Pinacol Rearrangement of Quinoline Analogs of Benzopinacol and Evidence for Rearrangement under the Conditions of Electron Impact

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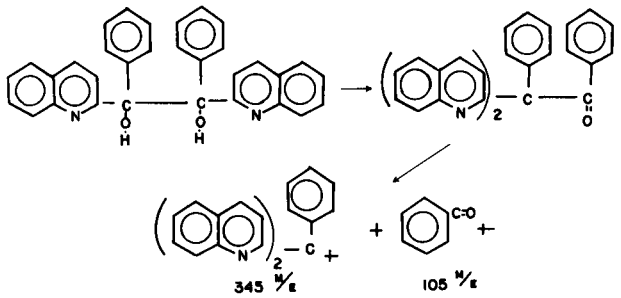
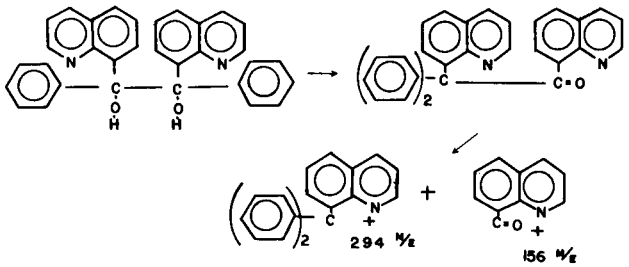
The pinacols, 1,2-di(2-quinolyl)-1,2-diphenylethane-1,2-diol and 1,2-di(8-quinolyl)-1,2-diphenylethane-1,2-diol, were prepared and rearranged. The mass spectrum of the phenyl-2-quinolylpinacolone showed fragment peaks corresponding to the pinacolone resulting from 2-quinolyl migration. The mass spectrum of the phenyl-8-quinolylpinacolone showed fragment peaks corresponding to the pinacolone resulting from phenyl migration. Evidence for the rearrangement by electron impact was observed in the mass spectrum of each pinacol.

In a continuation of our research into the pinacol rearrangement of heterocyclic analogs of benzopinacol, we wish to report the pinacol rearrangement of quinoline analogs of benzopinacol. In previous papers the thiophene (1), furan (1), and pyridine (2) analogs of benzopinacol were prepared, rearranged, and assigned a relative migratory aptitude based on that of the phenyl group. The groups, 2-furyl, 2-thienyl, and 2,5-dimethyl-3-thienyl, migrated to the complete exclusion of the phenyl group. The phenyl group migrated in perference to the 2-pyridyl and 3-pyridyl groups. The pinacols, 1,2-di(2-quinolyl)-1,2-diphenylethane-1,2-diol and 1,2-di(8-quinolyl)-1,2-diphenylethane-1,2-diol, have now been prepared and rearranged. Both pinacols were prepared by a bimolecular reduction reaction involving the phenyl ketone and a metal. Phenyl-2-quinolylpinacol was prepared by reduction of phenyl 2-quinolyl ketone with mercury (II) chloride and magnesium turnings in anhydrous pyridine-benzene solution. Phenyl-8-quinolylpinacol was prepared by two procedures, reduction of phenyl 8-quinolyl ketone with zinc dust in glacial acetic acid, and reduction of the same ketone with sodium amalgam in anhydrous tetrahydrofuran.



EQUATION 1



EQUATION 2

The pinacolone reaction products were purified by column chromatography, and only one pinacolone was found for each pinacol. A mass spectrum of each phenylquinolylpinacolone and phenylquinolylpinacol was taken. A table of m/e with relative abundance of each is presented in Table I. Attempted pinacolone scission by potassium hydroxide was unsuccessful, but identification was accomplished by mass spectrometry. The phenylquinolylpinacol mass spectra showed evidence for the rearrangement. It has been reported that pinacol (3) and benzopinacol (4) both rearrange to a pinacolone under the conditions of electron impact. The mass spectrum of the pinacolone from phenyl-2-quinolylpinacol showed a peak at 345 m/e and at 105 m/e, but no peak at 294 m/e or 156 m/e. Such a spectrum would be expected from the cleavage of the carbonyl carbon-α-carbon bond of the pinacolone resulting from 2-quinolyl migration (See Equation 1) and the pinacolone would be 1,2-diphenyl-2,2-di(2-quinolyl)-1-ethanone. If the spectrum had shown a peak at 294 m/e and 156 m/e and no peaks at 345 m/e and 105 m/e, the pinacolone would have resulted from phenyl migration. No such combination of peaks was found. The mass spectrum of pinacolone from phenyl-8-

TABLE I

m/e and Their Relative Abundance for the Pinacols and Pinacolones Studied

m/e	Relative Intensity			
	Phenyl-2-quinolyl Pinacolone	Phenyl-2-quinolyl Pinacol	Phenyl-8-quinolyl Pinacolone	Phenyl-8-quinolyl Pinacol
468	0	44	0	1
450	100	22	1	0
434	6	4	0	0
422	30	0	0	0
373	4	1	0	0
345	21	27	0	0
294	0	0	3	3
280	0	0	6	0
278	0	2	0	0
234	0	6	0	29
233	0	6	43	20
229	0	0	14	1
217	12	6	29	5
205	0	17	72	100
182	3	4	0	0
156	0	4	14	57
128	0	13	0	29
105	27	17	14	29
101	0	0	22	9
77	36	100	100	57

quinolylpinacol showed the presence of a peak at 294 m/e and the absence of a peak at 345 m/e. Peaks were observed at 156 m/e and 105 m/e. The peak at 294 m/e would result from cleavage of the carbonyl carbon-α-carbon bond of the pinacolone resulting from phenyl migration (see Equation 2) and the pinacolone would be 1,2-di-(8-quinolyl)-2,2-diphenyl-1-ethanone.

In a previous report (2) concerning the rearrangement of phenylpyridylpinacols it was found that the phenyl group migrated instead of the pyridyl group. This result was explained by assuming that the nitrogen on the pyridine ring was protonated thereby withdrawing electrons and reducing the nucleophilicity of the pyridyl group. In the case of phenyl-8-quinolylpinacol a similar argument may be used to explain the migration of the phenyl group instead of the 8-quinolyl group. For phenyl-2-quinolylpinacol evidence indicates that the 2-quinolyl group migrates in preference to the phenyl group. If the phenyl group were to migrate, the resulting species would have adjacent positive charges as a result of a resonance form of the protonated 2-quinolyl group.

A mass spectrum of each phenylquinolylpinacol was taken and studied for evidence of the rearrangement. Both showed a parent peak at m/e = 468. The spectrum of phenyl-2-quinolylpinacol showed a pinacolone peak at m/e = 450, a fragment peak at m/e = 345, but no peak at m/e = 294. The presence of the 345 m/e peak may be a result of cleavage of the carbonyl carbon-α-carbon bond of the pinacolone formed by 2-quinolyl migration. This evidence suggests that the same group, 2-quinolyl, which migrated in acidic media also migrated under the conditions of electron impact. The mass spectrum of phenyl-2-quinolylpinacol contained all of the peaks found in the spectrum of 1,2-diphenyl-2,2-di(2-quinolyl)-1-ethanone. The mass spectrum of phenyl-8-quinolylpinacol did not show a pinacolone peak at 450 m/e or a peak at 345 m/e, but did show a peak at 294 m/e. The presence of the 294 m/e peak may be a result of cleavage of the carbonyl carbon-α-carbon bond of the pinacolone formed by phenyl migration. This evidence suggests that the same group which migrated in acidic media also migrated under the conditions of electron impact. The mass spectrum of

phenyl-8-quinolylpinacol contained all of the peaks found in the mass spectrum of 1,2-di(8-quinolyl)-2,2-diphenyl-1-ethanone except the pinacolone peak at 450 m/e and a peak at 280 m/e. These cations may be unstable or formed in small quantities.

The presence of some peaks can be accounted for by a retrograde pinacol rearrangement. The presence of a peak at m/e = 182 in the spectrum of 1,2-diphenyl-2,2-di(2-quinolyl)-1-ethanone and 1,2-di(2-quinolyl)-1,2-diphenylethane-1,2-diol suggests that the phenyl group migrated in a retrograde pinacol rearrangement. For both 1,2-di(8-quinolyl)-2,2-diphenyl-1-ethanone and 1,2-di(8-quinolyl)-1,2-diphenylethane-1,2-diol, the absence of a peak at 284 m/e for a di(8-quinolyl)ketone suggests that the 8-quinolyl group does not migrate in the retrograde pinacol rearrangement. The presence of a peak at 233 m/e for phenyl 8-quinolyl ketone in the mass spectrum of 1,2-diphenyl-2,2-di(2-quinolyl)-1-ethanone suggests that the phenyl group does migrate in the retrograde rearrangement.

EXPERIMENTAL

2-Quinoline Aldehyde.

This was prepared from quinaldine by using freshly prepared selenium dioxide (5). The product was chromatographed on alumina from benzene. There was obtained 66% of the theoretical aldehyde which melted at 66-68° (6).

Phenyl-2-quinolylcarbinol.

Phenylmagnesium bromide and 2-quinoline aldehyde were reacted to give 80% of the theoretical carbinol which melted at 66-67° (7).

Phenyl 2-Quinolyl Ketone.

Phenyl-2-quinolyl carbinol was oxidized by chromic oxide (8) in sulfuric acid and acetone. Chromatography over alumina from benzene gave 64% of the theoretical amount of ketone which melted at 107-108° (9).

8-Quinolinecarboxylic Acid.

8-Methylquinoline was oxidized by chromic acid in sulfuric acid to give 38% of the theoretical amount of acid which melted at 185-186° (10).

Phenyl 8-Quinolyl Ketone.

This preparation was based on a procedure in Organic Syntheses (11) starting with 29 grams of acid. After the aluminum chloride addition, the mixture was heated at 60° for one hour. The chromatographic purification was performed as described above and evaporation of the benzene produced 25 g. (64%) of the ketone which melted at 92-93° (12).

1,2-Di(2-quinolyl)-1,2-diphenylethane-1,2-diol.

Phenyl 2-quinolyl ketone (20 g.) was dissolved in 90 ml. of anhydrous benzene and 10 ml. of pyridine treated with 3.2 g. of mercury (II) chloride and 3.2 g. of magnesium turnings. The mixture was heated to gentle reflux without stirring for several hours after which the reaction became exothermic. The black mixture was refluxed for 72 hours. Hydrolysis was accomplished by adding the mixture dropwise to a rapidly stirred 10% acetic acid solution. This mixture was then repeatedly extracted with benzene, the benzene was evaporated and the remaining oil was chromatographed over alumina in benzene. After evaporating the benzene, 15 ml. of 95% ethanol was added to the residue and the solid was collected by filtration to give 2.1 g. (10%) of the pinacol which melted at 198-200°. Infrared showed absorption at 3200 cm^{-1} to 3400 cm^{-1}.

Anal. Calcd. for $C_{32}H_{24}N_2O_2$: C, 82.05; H, 5.12; N, 5.98. Found: C, 82.24; H, 5.06; N, 6.08.

1,2-Di(8-quinolyl)-1,2-diphenylethane-1,2-diol. By Zinc Reduction.

Ten grams of phenyl 8-quinolyl ketone in 100 ml. of glacial acetic acid were treated with 10 g. of zinc powder. The mixture was treated with a gram of zinc powder for two subsequent days. After another two days the zinc was removed by filtration and washed with acetic acid. The acetic acid solution was added slowly with stirring to a liter of ice-water. The yellow precipitate was filtered and taken up in chloroform. After evaporation the residue was taken up in benzene and chromatographed on alumina. Evaporation of the solvent left 8.7 g. (87%) of the yellow pinacol which melted at 205-210° and showed infrared absorption at 3300-3400 cm^{-1}.

Anal. Calcd. for $C_{32}H_{24}N_2O_2$: C, 82.05; H, 5.12; N, 5.98. Found: C, 81.87; H, 5.23; N, 5.86.

1,2-Di(8-quinolyl)-1,2-diphenylethane-1,2-diol. By Sodium Reduction.

To a mixture of 200 ml. of anhydrous tetrahydrofuran and 122.4 g. of 2% sodium amalgam (13), was added 30 g. of phenyl 8-quinolyl ketone in 100 ml. of anhydrous tetrahydrofuran while stirring at room temperature under dry nitrogen. The mixture was then refluxed for 72 hours and hydrolyzed by the dropwise addition to 1 liter of 10% acetic acid. The hydrolysis mixture was extracted with chloroform and the chloroform was evaporated to leave a yellow oil which was dissolved in benzene and chromatographed over alumina. After evaporation of the benzene, the residue was dissolved in 20 ml. of acetone and precipitated by the addition of water. There was obtained 3 g. (10%) of pinacol which melted at 200-205° and had an infrared absorption at 3300-3400 cm^{-1}.

Anal. Calcd. for $C_{32}H_{24}N_2O_2$: C, 82.05; H, 5.12; N, 5.98. Found: C, 82.27; H, 5.17; N, 5.76.

Rearrangement of 1,2-Di(2-quinolyl)-1,2-diphenylethane-1,2-diol.

To a solution of 40 ml. of glacial acetic acid, 80 ml. of acetyl chloride and 160 ml. of benzene, was added 8 g. of phenyl-2-quinolyl-pinacol followed by a 78-hour reflux period and evaporation of all solvent. Water was added to the residue, the mixture was chloroform-extracted, and the chloroform was evaporated. The residue was taken up in benzene and the solution was chromatographed over alumina. Evaporation of the benzene left 7 g. (91%) of 1,2-diphenyl-2,2-di(2-quinolyl)-1-ethanone which melted at 228-230° and had an infrared absorption at 1650 cm^{-1}.

Anal. Calcd. for $C_{32}H_{24}N_2O_2$: C, 85.40; H, 4.89; N, 6.23. Found: C, 85.51; H, 4.78; N, 6.03.

Rearrangement of 1,2-Di(8-quinolyl)-1,2-diphenylethane-1,2-diol.

In the same manner as for the 2-isomer the diol was rearranged to give 7 g. (91%) of 1,2-di(8-quinolyl)-2,2-diphenyl-1-ethanone which melted at 290-295° and had an infrared absorption at 1650 cm^{-1}.

Anal. Calcd. for $C_{32}H_{24}N_2O_2$: C, 85.40; H, 4.89; N, 6.23. Found: C, 82.65; H, 5.01; N, 5.45.

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