism between H–D scrambling and p-FC_6H_4–C_6H_5 scrambling might suggest that the atoms to which these groups are attached themselves scramble. On the other hand, large differences in the amount of scrambling between the H–D-labeled compound and the p-FC_6H_4–C_6H_5-labeled compound would tend to weaken this argument; such data could suggest that the labels (one set or the other, or both to widely varying extents) rearrange on an intact ring or chain, rather than the atoms to which they are attached.

There have been several applications of the p-fluoro method to systems where H–D labeling is not easily available for comparison.[6,11–14] The one comparison that has been made, where the p-fluoro-labeling method was applied to the scrambling of groups in thiophenes but not furans, indicated that p-FC_6H_4–C_6H_5 scrambling resembles H–D scrambling in these heterocycles,[15] so that the suggestions based on the H–D scrambling results about the resemblance to photochemical behavior[4] were supported. Because of the interest in the mechanism of scrambling of hydrogen in six-membered rings, we present here further labeling results for the systems pyridine, pyrazine, and *as*-triazine, testing for the presence of scrambling; some of the results can be compared with previously published data for heterocycles. These rings contain one, two, and three nitrogen atoms, respectively.

The first compound studied, 3,5-diphenyl-2,4,6-tris(p-fluorophenyl)pyridine (I), mol wt 513, gave an intense M − 1 peak (Table I). The principal loss



I

from the M − 1 peak, supported by a metastable peak at m/e 338.0 (calculated, 338.0), is the loss of the elements of fluorobenzene to give the peak at m/e 416. By contrast, the loss of benzene to give a peak at m/e 434 is only one-tenth as favored as the loss of fluorobenzene. The mechanism of this series of reactions cannot be defined, but it is clear that scrambling is at best of only minor significance before the loss of C_6H_6 or C_6H_5F from the M − 1 ion. If it were complete, and therefore produced a statistical loss of the two labels, the relative intensities of C_6H_6 and C_6H_5F would have been 2:3, in the absence of a substituent effect

TABLE I

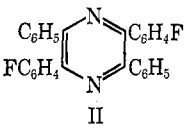
MASS SPECTRUM OF 3,5-DIPHENYL-2,4,6-TRIS(p-FLUOROPHENYL)PYRIDINE

m/e	Rel intensity	m/e	Rel intensity
55	2	247.5	2
57	2	256.5	3
60	2	414	2
196	2	416	4
225.5	2	494	2
226.5	2	495	2
234.5	2	512	100
237.5	2	513	88
238.5	2	514	27
246.5	2	515	5

of the p-fluoro group.[16] It is obviously unclear whether the ion loses C_6H_6 and C_6H_5F from a defined position (say the 2 and 6 positions) in a rearranged molecular ion, or whether it loses the fragments from each position by undefined amounts before rearranging at all. Thus, our results could fit a picture where there is no scrambling, but they cannot fit one where there is complete scrambling of positions. These are extreme pictures, and more likely the actual picture lies between them. The numerical data suggest that the real picture is closer to the first picture (no scrambling) by far.

Similarly, the peak at m/e 196 ($FC_6H_4C{\equiv}CC_6H_5^{+\cdot}$) is five times as intense as the peak at m/e 178 ($C_6H_5C{\equiv}CC_6H_5^{+\cdot}$) and ten times as intense as the peak at m/e 214 ($FC_6H_4C{\equiv}CC_6H_4F^{+\cdot}$). The origin of these could be $M^{+\cdot}$, $(M-1)^+$, or other larger fragments, even-electron precursors being less favorable, of course, for an odd-electron ion. The intensities of the small peaks are close to the doubly charged peaks on either side of them, and consequently the small peaks (*i.e.*, m/e 178 and 214) in particular have contributions of intensity from other pathways approaching the contribution from the immediate formation of the diphenylacetylene ion as written. The results do not conform to the ratio of intensities expected for complete randomization (m/e 178:196:214 = 1:6:3) before a correction is applied to the observed intensities. If it could be applied, the results would be in a direction even further from the statistical distribution; the intensities of neighboring peaks at half-integral masses suggest a correction to the intensities of the smaller peaks by at least a factor of four. Hence the scrambling is far from complete. Fragmentation without randomization would produce no m/e 178 or 214 ions, and the roughly corrected spectrum resembles this situation, though peaks are of too low intensity to claim that small relative contributions at these masses do not exist after correction of the data.

The compound containing two nitrogens, 2,5-bis(p-fluorophenyl)-3,6-diphenylpyrazine (II), mol wt 420, likewise does not give evidence of scrambling in the



II

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(10) For a review of heavy-atom migrations, see (a) P. Brown and C. Djerassi, *Angew. Chem., Intern. Ed. Engl.*, **6**, 477 (1967); (b) R. G. Cooks, *Org. Mass Spectry*, **2**, 481 (1969). The latter deals more specifically with bond formation on electron impact.

(11) M. M. Bursey and T. A. Elwood, *Org. Mass Spectrom.*, **1**, 531 (1968).

(12) T. A. Elwood and M. M. Bursey, *ibid.*, **1**, 537 (1968).

(13) M. M. Bursey, T. A. Elwood, and P. F. Rogerson, *Tetrahedron*, **25**, 605 (1969).

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(15) T. A. Elwood, P. F. Rogerson, and M. M. Bursey, *J. Org. Chem.*, **34**, 1138 (1969).

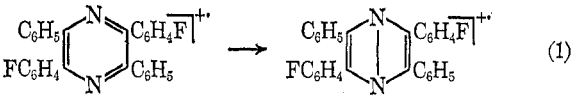
(16) Peaks for the losses of C_6H_6 and C_6H_5F from the molecular ion of the unsymmetrical 2,4-bis(p-fluorophenyl)-3,5-diphenylthiophene are equally intense.[15] There is therefore no observed p-fluoro substituent effect in this fairly comparable case.

TABLE II

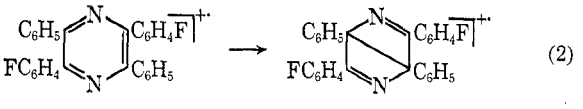
MASS SPECTRUM OF 2,5-BIS(*p*-FLUOROPHENYL)-3,6-DIPHENYLPYRAZINE

m/e	Rel intensity	*m/e*	Rel intensity
170	3	220	1
175	2	298	2
194	6	316	2
195	3	323	3
196	10	341	2
197	6	419	49
210	10	420	100
210.5	3	421	29
		422	4

molecular ion (Table II) before the major decomposition, which is in this case the formation of the *m/e* 196 ion, $FC_6H_4C{\equiv}CC_6H_5^{+\cdot}$. For this molecule the peak at *m/e* 178 is 0.0015 times as intense as that at *m/e* 196, and *m/e* 214 has 0.003 times the intensity of *m/e* 214. Thus the peaks that would indicate scrambling of positions before this fragmentation are virtually absent. The only possible reorganization of the molecular ion, in light of their absence, is that indicated in eq 1; if a process like eq 2 occurs, it cannot lead to



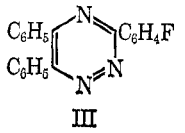
(1)



(2)

formation of a fragment ion from the newly connected atoms. It is not clear why the Dewar form of eq 1 would be more favorable than the Dewar form of eq 2, and, in fact, there is no loss of N_2 to support even eq 1. The losses of C_6H_6 and C_6H_5F from the M − 1 ion to give *m/e* 341 and 323 seem to be of comparable rate, as are the losses of C_6H_5CN and FC_6H_4CN, producing *m/e* 316 and 298. The equivalence within these pairs is expected on the basis of the symmetry of the molecule and the absence of a substituent effect.

Finally, the spectrum of 5,6-diphenyl-3-*p*-fluorophenyl-1,2,4-triazine (III), mol wt 327, is given in



III

Table III. Again, the principal decomposition of the molecular ion is the formation of a diphenylacetylene ion (*m/e* 178, $C_6H_5C{\equiv}CC_6H_5^{+\cdot}$), in this case unsubstituted. The intensity of the monosubstituted ion, which might have been formed if scrambling had occurred, is at the background level. The data again suggest virtually no scrambling of the label before fragmentation. The same arguments about the intervention of Dewar structures may be made as before.

The spectra of these three compounds do not indicate significant scrambling before the major fragmentations. These results are in contrast to the deuterium–protium scrambling results reported earlier[2,3] for six-membered rings; in particular, our phenylated pyridine and the deuterated pyridine studied earlier[3] show entirely

TABLE III

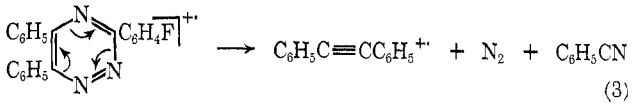
MASS SPECTRUM OF 5,6-DIPHENYL-3-*p*-FLUOROPHENYL-1,2,4-TRIAZINE

m/e	Rel intensity	*m/e*	Rel intensity
41	3	126	2
43	2	135	2
55	3	151	4
57	2	152	4
76	2	163.5	1
81	2	176	8
83	2	177	4
95	2	178	100
97	2	179	16
103	2	327	19
121	3	328	5
		329	1

different results for randomization, for the deuterium-labeling studies indicated statistical losses (*i.e.*, complete scrambling); and our results for the pentaphenylpyridine are far from the statistical distribution. Our other compounds give results even further removed from statistical distributions.

We may draw several possible conclusions from this study. The first one was suggested at the beginning of this report: the scrambling results are incompatible with a randomization mechanism based on valence isomers of the heterocyclic ring. They rather indicate H–D scrambling on an intact aromatic carbon–nitrogen skeleton, on the one hand, and C_6H_5–FC_6H_4 scrambling on an intact aromatic carbon–nitrogen skeleton, on the other. That is, the explanation for the deuterium scrambling is not valence-isomer formation, as suggested earlier.

An alternate explanation is that the phenyl groups change the relative rates of isomerization and fragmentation, so that eq 3, for example, is much more rapid



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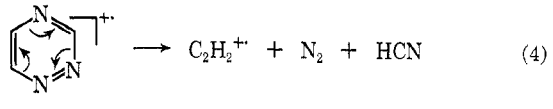
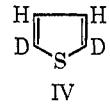
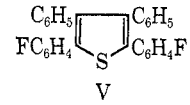


(4)

relative to heterocyclic valence isomer formation than eq 4 is. This argument seems weakened by the observation[15] that the results of H–D and FC_6H_4–C_6H_5 scrambling studies in thiophenes do not suggest that the heavier label influences the relative rates of cleavage and isomerization by so great an extent as would be needed to explain away the results of this new work. Labeling results in the thiophene system for the formation of HCS^+ from IV and $C_6H_5CS^+$ from V indicate scram-



IV



V

bling of the same order of magnitude before fragmentation. Our results for the azines could be explained by this second model only if phenylation unexpectedly increased the rate of fragmentation, relative to the rate of fragmentation of the thiophene, by a factor of about three orders of magnitude. The relative intensities of

the peaks in the spectra do not seem to support such an acceleration of the rate, and this explanation appears less acceptable to us as a result. It would be helpful to have the results of ^{13}C labeling in both the fundamental and the phenylated systems to answer this new question.

It is interesting that I loses H easily in its mass spectral fragmentation, a route not found in the other compounds. Perhaps the loss of larger groups is made less favorable by the higher degree of substitution of the more stable pyridine ring in I, and the only important route available remains the loss of H. It would be of some interest to know the origin of this hydrogen, or the extent of hydrogen scrambling before the loss, but the technique applied here does not permit an answer at the moment.

Experimental Section

General.—Melting points, reported uncorrected, were recorded on a Thomas–Kofler apparatus. Combustion analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. High-resolution mass-spectrometric elemental analyses were obtained on an MS-902 instrument at the Research Triangle Institute, Research Triangle Park, N. C.

3,5-Diphenyl-2,4,6-tris(*p*-fluorophenyl)pyridine (I) was prepared from *p*-fluorobenzaldehyde (Aldrich Chemical Co.) and 4′-fluorodeoxybenzoin (Aldrich) by the method of Weiss.[17] The crystals which separated from the reaction mixture were recrystallized from acetic acid–methanol, mp 215–217°.

Anal. Calcd for $C_{35}H_{22}F_3N$: C, 81.86; H, 4.32; monoisotopic mol wt, 513.1704. Found: C, 81.72; H, 4.29; mol wt, 513.1701.

2,5-Bis(*p*-fluorophenyl)-3,6-diphenylpyrazine (II).—Crude 4′-fluorobenzoin, prepared from 4′-fluorodeoxybenzoin by a standard procedure,[18] was heated with ammonium acetate according to Japp and Wilson's procedure.[19] The product was recrystallized from acetone, mp 248–248.5°.

Anal. Calcd for $C_{28}H_{18}F_2N_2$: C, 79.98; H, 4.31; monoisotopic mol wt, 420.1437. Found: C, 80.11; H, 4.20; mol wt, 420.1433.

5,6-Diphenyl-3-*p*-fluorophenyl-1,2,4-triazine (III) was prepared from benzil, *p*-fluorobenzhydrazide, and ammonium acetate by a literature procedure[20] and recrystallized from ethanol, mp 144.5–145.5°.

Anal. Calcd for $C_{21}H_{14}FN_3$: C, 77.05; H, 4.31; monoisotopic mol wt, 327.1170. Found: C, 76.93; H, 4.20; mol wt, 327.1170.

Mass Spectra.—The mass spectra were recorded on an AEI MS-902 instrument at the Research Triangle Institute and a Hitachi RMU-6E instrument at the University of North Carolina. The approximate resolution was 800 for the MS-902 and 500 for the RMU-6E. The samples were introduced by the direct probe at temperatures of 150, 170, and 120° for compounds I, II, and III, respectively.

Registry No.—I, 22158-33-4; II, 22158-34-5; III, 22158-35-6.

Acknowledgment.—This work was partially supported by the University of North Carolina Materials Research Center through Contract SD-100 with the Advanced Research Projects Agency. The MS902 mass spectrometer was purchased through funds made available by the Special Research Resources Branch of the National Institutes of Health. Spectra on this instrument were obtained by Dr. David Rosenthal and Mr. Fred Williams, to whom we express our thanks for their kind assistance.

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Alcoholysis of 4-Chloroquinolines to 4(1H)-Quinolones[1]

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4-Chloroquinolines bearing a carbethoxy or nitro substituent in the 3 position have been found to undergo "alcoholysis" to 4-quinolones. The intermediacy of a 4-alkoxyquinoline has been indicated. Both the initial substitution of the 4-chloroquinoline and the cleavage of the 4-alkoxyquinoline have been found to be acid-catalyzed.

During our studies on the preparation of some 4-chloroquinolines, required as intermediates in the synthesis of potential antimalarial agents, it was discovered that purification of the crude halo heterocycles by recrystallization from alcohols often resulted in the generation of 4-(1H)-quinolones, even when thoroughly anhydrous alcohols were employed as solvents.[2] Nucleophilic displacement of "activated" halo heterocycles was originally demonstrated by Banks to be an acid-catalyzed process presumably proceeding *via* a protonated iminium salt.[3–5] Although a few particularly reactive substrates are known which undergo noncatalyzed ethanolysis,[4,6] the overall conversion of a 4-Cl into a 4-quinolone in pure alcohol appears to be without precedent.

As we have noted,[7] 4-chloroquinolines lacking special electron-withdrawing functions at C-3 are totally inert to alcoholysis unless traces of HCl are present, in which case excellent yields of 4-alkoxyquinolines are obtained. However, with more activated halo heterocycles, such as 3-carbethoxy-4-chloro- and 3-nitro-4-chloroquinolines, one might anticipate an autocatalyzed displacement of halogen by alcohol. Several examples are known where autocatalytic attack of ROH has been indicated.[4,6] That the formation of quinolones from our chloroquinolines is definitely an acid-autocatalyzed effect has been established by experiments in which 1 equiv of tertiary amine base was added as proton

(1) Supported in part by Contract DA-49-193-MD-3011 from the U. S. Army Medical Research and Development Command. This paper represents Contribution No. 723 from the Army Research Program on Malaria.

(2) Alcohols are often recommended as solvents for recrystallization of haloquinolines. See, for example, H. R. Snyder, H. E. Freier, P. Kovacic, and E. M. Van Heyningen, *J. Amer. Chem. Soc.*, **69**, 371 (1947).

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