overnight at room temperature. The yield was 14 g. of *4-trityl-1-naphthol,* crystallizing from ethanol in colorless prisms, m.p. 205°; this product, dissolved in hot ethanol, gave with ferric chloride a brown-violet coloration which faded on cooling.

Condensation of this naphthol with 2,3-dichloro-1,4-naphthoquinone in pyridine yielded *5-trityldinaphtho[1,2-2',3]furan-7,12-dione* (IV), crystallizing from pyridine in silky golden yellow needles, m.p. 352–353°, giving, with sulfuric acid, a cobalt-blue halochromy; yield 80%.

Anal. Calcd. for $C_{39}H_{24}O_3$: C, 86.7; H, 4.5. Found: C, 86.3; H, 4.5.

2-Hydroxy-5-trityldiphenyl (V). A solution of 3 g. of 2-hydroxydiphenyl and 3 g. of triphenylcarbinol in 30 ml. of warm acetic acid was treated in the usual way with 5 g. of sulfuric acid, and the red mixture obtained was left for a week at room temperature. The precipitate (4 g.) was treated as above, and yielded on recrystallization from a mixture of benzene and ethanol, shiny, colorless, sublimable needles, m.p. 246–247°.

Anal. Calcd. for $C_{31}H_{24}O$: C, 90.3; H, 5.9. Found: C, 89.9; H, 6.1.

From similar experiments performed with 3-chloro-2-hydroxybiphenyl and 4-hydroxybiphenyl (1 month at room temperature), only the starting materials were recovered, along with some triphenylmethane.

2-Trityl-1,4-naphthoquinone (VII). A mixture of 3 g. of 1,4-dihydroxynaphthalene and 3 g. of triphenylcarbinol in 50 ml. of acetic acid was treated with 5 g. of sulfuric acid in the usual way. The precipitate (3 g.), obtained after 3 days on addition of water, was washed with water, and crystallized several times from a mixture of ethanol and benzene, to give *2-trityl-1,4-naphthoquinone* in the form of canary yellow prisms, m.p. 222–223°, giving a deep green coloration in sulfuric acid. This compound was insoluble in aqueous alkalis, and yielded phthalic acid on oxidation with potassium permanganate.

Anal. Calcd. for $C_{29}H_{20}O_2$: C, 87.0; H, 5.0. Found: C, 87.2; H, 5.2.

1,5-Dihydroxy-4,8-ditritylnaphthalene (VIII). A mixture of 3 g. of 1,5-dihydroxynaphthalene and 6 g. of triphenylcarbinol in 60 ml. of acetic acid was treated with 5 g. of sulfuric acid. The precipitate which formed after 2 days was washed with ethanol, then with hot dioxane, and recrystallized from tetralin, giving 3 g. of fine, colorless prisms, m.p. 429–430°.

Anal. Calcd. for $C_{48}H_{36}O_2$: C, 89.4; H, 5.6. Found: C, 89.2; H, 5.9.

2,7-Dihydroxy-1,x-ditritylnaphthalene. This compound, prepared from 2,7-dihydroxynaphthalene as for β-naphthol, crystallized from a mixture of ethanol and benzene in silky colorless needles, m.p. 318–320°; yield 60%.

Anal. Calcd. for $C_{48}H_{36}O_2$: C, 89.4; H, 5.6. Found: C, 89.1; H, 5.9.

This compound failed to give a furanoquinone on heating with 2,3-dichloro-1,4-naphthoquinone in pyridine medium.

2,3,5-Trimethyl-4-tritylphenol (IX). Prepared from 2,3,5-trimethylphenol (3 g.), this compound crystallized from ethanol in silky colorless needles (1 g.), m.p. 170–171°.

Anal. Calcd. for $C_{28}H_{26}O$: C, 88.9; H, 6.9. Found: C, 88.6; H, 6.6.

Similar experiments performed with *p-tert.* amylphenol, 2,4-dihydroxybenzaldehyde, gallacetophenone, and lawsone were completely negative.

PARIS (V^e), FRANCE

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, RADIUM INSTITUTE, UNIVERSITY OF PARIS]

Friedel-Crafts Acylations of 3-Chloro-4-methoxybiphenyl

NG. PH. BUU-HOÏ, MICHEL SY, AND JEAN RICHÉ

Received December 26, 1956

Friedel-Crafts acylations of 3-chloro-4-methoxybiphenyl with aliphatic and aromatic acid chlorides are shown to give 4'-acyl-3-chloro-4-methoxybiphenyls, several of which were prepared and their reactions investigated. In the course of this work, a large number of new derivatives of 3-chloro-4-hydroxybiphenyl and its methyl ether (ketones, phenols, quinolines) were synthesized.

Substitution reactions in the biphenyl series present an interesting subject of research, because of the possibility for substitutions to be homonuclear or heteronuclear. For instance, 4-methoxybiphenyl has been shown to undergo Friedel-Crafts acylations[1] mainly at position 4', with some substitution at position 3. When the directing effect of the first substituent is weaker, as is the case with 4-alkyldiphenyls,[2] acylations have been found to occur almost exclusively at position 4'. It was now thought of interest to investigate similar Friedel-Crafts reactions with 3-chloro-4-methoxybiphenyl (I), a readily accessible molecule in which the position *ortho* to the methoxy group is deactivated by the chlorine atom present in the *meta* position. (It is known that bromination of 4-hydroxybiphenyl leads to a monobromo derivative, even in relatively drastic conditions.)[3]

The starting material, 3-chloro-4-hydroxybiphenyl, possesses to some extent the properties of a cryptophenol, and could be completely methylated with sodium hydroxide and dimethyl sulfate only in the presence of methanol or ethanol;[4] acylation of 3-chloro-4-methoxybiphenyl by acetyl chloride in the presence of aluminum chloride in nitrobenzene medium gave, in excellent yields, a ketone which must have been 4'-acetyl-3-chloro-4-methoxybiphenyl (II; R = H), as its demethylation afforded a substance which, since it did not show the proper-

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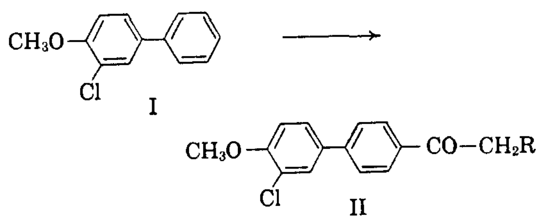
[1] See Fieser and Bradsher, *J. Am. Chem. Soc.,* **58,** 1738, 2337 (1936).

[2] Buu-Hoï and Royer, *Rec. trav. chim.,* **70,** 825 (1951); *Bull. soc. chim. France,* **17,** 489 (1950).

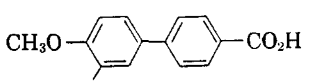
[3] Bell and Robinson, *J. Chem. Soc.,* 1132 (1927).

[4] For other instances of methylation of cryptophenols. see Buu-Hoï and Lavit, *J. Chem. Soc.,* 2412 (1956).


I

II

ties of an *o*-hydroxy ketone, must have been the expected 4′-acetyl-3-chloro-4-hydroxybiphenyl. No appreciable amount of an isomeric ketone could be isolated, and this confirms the theoretical prediction concerning the deactivation of position 5 by the chlorine atom occupying position 3. Replacement of acetyl chloride by propionyl, *n*-butyryl, and phenacetyl chloride yielded 3-chloro-4-methoxy-4′-propionyl- (II; R = C_2H_5), 3-chloro-4-methoxy-4′-*n*-butyryl- (II; R = n-C_3H_7), and 3-chloro-4-methoxy-4′-phenacetylbiphenyl (II; R = $CH_2C_6H_5$), respectively. In the case of benzoyl chloride, the ketone obtained was 4′-benzoyl-3-chloro-4-methoxybiphenyl (IV), as it was identical with the product of a Friedel-Crafts reaction between benzene and the chloride of 3-chloro-4-methoxybiphenyl-4′-carboxylic acid (III); this acid was prepared by sodium hypobromite oxidation of 4′-acetyl-3-chloro-4-methoxybiphenyl. This proof of constitution was thought useful, in view of the differences observed between aliphatic acid chlorides and nuclear aromatic acid chlorides in respect of orientation in Friedel-Crafts acylations.[5]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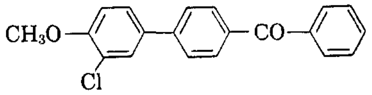
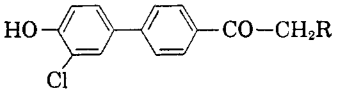
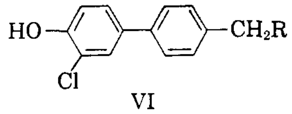
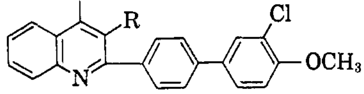

IV

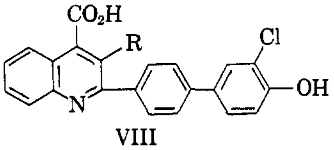
Demethylation of the ketones of general formula II by means of pyridine hydrochloride[6] readily yielded the corresponding 4′-acyl-3-chloro-4-hydroxybiphenyls (V), which showed pronounced bacteriostatic activity against several germs (tubercle bacilli, staphylococci, etc.).[7] Kishner-Wolff reduction of 4′-acyl-3-chloro-4-methoxybiphenyls, using the Huang-Minlon technique,[8] readily gave the corresponding 4′-alkyl- and 4′-arylalkyl-3-chloro-4-methoxybiphenyls; demethylation of these ethers yielded 4′-alkyl- and 4′-arylalkyl-3-chloro-4-hydroxybiphenyls of general formula VI, which also showed antibacterial properties.


V


VI

The ready availability of ketones of type II prompted an investigation of their Pfitzinger reactions with isatin. In several previous papers, it had been pointed out that this type of reaction is highly sensitive to steric hindrance,[9] and this was again found to be the case. Thus, in ethanol medium, isatin reacted with 4′-acetyl- and 4′-propionyl-3-chloro-4-methoxybiphenyl to give in 85–90% yield 2-(3-chloro-4-methoxy-4′-xenyl)cinchoninic acid (VII; R = H) and its 3-methyl derivative (VII; R = CH_3) after 68 hr., while 4′-*n*-butyryl-3-chloro-4-methoxybiphenyl gave only 18% yield of 3-ethyl-2-(3-chloro-4-methoxy-4′-xenyl)cinchoninic acid (VII; R = C_2H_5) after 120 hrs. The corresponding hydroxy cinchoninic acids (VIII), which could not be synthesized by the Pfitzinger reaction with 4′-acyl-3-chloro-4-hydroxybiphenyls, were prepared by pyridine hydrochloride-demethylation of the methoxy acids (VII). Thermal decomposition of these latter acids gave the corresponding 2-(3-chloro-4-methoxy-4′-xenyl)quinolines.


VII


VIII

EXPERIMENTAL

4′-Acetyl-3-chloro-4-methoxybiphenyl (II; R = H). Into an ice-cooled solution of 3-chloro-4-methoxybiphenyl (1 mole; prepared by methylation of commercial 3-chloro-4-hydroxybiphenyl with dimethyl sulfate and sodium hydroxide in aqueous ethanol) and acetyl chloride (1.2 moles) in dry carbon disulfide, finely powdered aluminum chloride (1.1 moles) was stirred portionwise, and the mixture left overnight at room temperature. The reaction mixture was then treated with ice-cooled hydrochloric acid, the carbon disulfide layer was washed with aqueous sodium carbonate, then with water, and dried over sodium sulfate. The solvent was distilled and the oily residue fractionated under reduced pressure. Yield: 88% of a *ketone*, b.p. 244–246°/15 mm., which crystallized from ethanol in shiny colorless needles, m.p. 109°.

Anal. Calcd. for $C_{15}H_{13}ClO_2$: C, 69.1; H, 5.0. Found: C, 69.1; H, 5.1.

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(5) Haworth and Sheldrick, *J. Chem. Soc.*, 864 (1934).

(6) Buu-Hoï, *Rec. trav. chim.*, **68**, 759 (1949).

(7) Unpublished results.

(8) Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946); **71**, 3301 (1949); Buu-Hoï, Hoán, and Xuong, *Rec. trav. chim.*, **71**, 285 (1952).

(9) Buu-Hoï and Cagniant, *Rec. trav. chim.*, **62**, 519, 713 (1943); **64**, 214 (1945); *Bull. soc. chim. France*, **13**, 123, 134 (1946); Buu-Hoï, *J. Chem. Soc.*, 795 (1946); Buu-Hoï and Royer, *Bull. soc. chim. France*, **13**, 374 (1946); **17**, 489 (1950); *J. Chem. Soc.*, 106 (1948); *Rec. trav. chim.*, **70**, 825 (1951); Buu-Hoï, Royer, Xuong, and Jacquignon, *J. Org. Chem.*, **18**, 1209 (1953).

TABLE I

4′-SUBSTITUTED DERIVATIVES OF 3-CHLORO-4-HYDROXYBIPHENYL

Acetyl group	Formula	M.P., °C.	Analyses Calcd. C	Analyses Calcd. H	Analyses Found C	Analyses Found H
4′-Acetyl-	$C_{14}H_{11}ClO_2$	143	68.2	4.5	68.2	4.2
4′-Propionyl-	$C_{15}H_{13}ClO_2$	139–140	69.1	5.0	69.2	5.0
4′-Benzoyl-	$C_{19}H_{13}ClO_2$	151	73.9	4.2	73.7	4.3
4′-Phenacetyl-	$C_{20}H_{15}ClO_2$	208	74.4	4.7	74.2	4.4
4′-Ethyl-	$C_{14}H_{13}ClO$	97	72.3	5.6	72.3	5.7
4′-*n*-Propyl-	$C_{15}H_{15}ClO$	104	73.0	6.1	72.9	6.1

TABLE II

QUINOLINE DERIVATIVES

Substance	Formula	M.P., °C.	Analyses Calcd. C	Analyses Calcd. H	Analyses Found C	Analyses Found H
2-(3-Chloro-4-methoxy-4′-xenyl)-cinchoninic acid	$C_{23}H_{16}ClNO_3$	283–284	70.9	4.1	70.6	4.0
2-(3-Chloro-4-methoxy-4′-xenyl)-quinoline[a]	$C_{22}H_{16}ClNO$	221	76.4	4.6	76.3	4.5
2-(3-Chloro-4-hydroxy-4′-xenyl)-cinchoninic acid	$C_{22}H_{14}ClNO_3$	316	70.3	3.7	70.0	3.5
2-(3-Chloro-4-methoxy-4′-xenyl)-3-methylcinchoninic acid	$C_{24}H_{18}ClNO_3$	325	71.4	4.5	71.5	4.4
2-(3-Chloro-4-methoxy-4′-xenyl)-3-methylquinoline	$C_{23}H_{18}ClNO$	183	76.8	5.0	76.6	5.1
2-(3-Chloro-4-hydroxy-4′-xenyl)-3-methylcinchoninic acid	$C_{23}H_{16}ClNO_3$	371	70.9	4.1	70.8	4.0
2-(3-Chloro-4-methoxy-4′-xenyl)-3-ethylcinchoninic acid	$C_{25}H_{20}ClNO_3$	307	71.9	4.8	71.6	4.6
2-(3-Chloro-4-methoxy-4′-xenyl)-3-ethylquinoline	$C_{24}H_{20}ClNO$	136	77.1	5.4	77.0	5.4
2-(3-Chloro-4-hydroxy-4′-xenyl)-3-ethylcinchoninic acid	$C_{24}H_{18}ClNO_3$	331	71.4	4.5	71.1	4.4
2-(3-Chloro-4-methoxy-4′-xenyl)-3-phenylcinchoninic acid[b]	$C_{29}H_{20}ClNO_3$	309	74.8	4.3	74.7	4.1
2-(3-Chloro-4-methoxy-4′-xenyl)-3-phenylquinoline	$C_{28}H_{20}ClNO$	172	79.7	4.7	79.6	4.8
2-(3-Chloro-4-hydroxy-4′-xenyl)-3-phenylcinchoninic acid	$C_{28}H_{18}ClNO_3$	344–346	74.4	4.0	74.1	3.9
2-(3-Chloro-4-hydroxy-4′-xenyl)-3-phenylquinoline	$C_{27}H_{18}ClNO$	220	79.5	4.4	79.3	4.3

[a] The quinolines were prepared by heating the corresponding cinchoninic acids above their melting points, and crystallizing the residue from a mixture of benzene, to give colorless prisms. [b] Obtained in 80% yield.

TABLE III

4′-ALKYL AND 4′-ARYLALKYL DERIVATIVES OF 3-CHLORO-4-METHOXYBIPHENYL

Alkyl group	Formula	M.P. °C.	Analyses Calcd. C	Analyses Calcd. H	Analyses Found C	Analyses Found H
4′-Ethyl-	$C_{15}H_{15}ClO$	72	73.0	6.1	72.9	6.3
4′-*n*-Propyl-	$C_{16}H_{17}ClO$	64	73.7	6.5	73.5	6.5
4′-*n*-Butyl-	$C_{17}H_{19}ClO$	52	74.3	6.9	74.3	7.0
4′-Benzyl-[a]	$C_{20}H_{17}ClO$	88	77.8	5.5	77.5	5.5
4′-(β-Phenylethyl)-	$C_{21}H_{19}ClO$	92	78.1	5.9	78.0	5.8

[a] Demethylation yielded a compound m.p. 82°.

The corresponding *semicarbazone* crystallized from a mixture of benzene and ethanol in shiny colorless prisms, m.p. 254°.

Anal. Calcd. for $C_{16}H_{16}ClN_3O_2$: N, 13.2. Found: N, 12.9.

Chalcones derived from 4′-acetyl-3-chloro-4-methoxybiphenyl. The *benzylidene derivative*, prepared with benzaldehyde in ethanol medium and in the presence of a few drops of 20% aqueous sodium hydroxide, crystallized from a mixture of benzene and ethanol in shiny yellowish leaflets, m.p. 157°, giving an orange coloration with sulfuric acid.

Anal. Calcd. for $C_{22}H_{17}ClO_2$: C, 75.8; H, 4.9. Found: C, 75.8; H, 4.8.

p-Methoxybenzilidene derivative, pale yellow leaflets, m.p. 145°, gave a bright red coloration with sulfuric acid.

Anal. Calcd. for $C_{23}H_{19}ClO_3$: C, 72.9; H, 5.0. Found: C, 73.1; H, 5.0.

Piperonylidene derivative, pale yellow leaflets, m.p. 158°, gave a violet-red coloration with sulfuric acid.

Anal. Calcd. for $C_{23}H_{17}ClO_4$: C, 70.3; H, 4.3. Found: C, 70.3; H, 4.3.

2-Furfurylidene derivative, shiny yellow leaflets, m.p. 148°, gave a bright red coloration with sulfuric acid.

Anal. Calcd. for $C_{20}H_{15}ClO_3$: C, 70.9; H, 4.4. Found: C, 70.7; H, 4.5.

2-Thenylidene derivative, pale yellow needles, m.p. 165°, gave a red coloration with sulfuric acid.

Anal. Calcd. for $C_{20}H_{15}ClO_2S$: C, 67.7; H, 4.2. Found: C, 67.7; H, 4.2.

3-Chloro-4-methoxybiphenyl-4'-carboxylic acid (III). A fine suspension of 4'-acetyl-3-chloro-4-methoxybiphenyl (1 mole) in an aqueous solution of sodium hypobromite (1.2 moles) was shaken with some dioxane for 4 hr., then heated for 1 hr. on the water bath. After addition of sodium hydrogen sulfite and filtration, the filtrate was acidified with hydrochloric acid, and the precipitate washed with water and recrystallized from dioxane. Yield: 80% of fine colorless prisms, m.p. 280–281°.

Anal. Calcd. for $C_{14}H_{11}ClO_3$: C, 64.0; H, 4.2. Found: C, 63.7; H, 4.3.

The corresponding *amide* crystallized from ethanol in fine colorless needles, m.p. 243°.

Anal. Calcd. for $C_{14}H_{12}ClNO_2$: C, 64.2; H, 4.6. Found: C, 64.1; H, 4.9.

4'-Propionyl-3-chloro-4-methoxybiphenyl (II; R = CH_3). Prepared in 86% yield as for the lower homolog, this ketone, b.p. 260–262°/15 mm., crystallized from ethanol in lustrous colorless leaflets, m.p. 111°.

Anal. Calcd. for $C_{16}H_{15}ClO_2$: C, 69.9; H, 5.5. Found: C, 70.0; H, 5.5.

4'-n-Butyryl-3-chloro-4-methoxybiphenyl (II; R = C_2H_5). This ketone (65% yield), b.p. 272–274°/18 mm., crystallized from ethanol in colorless leaflets, m.p. 86°.

Anal. Calcd. for $C_{17}H_{17}ClO_2$: C, 70.7; H, 5.9. Found: C, 70.5; H, 6.1.

4'-Phenacetyl-3-chloro-4-methoxybiphenyl (II; R = C_6H_5). This ketone (65% yield), b.p. 332–334°/17 mm., crystallized from a mixture of benzene and ethanol in colorless prisms, m.p. 144°.

Anal. Calcd. for $C_{21}H_{17}ClO_2$: C, 74.9; H, 5.1. Found: C, 74.8; H, 5.3.

The *semicarbazone* crystallized from acetic acid in fine colorless prisms, m.p. 245°.

4'-Benzoyl-3-chloro-4-methoxybiphenyl (IV). (a) *From benzoyl chloride* the yield was 68% of a ketone, m.p. 310–315°/20 mm., which crystallized from a mixture of ethanol and benzene in long colorless needles, m.p. 138°.

Anal. Calcd. for $C_{20}H_{15}ClO_2$: C, 74.4; H, 4.7. Found: C, 74.1; H, 4.5.

(b) *From 3-chloro-4-methoxybiphenyl-4'-carboxylic acid.* This acid was converted into its chloride by means of thionyl chloride in benzene solution on the water bath. The solvent was then distilled off and replaced by more benzene, aluminum chloride was added with cooling, and the mixture was left overnight. After the usual treatment, a ketone was obtained in 75% yield, identical with the one prepared from benzyl chloride.

Pfitzinger reactions with ketones II. The appropriate ketone was condensed with isatin in the usual way, the duration of reaction being 68 hr. for ketones II; R = H and R = CH_3, 100 hr. for ketone II; R = C_6H_5, and 120 hr. for ketone II; R = C_2H_5. Crystallization was from nitrobenzene producing fine yellowish prisms.

Demethylation of methoxy ketones II. A mixture of one part of the appropriate 4'-acyl-3-chloro-4-methoxybiphenyl and six parts of redistilled pyridine hydrochloride was gently refluxed for 15 to 30 min., and the cooled reaction product treated with dilute hydrochloric acid; the precipitate obtained was collected, washed, and purified *via* its sodium salt. Recrystallization was from benzene.

Reduction of methoxy ketones II. A solution of the methoxy ketone (1 mole) and 95% hydrazine hydrate (4 moles) in diethylene glycol was heated for a few minutes to allow formation of the hydrazone; potassium hydroxide (same weight as the hydrazine hydrate) was added after cooling, and the mixture refluxed for 1 hr. with removal of water. After cooling, water was added, the reduction product was taken up in benzene, the benzene solution was washed first with dilute hydrochloric acid, then with water, and dried over sodium sulfate. The solvent was removed, and the residue vacuum-distilled. Crystallization was from ethanol. Yield: 80 to 85%.

PARIS (V^e), FRANCE

[CONTRIBUTION FROM THE RESEARCH DIVISION, AMERICAN CYANAMID COMPANY, BOUND BROOK LABORATORIES]

Pyrido[2,3,4,5-*lmn*]phenanthridine

W. L. MOSBY

Received November 13, 1956

The synthesis of pyrido[2,3,4,5-*lmn*]phenanthridine and its 5,10-dimethyl homolog is described.

The only pyrido[2,3,4,5-lmn]phenanthridines thus far described have been aryl derivatives. These have been obtained[1,2] in the preparation of the yellow vat dye flavanthrone, and in the synthesis of trypanocidal drugs.[3] An aluminum chloride-sodium chloride melt was used[1,2] to cyclize 2,2'-diphthalimidobiphenyl, although 10-benzamido-5-phenylphenanthridine cyclized readily upon treatment with phosphorus oxychloride in nitrobenzene.[3] The third synthesis employed[3] was the reduction and simultaneous cyclodehydration of 2,2'-diaroyl-6,6'-dinitrobiphenyls. By a modification of the first of these methods, we have now prepared the prototype of this ring system, and its dimethyl homolog.

A few simple modifications of Ullmann's synthesis[4] of 2,2'-dinitrobiphenyl permitted the convenient preparation of quantities of this material in

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(1) F. Ebel, German Patent **614,196**; *Frdl.*, **22**, 1126 (1939); British Patent **431,790**; U. S. Patent **2,069,473**.

(2) V. Krepela and R. Štefec, *Collection Czechoslov. Chem. Commun.*, **9**, 29 (1937).

(3) A. E. S. Fairfull, D. A. Peak, W. F. Short, and T. I. Watkins, *J. Chem. Soc.*, 4700 (1952).

(4) F. Ullmann and J. Bielecki, *Ber.*, **34**, 2176 (1901).