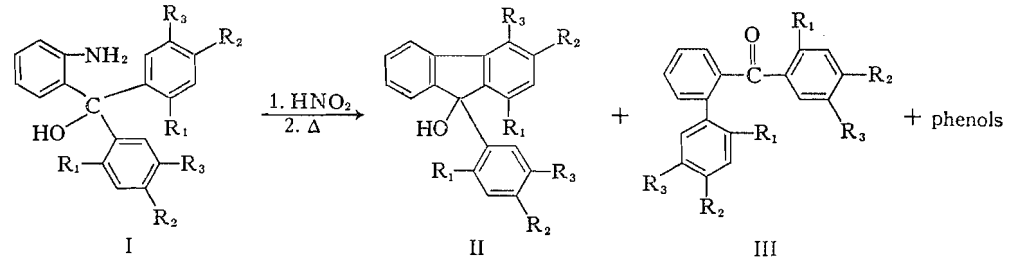
MOLECULAR REARRANGEMENT OF DIAZOTIZED *o*-AMINOPHENYLCARBINOLS

A. J. SISTI AND R. L. COHEN

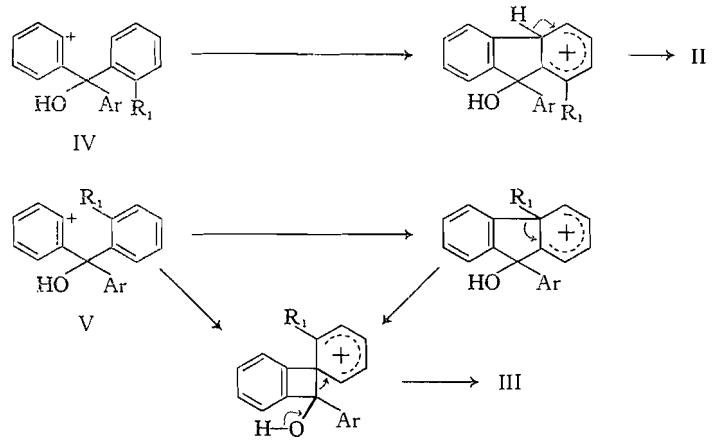
Two new reaction paths[1] have recently been observed in the decomposition of diazonium salts: in certain instances, molecular rearrangement (2, 3), and a fragmentation reaction yielding a benzyne intermediate (2, 4).

The first example of the rearrangement involved the conversion of 9-*o*-aminophenylfluorenol into tribenzotropone (5). More recently (2), the scope of the rearrangement was extended to a group of *o*-aminophenylcarbinols (I), yielding substituted 9-fluorenols II, ketones III (resulting from molecular rearrangement), and phenols (eq. [1]).

[1] 

I II III

The previous study demonstrated the necessity of an *o*-substituent (only the *o*-methyl substituent was studied (I, $R_1 = CH_3$)) for the production of ketone III. These results (Table I (*a*–*e*)) suggested that the lifetime of the aryl cation formed by the loss of nitrogen is very short compared with the time required for rotational equilibrium within the molecule (2). The following rationale was postulated.



Structures IV and V represent conformations in which the unsubstituted *o*-position is within and without incipient bonding distance to the aryl cation.[2]

Two new *o*-substituents, chloro and ethyl, were introduced to increase further the scope of the rearrangement and to offer more evidence to substantiate the previously postulated rationale.

[1] *For the more established reactions of the highly reactive aryl cation, see ref. 1.*
[2] *Structures IV and V are not intended to imply that the two rings are coplanar.*

The aminocarbinols listed in Table II were prepared from the corresponding Grignard reagents and acetyl anthranil, yielding the amido alcohols (6). The amido alcohols were subsequently hydrolyzed with alcoholic potassium hydroxide to the aminocarbinols.

The amino alcohols were diazotized in aqueous sulfuric acid and the diazonium salts were allowed to decompose at room temperature. Column chromatography on alumina was employed to separate the neutral materials.

Since all the diazonium salt decompositions were carried out in strong acid conditions, the heterolytic mechanism is most probably operating (1*c*).[3] The results are presented in Table I.

TABLE I

Yields of ketones and fluorenols from diazonium salts

	Amine I				
	R_1	R_2	R_3	% ketone III*	% fluorenol II†
a‡	H	H	H	0	46
b‡	H	OCH_3	H	0	48
c‡	CH_3	H	H	16.5 (15)	19
d‡	CH_3	CH_3	H	21.0 (16.6)	19
e‡	CH_3	OCH_3	H	28.6 (22.6)	21
f§	CH_3	OCH_3	CH_3	38 (27)	16
g	Cl	H	H	2.9	9.5
h	Cl	CH_3	H	8.8	9.9
i	Cl	OCH_3	H	11.0	8.7
j	CH_2CH_3	H	H	16.9 (13.0)	31.3
k	CH_2CH_3	OCH_3	H	33 (28)	28.4

*Yields in parentheses refer to recrystallized ketone; those without parentheses refer to chromatographed but not recrystallized material.
†In all cases, yields are based on recrystallized material.
‡Previously reported (2).
§This reaction, which was described previously (3), also gave a 7% yield of 2-(2,5-dimethyl-4-methoxybenzoyl)-2′,5′-dimethyl-4′-methoxyazobenzene.

The most significant feature of the results presented in Table I is that ketone is only obtained from the triphenylcarbinol derivatives possessing an *o*-substituent. The effect of the three *o*-substituents (chloro, methyl, and ethyl) cannot be solely electrical, since compound I*b*, containing the powerful electron-donating *p*-methoxyl group, yields no ketone. It may be noted that electron-donating substituents in the *p*-position of the migrating aryl group increase the yields of ketone significantly provided an *o*-substituent is present (I*d*, I*e*, I*h*, I*i*, and I*k*). In addition, one observes that ketone formation also appears to be dependent upon the electrical properties of the *o*-substituent (compare I*c* and I*j* with I*g*). These electrical effects are not unexpected since the rearrangement involves the migration of an aryl group to an electron-deficient site.

Another striking feature of Table I is that for a *given* *o*-substituent the yield of fluorenol remains unaltered when electron-donating *p*-substituents are introduced (I*g*–I*i*, I*c*–I*f*, and I*j*–I*k*). These data are consistent with the rationale previously postulated, based upon a very short lifetime for the aryl cation, the total number of free *o*-positions, and the relative populations of conformations IV and V. One additional observation, however, can be made. If the same relative population of conformations IV and V is assumed for R_1 = Cl, CH_3, and CH_2CH_3, the lower yield of fluorenol for *o*-chloro versus *o*-methyl and *o*-ethyl (I*g* versus I*c* and I*j*) may be ascribed to an adverse electrical effect.

The evidence presently available indicates that ketone formation resulting from the aryl cation is directly related to the total number of substituted *o*-positions and the electrical property of the *o*-substituent.

[3]*Recently an ion–diradical has been postulated as the intermediate (7).*

EXPERIMENTAL[4]

Aryl halides were prepared as follows: *o*-chlorobromobenzene (8), b.p. 197–200° (reported (8) b.p. 199–200°); 4-bromo-3-chlorotoluene (9), b.p. 75° at 2 mm (reported (9) b.p. 115–116° at 25 mm); 3-chloro-4-iodoanisole (10), b.p. 93–97° at 0.7 mm (reported (11) b.p. 127–130° at 6 mm); *o*-iodoethylbenzene (12), b.p. 56° at 0.7 mm (reported (12) b.p. 92–95° at 13 mm); 3-ethyl-4-iodoanisole, b.p. 125–126° at 5.5 mm (reported (10) b.p. 120–125° at 5 mm).

Synthesis of Acetamido Alcohols

All of the acetamido alcohols were prepared by the reaction of the appropriate arylmagnesium halide with acetyl anthranil (13). In each case a threefold excess of Grignard reagent was used. The ethereal solution of the Grignard reagent was cooled in an ice bath during the addition of a benzene solution of acetyl anthranil. The reactions were then completed by refluxing the solutions for 3 h followed by stirring at room temperature overnight. The reaction mixture was then hydrolyzed with an ammonium chloride solution, and the organic layer was separated and washed with 6 *M* sodium hydroxide followed by water. After the ether layer was dried over calcium sulfate and the solvent removed, the residue was crystallized, and recrystallized from benzene. The yields ranged from 18 to 32%. Three acetamido alcohols were characterized; the others were directly hydrolyzed to the amino alcohols listed in Table II.

The following acetamido alcohols were characterized.

2-Acetaminophenyldi-(2-chlorophenyl)carbinol had m.p. 188–189°.

Anal. Calcd. for $C_{21}H_{17}Cl_2NO_2$: C, 65.29; H, 4.44; N, 3.63. Found: C, 65.14; H, 4.55; N, 3.69.

2-Acetaminophenyldi-(2-chloro-4-methylphenyl)carbinol had m.p. 171–172°.

Anal. Calcd. for $C_{23}H_{21}Cl_2NO_2$: C, 66.68; H, 5.10; N, 3.38. Found: C, 66.57; H, 5.20; N, 3.40.

2-Acetaminophenyldi-(2-ethylphenyl)carbinol had m.p. 184–186°.

Anal. Calcd. for $C_{25}H_{27}NO_2$: C, 80.39; H, 7.29; N, 3.75. Found: C, 80.33; H, 7.28; N, 3.66.

Synthesis of Amino Alcohols

The amino alcohols listed in Table II were prepared by the hydrolysis of the corresponding acetamido alcohols. The hydrolysis was accomplished by refluxing the acetamido alcohols with a 20% alcoholic potassium hydroxide solution for 24–30 h. The mixture was then poured into water and extracted with ether, and the ether layer was dried over calcium sulfate. After removal of the ether the residue was crystallized from benzene – petroleum ether (b.p. 30–60°).

Diazotizations

The amino alcohols were diazotized in 100–150 ml of 5–10% sulfuric acid and 50 ml of dioxane at 0–5° with slightly more than an equivalent quantity of sodium nitrate. The aqueous acid (100–150 ml) was cooled to 0–5°, and the amino alcohol (8–17 mmoles) dissolved in 50 ml of dioxane was added. To the cooled solution was added the sodium nitrate in 10 ml of water. The solution was then allowed to stand at 0–10° for 1–2 h, after which time the solution was permitted to warm to room temperature and remain overnight. The mixture was then warmed to 40–50° to complete the decomposition (0.5–1 h). The mixture was extracted three times with ether and the ether extracts were washed with 5% sodium hydroxide to remove phenolic material, which was not characterized further. The dried ether solution was then evaporated and the residue examined as described below.

Products from Ig

The neutral residue was dissolved in 75% petroleum ether – benzene and adsorbed on alumina.[5] Elution with more of the same solvent mixture yielded 0.165 g (2.9%) of an oil, ν 1 685 cm^{-1} (chloroform). The oil resisted all attempts at crystallization. The ketone, however, was assigned the structure of *2-chloro-2'-(2-chlorophenyl) benzophenone* (IIIg).

Elution of the column with 70% benzene–chloroform gave an oil which was crystallized from benzene – petroleum ether, yielding 0.538 g (9.5%) of *1-chloro-9-(2-chlorophenyl)-9-fluorenol* (IIg), m.p. 131–132°.

Anal. Calcd. for $C_{19}H_{12}Cl_2O$: C, 69.74; H, 3.70. Found: C, 69.44; H, 3.58.

A duplicate diazotization with Ig yielded essentially the same results: 3.2% ketone (IIIg) and 8.9% fluorenol (IIg).

Products from Ih

The neutral residue was dissolved in equal volumes of benzene – petroleum ether and adsorbed on alumina. Elution with the same solvent mixture yielded 0.418 g (8.8%) of a yellow oil, ν 1 677 cm^{-1} (chloroform). The oil could not be crystallized; however, it was assigned the structure of *2-chloro-4-methyl-2'-(2-chloro-4-methylphenyl) benzophenone* (IIIh).

Elution of the column with benzene gave an oil which was crystallized from benzene – petroleum ether, yielding 0.470 g (9.9%) of *2-chloro-4-methyl-9-(2-chloro-4-methylphenyl)-9-fluorenol* (IIh), m.p. 163–164°.

Anal. Calcd. for $C_{21}H_{16}Cl_2O$: C, 71.00; H, 4.54. Found: C, 70.88; H, 4.74.

[4]*Microanalyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Michigan. Melting points and boiling points are not corrected.*

[5]*All chromatograms described herein were conducted with ordinary Merck alumina (20 g/g of compound).*

TABLE II

Amino alcohols

	Melting point (°C)	% yield	Calculated (%)			Found (%)		
			C	H	N	C	H	N
2-Aminophenyldi-(2-chlorophenyl)carbinol (I*g*)	141.5–143	82	66.29	4.39	4.07	66.35	4.46	3.97
2-Aminophenyldi-(2-chloro-4-methylphenyl)carbinol (I*h*)	162–164	78	67.75	5.14	3.76	67.87	5.19	3.82
2-Aminophenyldi-(2-chloro-4-methoxyphenyl)carbinol (I*i*)	119–121	7	62.39	4.73	3.47	62.29	4.84	3.68
2-Aminophenyldi-(2-ethylphenyl)carbinol (I*j*)	100–102	54	83.34	7.60	4.23	83.33	7.65	4.36
2-Aminophenyldi-(2-ethyl-4-methoxyphenyl)carbinol (I*k*)	96–98	3	76.69	7.47	3.58	76.76	7.48	3.64

Products from Ii

The neutral residue was dissolved in equal volumes of benzene – petroleum ether and adsorbed on alumina. Elution with benzene yielded 0.301 g (11%) of a light-yellow oil, ν 1 672 cm^{-1} (chloroform). The oil resisted crystallization; however, it was assigned the structure of *2-chloro-4-methoxy-2'-(2-chloro-4-methoxyphenyl) benzophenone* (III*i*).

Elution of the column with equal volumes of benzene–chloroform gave, after recrystallization from benzene – petroleum ether, 0.249 g (8.7%) of *2-chloro-4-methoxy-9-(2-chloro-4-methoxyphenyl)-9-fluorenol* (II*i*), m.p. 191–193°.

Anal. Calcd. for $C_{21}H_{16}Cl_2O_3$: C, 65.13; H, 4.17. Found: C, 65.20; H, 4.28.

Products from Ij

The neutral residue was dissolved in 35% benzene – petroleum ether and adsorbed on alumina. Elution with petroleum ether yielded 0.803 g (16.9%) of a light-yellow oil, ν 1 685 cm^{-1} (chloroform). Recrystallization from petroleum ether yielded 0.616 g (13%) of *2-ethyl-2'-(2-ethylphenyl) benzophenone* (III*j*), m.p. 45–47°.

Anal. Calcd. for $C_{23}H_{22}O$: C, 87.86; H, 7.05. Found: C, 87.76; H, 7.04.

Further elution of the column with benzene yielded, after recrystallization from benzene – petroleum ether, 1.487 g (31.3%) of *2-ethyl-9-(2-ethylphenyl)-9-fluorenol* (II*j*), m.p. 91–93°.

Anal. Calcd. for $C_{23}H_{22}O$: C, 87.86; H, 7.05. Found: C, 87.67; H, 7.11.

Products from Ik

The neutral material was dissolved in equal volumes of benzene – petroleum ether and adsorbed on alumina. Elution with the same solvent mixture gave 0.928 g (33%) of a light-yellow oil, ν 1 665 cm^{-1} (chloroform). The oil was crystallized from ethanol, yielding 0.780 g (28%) of *2-ethyl-4-methoxy-2'-(2-ethyl-4-methoxyphenyl) benzophenone* (III*k*), m.p. 65–67°.

Anal. Calcd. for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00. Found: C, 80.23; H, 7.09.

Elution of the column with equal volumes of benzene–chloroform yielded, after recrystallization from benzene – petroleum ether, 0.804 g (28.4%) of *2-ethyl-4-methoxy-9-(2-ethyl-4-methoxyphenyl)-9-fluorenol* (II*k*), m.p. 153–155°.

Anal. Calcd. for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00. Found: C, 80.23; H, 7.09.

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Department of Chemistry,
Adelphi University,
Garden City, New York.

THE STRUCTURE OF THE MALEIC ANHYDRIDE – ACETYLACETONE ADDUCT

R. D. Bailey and G. M. Strunz

The reaction of maleic anhydride with acetylacetone was reported by Berner (1) in 1946 to give rise to a 2:1 adduct, m.p. 180° (decomp.), $C_{13}H_{12}O_8$. Similarly, ethyl acetoacetate was shown to give rise to an analogous adduct, $C_{14}H_{14}O_9$. The structures I*a* and I*b*, respectively, were assigned to these adducts, largely on the basis of their degradation