Experimental

The Condensation of Substituted Acetophenones in Alcoholic Hydrogen Chloride. Procedure A.—A solution of 3.0 g. of the acetophenone in 15 ml. of a 50% methanol-dioxane mixture was placed in a 50-ml. erlenmeyer flask and was saturated, with cooling, with dry hydrogen chloride. After constant weight was reached, a gain in weight of about 10 g., the flask was closed except for a small capillary outlet which allowed the escape of hydrogen chloride expelled from the solution on warming to room temperature.

After 10 days, any solid which had precipitated was removed by filtration, and the solution again saturated with hydrogen chloride. After standing a total of 18 days, the solution was filtered and the residue combined with the solid from the original filtration. The filtrate was poured into about 200 ml. of water, and the mixture was extracted with petroleum ether. Any solid remaining undissolved was filtered off and added to that above. From the petroleum ether solution could be recovered unreacted acetophenone, small amounts of dypnone, and polymers.

The yields listed in Table I, with the exception of 1,3,5-tris-*m*-chlorophenylbenzene, were based on the weight of unrecrystallized solid recovered from the reaction. These yields do not include consideration of recovered starting material.

Procedure B.—To 50 ml. of absolute ethanol saturated with hydrogen chloride was added 10 g. of the substituted acetophenone. After standing for 30 days, the reaction mixtures were filtered, and the solid residue was washed with cold alcohol giving pure 1,3,5-triarylbenzene or dypnone. A small amount of product was obtained by pouring the above filtrate into water and filtering the mixture. The crude product from this operation was oily and required washing with alcohol before it could be considered as yield.

p-Methoxyacetophenone was allowed to stand for four months before being treated as above. (The yield at the end of 34 days was 2%.) The solid residue was extracted with ether and on evaporation of the ether solution 1,3,5-tri-*p*-methoxyphenylbenzene was obtained. The small amount of ether insoluble residue was identified as 2,4,6-tri-*p*-methoxyphenylpyrylium chloride, m.p. 197–204° (dec.), for it could be converted to the known 2,4,6-tri-*p*-methoxyphenylpyrylium picrate, m.p. 276–283° (dec.) (lit.[2e] m.p. 283–284°).

Procedure C.—A solution of 1 g. of the acetophenone in 15 ml. of 60% absolute methanol–40% dioxane mixture was saturated with hydrogen chloride and treated as in Procedure B.

Procedure D.—A solution of 3 g. of the acetophenone in 7 ml. of absolute methanol was treated as in Procedure A.

DURHAM, NEW HAMPSHIRE

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF FORDHAM UNIVERSITY]

The Pinacol Rearrangement in the Heterocyclic Series. II. Thiophene and Furan Analogs of Benzopinacol

BY MATTHEW R. KEGELMAN AND ELLIS V. BROWN

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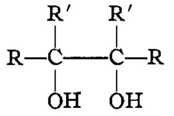
Symmetrical analogs of benzopinacol containing two phenyl groups with either two 2-thienyl groups, two 2,5-dimethyl-3-thienyl groups or two 2-furyl groups have been synthesized and rearranged. The structures of the products of rearrangement have been determined by characterization of their degradation products.

In a previous report,[1] the authors have described their extension to the pyridine series of the studies of earlier workers on the migratory aptitudes of aromatic groups. These migratory aptitudes were determined by rearranging pinacols of the type shown in I, where R and R′ are aryl, and determining the structures of the resulting pinacolones by degradation. It was found in this way that the migratory aptitudes of the 2-pyridyl and 3-pyridyl groups were very small compared to that of the phenyl group. An explanation of this fact was offered.



$$\mathrm{R{-}\overset{R'}{\underset{OH}{C}}{-}\overset{R'}{\underset{OH}{C}}{-}R}$$

I

Turning next to the five-membered heterocycles, we have examined the 2-thienyl, the 2,5-dimethyl-3-thienyl and the 2-furyl groups in a similar manner.

The magnesium–magnesium iodide reducing reagent of Gomberg and Bachmann,[2] which is ordinarily very effective in converting diaryl ketones into the corresponding pinacols, furnished only an insoluble complex when applied to phenyl 2-thienyl ketone. (This had also been found to be the case with the ketones of the pyridine series.) Hydrolysis of this complex resulted in recovery of the original ketone. Treatment of 2,2′-thenil with phenylmagnesium bromide produced a tarry mass. The reaction of 2-thienylmagnesium iodide with benzil, on the other hand, did give rise to the desired pinacol although in very small yield. The same pinacol was eventually found to be produced in excellent yield by reducing phenyl 2-thienyl ketone with zinc and acetic acid.

When this pinacol was rearranged and the resulting pinacolone cleaved, there were only two products of degradation, *i.e.*, benzoic acid and phenyldi-(2-thienyl)-methane. The latter substance was identified by comparison with an authentic sample. Since no 2-thenoic acid was produced, the 2-thienyl group had migrated to the exclusion of the migration of the phenyl group.

In order to determine whether the pronounced tendency for the thienyl group to migrate would be overcome by the influence of substituents in the ortho position, which are notoriously detrimental to migration in the pinacol rearrangement, a symmetrical pinacol containing two phenyl groups and two 2,5-dimethyl-3-thienyl groups was synthesized. This was accomplished by the action of 2,5-dimethyl-3-thienylmagnesium iodide on benzil. The results of the rearrangement of this pinacol exactly paralleled those obtained with the 2-thienyl analog. Thus, the 2,5-dimethyl-3-thienyl group also migrates to the exclusion of migration of the phenyl group. The di-(2,5-dimethyl-3-thienyl)-phenylmethane was characterized by independent synthesis.

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[1] M. R. Kegelman and E. V. Brown, THIS JOURNAL, **75**, 4649 (1953).

[2] M. Gomberg and W. E. Bachmann, *ibid.*, **49**, 236 (1927).

With magnesium–magnesium iodide, phenyl 2-furyl ketone behaved as had the other heterocyclic ketones. Furthermore, no pinacol could be isolated from the reduction of this ketone either by zinc and acetic acid or photochemically. The Grignard method, however, furnished the desired compound when furil was treated with phenylmagnesium bromide.

When this pinacol was subjected to the conditions of rearrangement and the resulting pinacolone cleaved, the acid fraction of the degradation products was found to consist of pure benzoic acid with no furoic acid. Attempts to characterize the triarylmethane fraction were not successful; the indication was, nevertheless, that the furyl group migrated much more readily than did the phenyl group.

The behavior of the thienyl and furyl groups as extremely active migrators might have been predicted. As a result of the presence of the unshared pairs of electrons at the hetero atom, these groups have an enhanced capacity for supplying electrons and consequently would be expected to be attracted to the positive center toward which migration takes place.

It is interesting to note in the case of the 2,5-dimethyl-3-thienylpinacol which was studied that this effect is evidently sufficiently powerful to overcome the steric influence of the ortho substituent. However, it must be conceded that this steric effect is somewhat lessened owing to the five-membered ring.[3]

Experimental

1,2-Di-(2-thienyl)-1,2-diphenylethane-1,2-diol. Reduction Method.—To a solution of 10.0 g. (0.053 mole) of phenyl 2-thienyl ketone[4] in 100 ml. of glacial acetic acid in a glass-stoppered bottle was added 10.0 g. of zinc dust. This mixture was allowed to stand for 10 days at room temperature with occasional shaking and the addition of 1.0 g. of zinc dust every day. The mixture was then filtered and the excess zinc dust washed with acetic acid. The combined filtrate and washings were added dropwise to 1.5 l. of ice-water with vigorous mechanical stirring. The resulting pink precipitate was separated by filtration, washed thoroughly with water and dried. The resulting 9.5 g. (95%) of crude pinacol melted at 122–125°. The purified material obtained after two recrystallizations from aqueous ethanol (discarding any oily fractions) melted at 137–137.5°.

Anal. Calcd. for $C_{22}H_{18}O_2S_2$: C, 69.78; H, 4.80; S, 16.95. Found: C, 70.10; H, 4.86; S, 16.90.

Grignard Method.—A solution of 2-thienylmagnesium iodide was prepared from 5.4 g. (0.2 mole) of magnesium turnings and 42.0 g. (0.2 mole) of 2-iodothiophene[5] dissolved in 100 ml. of absolute ether and 100 ml. of dry benzene. This was decanted quickly from a trace of unreacted metal into a second flask and cooled to 3° while protected from the atmosphere. At this temperature, 10.5 g. (0.05 mole) of benzil was added in small portions with mechanical stirring. After coming to room temperature, the mixture was allowed to stand protected from the atmosphere for two days. The clear red solution was then added to 1 l. of ice-water and the resulting mixture acidified with dilute hydrochloric acid. The organic layer was separated, washed twice with water and dried. Evaporation of the solvent *in vacuo* at room temperature left a black solid which, after repeated recrystallization from aqueous ethanol using Norit, afforded 1.0 g. (5.4%) of purified pinacol, melting at 137–138°. This material showed no depression in melting point when mixed with the product obtained by the reduction method.

Rearrangement of 1,2-Di-(2-thienyl)-1,2-diphenylethane-1,2-diol and Scission of the Pinacolone.—A 2.69-g. (0.007 mole) sample of this pinacol was refluxed for 44 hours with a mixture of 55 ml. of dry benzene, 15 ml. of glacial acetic acid and 30 ml. of acetyl chloride while protected from the atmosphere by a drying tube. The heating bath was maintained at 90°. The bulk of the volatile material was then removed *in vacuo* (bath at 90°). The residue was freed of the last of the acetic acid by storage in a vacuum desiccator over potassium hydroxide. The resulting pinacolone residue was next refluxed for 36 hours with a solution of 4.2 g. of potassium hydroxide in 70 ml. of absolute ethanol. The heating bath was maintained at 90° and the reaction mixture was protected from moisture by a drying tube. Most of the ethanol was then removed *in vacuo*. The last traces of ethanol were removed by storage in a vacuum desiccator over sulfuric acid. To the residue was added 70 ml. of water and the mixture was extracted with 70 ml. of benzene in several portions.

The combined benzene extracts were dried and the solvent evaporated under vacuum at room temperature. There remained a reddish-brown crystalline solid residue of 1.77 g. (97%) of crude phenyldi-(2-thienyl)-methane melting at 67°. After two recrystallizations from ethanol, using Norit, the substance melted at 74–75° and showed no depression in melting point when mixed with an authentic sample[6] of the triarylmethane.

The basic aqueous layer from the above extraction was acidified carefully with dilute hydrochloric acid. The light tan solid which precipitated, together with the supernatant liquid, was exhaustively extracted with ether, the combined extracts dried over sodium sulfate and the solvent evaporated. The remaining brown crystalline residue was transferred quantitatively to a vacuum sublimator. The residue was sublimed at 10 mm. and a bath temperature of 90°. The yield was 0.75 g. (87%) of white crystals, m.p. 120–122°. The material showed no depression in melting point when mixed with a sample of benzoic acid.

Anal. Calcd. for $C_7H_6O_2$: C, 68.85; H, 4.96. Found: C, 68.70; H, 4.65.

1,2-Di-(2,5-dimethyl-3-thienyl)-diphenylethane-1,2-diol.—The Grignard reagent prepared from 5.4 g. (0.2 mole) of magnesium turnings and 48.0 g. (0.2 mole) of 2,5-dimethyl-3-iodothiophene[7] dissolved in 100 ml. of absolute ether and 100 ml. of dry benzene was allowed to react with 10.5 g. (0.05 mole) of benzil, exactly as described above for the 2-thienyl analog. However, in this case, the solvent was evaporated only to a volume of 25 ml. At this point, the tan solid which had precipitated, was separated and combined with an additional amount of similar material obtained by adding ethanol to the mother liquor. Three recrystallizations from ethanol–chloroform furnished 2.8 g. (13%) of purified pinacol. The white needles, which melted at 176–177°, darkened slightly after prolonged storage.

Anal. Calcd. for $C_{26}H_{26}O_2S_2$: C, 71.84; H, 6.04; S, 14.76. Found: C, 72.20; H, 5.73; S, 14.60.

Rearrangement of 1,2-Di-(2,5-dimethyl-3-thienyl)-1,2-diphenylethane-1,2-diol.—A 2.46-g. (0.0057 mole) sample of this pinacol was treated just as described above for the rearrangement of the 2-thienyl analog. The triarylmethane fraction afforded 0.78 g. (44%) of crude di-(2,5-dimethyl-3-thienyl)-phenylmethane. This was recrystallized several times from petroleum ether to give white crystals melting at 96–97.5°. There was no depression in melting point when this material was mixed with an authentic sample prepared as described below.

There was obtained from the acid fraction after sublimation 0.68 g. (98%) of white crystals melting at 120–122°. The material showed no depression in melting point when mixed with benzoic acid.

Anal. Calcd. for $C_7H_6O_2$: C, 68.85; H, 4.96; S, 0.00. Found: C, 69.03; H, 4.73; S, 0.00.

Di-(2,5-dimethyl-3-thienyl)-phenylmethane.—A mixture of 14 g. (0.125 mole) of 2,5-dimethylthiophene,[8] 6.2 g.

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[3] L. J. Owen and F. F. Nord, *J. Org. Chem.*, **16**, 1864 (1951); A. Khawam and E. V. Brown, THIS JOURNAL, **74**, 5603 (1952).

[4] W. Minnis, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 520.

[5] W. Minnis, ref. 4, p. 357.

[6] A. Tohl and A. Nahke, *Ber.*, **29B**, 3205 (1896).

[7] W. Steinkopf, I. Poulsson and O. Herdey, *Ann.*, **536**, 128 (1938).

[8] C. Paal, *Ber.*, **18B**, 2251 (1885).

(0.058 mole) of benzaldehyde, 30 ml. of petroleum ether (b.p. 60–75°) and 12.4 g. of phosphorus pentoxide was allowed to stand protected by a drying tube for three days with occasional shaking. The yellow crystals, which had deposited, were then dissolved by boiling the mixture on a steam-bath. The resulting clear solution was then decanted from the brown gummy residue and the latter extracted by stirring with several portions of boiling petroleum ether. The combined solutions, which exhibited a strong green fluorescence, were then evaporated until crystallization began. Upon cooling, 11.1 g. (61%) of crude triarylmethane deposited. These crystals, which melted at 90–97°, were recrystallized twice from petroleum ether and once from ethanol to furnish pure di-(2,5-dimethyl-3-thienyl)-phenylmethane melting at 96.5–97.5°.

Anal. Calcd. for $C_{19}H_{20}S_2$: C, 73.00; H, 6.46. Found: C, 72.98; H, 6.93.

1,2-Di-(2-furyl)-1,2-diphenylethane-1,2-diol.—Phenylmagnesium bromide was prepared from 5.4 g. (0.2 mole) of magnesium turnings and 31.4 g. (0.2 mole) of bromobenzene dissolved in 100 ml. of absolute ether and 100 ml. of dry benzene. This was quickly decanted from a trace of unused metal and cooled in another flask to 0° while protected by a drying tube. With mechanical stirring there was slowly added 9.5 g. (0.05 mole) of 2,2′-furil. The dark orange solution was stirred while being allowed to come to room temperature and was permitted to stand for two days protected by a drying tube. The mixture was then hydrolyzed by the addition of an iced, concentrated aqueous solution of 60 g. of ammonium chloride, the organic layer was washed twice with water and dried. The solvent was evaporated *in vacuo* at room temperature. The yellow residue was washed twice with petroleum ether (b.p. 30–60°) and dried. It weighed 16.3 g. and melted at 113–116°. After two recrystallizations from ethanol, the pure white crystals of pinacol melted at 130–131°. They assumed a yellow coloration upon prolonged standing.

Anal. Calcd. for $C_{22}H_{18}O_4$: C, 76.27; H, 5.25. Found: C, 76.10; H, 5.11.

Rearrangement of 1,2-Di-(2-furyl)-1,2-diphenylethane-1,2-diol and Scission of the Pinacolone.—A 3.64-g. (0.01 mole) sample of the pinacol was treated as described above for the 2-thienyl analog. Sublimation of the acid fraction furnished 1.19 g. (98%) of white crystals melting at 118–120°. The melting point of a mixture of these with a sample of benzoic acid showed no depression.

Anal. Calcd. for $C_7H_6O_2$: C, 68.85; H, 4.96. Found: C, 69.13; H, 4.91.

NEW YORK 58, NEW YORK

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

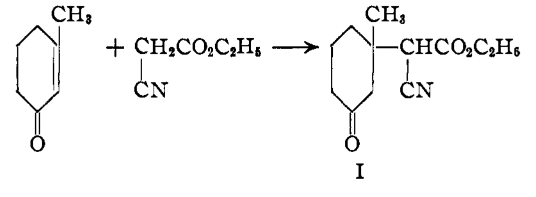
Structure of the Adduct of 3-Methyl-2-cyclohexenone and Ethyl Cyanoacetate. The Question of "Meta"- and "Para"- Bridged Rings

BY P. R. SHAFER,[1] WILLIAM E. LOEB AND WILLIAM S. JOHNSON

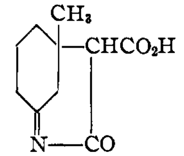
RECEIVED JULY 27, 1953

The structures assigned by Farmer and Ross to this adduct and to several products derived therefrom are challenged. A new structural interpretation, which does not necessitate the assumption of "meta"- and "para"- bridged ring intermediates, is given to these previously described transformations, and new supporting experimental evidence is provided.

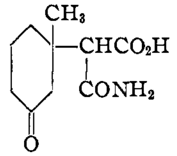
Farmer and Ross[2] have described the reaction of ethyl cyanoacetate with 3-methyl-2-cyclohexenone in the presence of one equivalent of sodium ethoxide in excess ethanol. In addition to 3-methyl-2-cyclohexenylidenecyanoacetic acid, they obtained a neutral oil b.p. 197° (2 mm.) in 21% yield. Since the latter was a ketonic adduct, $C_{12}H_{17}O_3N$, (semicarbazone, m.p. 166°) and failed to give a color with ferric chloride, they considered it to be the product I of a normal Michael reaction. Mild hydrolysis of the adduct with sodium carbonate effected saponification to give the free cyano acid, $C_{10}H_{13}O_3N$, m.p. 106°, which on boiling for 15 minutes with 15% hydrochloric acid was practically quantitatively isomerized to a new acid, m.p. 181°. This same product was also produced in almost quantitative yield by somewhat longer treatment of I with aqueous alcoholic hydrochloric acid. On the basis of its mode of formation and further reactions (see below) Farmer and Ross assigned to the 181° acid the "meta"-bridged structure II. In the present paper we challenge the structures I and II as well as those of several products derived therefrom, and present another interpretation of the transformations.



I



II



III

Farmer and Ross found their 181° acid II to be monobasic, to give an intense color with ferric chloride, and to react with bromine to give a dibromide, m.p. 186°, to which they assigned the molecular formula $C_{10}H_{13}O_3NBr_2$, but proposed no structure. On heating with 10% potassium hydroxide for 5 minutes, the 181° acid was hydrolyzed to a mixture of two nitrogen-containing acidic products formed in about equal amounts. One of these was a crystalline keto acid, $C_{10}H_{15}O_4N$, m.p. 151° (dec.), which was assigned the structure III. It gave no color with ferric chloride and reverted to the 181° acid II on heating with 15% hydrochloric acid. The other acidic product was a sirup, formulated as IV, since it was dibasic, and evolved ammonia upon prolonged heating with aqueous potassium hydroxide to give the known tribasic acid V, m.p. 125°, which was compared with authentic material prepared by independent synthesis. The oily dibasic acid IV, upon treatment

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[1] Wisconsin Alumni Research Foundation Research Assistant, 1949-1950; U. S. Rubber Co., Fellow, 1950-1951.

[2] E. H. Farmer and J. Ross, *J. Chem. Soc.*, 3233 (1926).