James Woodyard, were recorded with a Varian A-60 spectrophotometer. The elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Melting points were taken on a Mel-Temp capillary melting point apparatus and are uncorrected. All chromatographic columns were prepared by pouring Merck reagent grade aluminum oxide, previously dried for 2 hr at 100°, onto a column filled with chloroform (reagent grade). The elutant from the column was analyzed by thin layer chromatography using microslides prepared by the method of Peifer[6] from silica gel G (according to Stahl), 1:1 ether–methanol as developing solvent, and iodine vapor for visualization of spots.

Sealed Tube Reaction between Imidazole and Formaldehyde. A solution of 13.6 g (0.20 mol) of imidazole (Sigma Chemical Co.) and 50 g of 37% aqueous formaldehyde solution in sealed Pyrex tubes was heated for 15 hr in an oil bath at 120–130° and was then evaporated in vacuo to give 17.8 g of colorless, viscous syrup. A drop of crude product treated with picric acid gave a resinous picrate derivative. The syrup was extracted with a hot mixture of 140 ml of acetone, 15 ml of methanol, and 15 ml of chloroform. After cooling, the supernatant was decanted from an insoluble syrup. This syrup was dissolved in a small volume of methanol and 35 ml of a 1:1 mixture of chloroform–acetone was added. After cooling overnight at 10° the supernatant was decanted from about 1.5 g of insoluble syrup. The solvents were evaporated from the two extracts, leaving syrupy residues: 10 g of more soluble material; 6 g of less soluble material. These two fractions were separately chromatographed on alumina.

1,2-Dihydroxymethylimidazole. The 10 g of more soluble material was dissolved in an acetone–chloroform mixture, placed on a 15.5 × 4 cm column, and eluted with six 25-ml portions of 3:1 chloroform–acetone, four 24-ml portions of chloroform–acetone mixture plus 1 ml of methanol, and three fractions with increasing amounts of methanol. By digesting the first nine fractions with acetone a total of 3.25 g of white, crystalline solid was obtained. Melting points of the different fractions ranged from 90–115° to 121–125° but all gave identical ir spectra. A sample for analysis recrystallized twice from acetone melted at 126–127°. The NMR spectrum and analysis indicated this material to be 1,2-bis(hydroxymethyl)imidazole.

Anal. Calcd for $C_5H_8N_2O_2$: C, 46.87; H, 6.29; N, 21.86. Found: C, 46.79; H, 6.16; N, 22.03.

2-Imidazolemethanol was prepared by the method of Jones;[5] purification by chromatography yielded a white, crystalline solid, mp 112–112.5° (lit.[7] mp 114–115°). The NMR sample of the 1,2-dihydroxymethylimidazole (0.1413 g) was repeatedly digested with water to remove deuterium. The final residue (72 mg after one recrystallization from acetone) melted at 108–109° and gave an ir spectrum identical with that of 2-imidazolemethanol.

The syrupy residues (2.4 g) from recrystallizations of different fractions of 1,2-dihydroxymethylimidazole were combined, boiled with water, and chromatographed, yielding 0.25 g of imidazole, mp 91–92° (identified by ir), and 1.5 g of crude 2-imidazolemethanol (identified by ir).

2,4,5-Trihydroxymethylimidazole. After fractions 10–13 were extracted from the above chromatography with acetone, the combined acetone-insoluble residues were dissolved in methanol. White, crystalline solid slowly separated from solution and after cooling overnight at 10°, 0.2 g of solid, mp 154–155°, was separated by filtration. After one recrystallization from methanol–acetone, a sample for analysis melted at 158–159°.

Anal. Calcd for $C_6H_{10}N_2O_3$: C, 45.57; H, 6.37; N, 17.71. Found: C, 46.14, 45.99; H, 6.52, 6.60; N, 18.26, 18.16.

A sample (50 mg) for NMR analysis was dissolved in 0.3 ml of D_2O. Only two adsorptions occurred at δ 4.81 (HOD) and 4.57. The integration data showed a ratio of HOD to $-CH_2$ of 1:1.48. The recovered sample, after boiling with water to remove deuterium, was identical in melting point and mixture melting point with the original sample and gave an identical ir spectrum. This indicates this material to be 2,4,5-trihydroxymethylimidazole.

The remaining materials from this column were divided into 6.5 g of an acetone-soluble residue and a small amount of acetone-insoluble syrup residue.

1-Imidazolemethanol. The above acetone-soluble residue was rechromatographed. The first eight fractions, eluted with 3:1 chloroform–acetone, showed only one component on TLC slides with the major amounts in fractions 2 and 3. The residue from fractions 2–4 (identical ir spectra) weighed 5.2 g and was a colorless liquid. The NMR spectrum of this material in D_2O solution indicates it is 1-imidazolemethanol. No attempt was made to purify this material. Treatment of 0.5 g of this liquid with a saturated alcoholic solution of picric acid yielded 0.49 g of crystalline picrate (**6**), mp 201–202°. A sample recrystallized for analysis from absolute alcohol melted at 202–203°.

Anal. Calcd for $C_{10}H_9N_5O_8$: C, 36.71; H, 2.77; N, 21.40. Found: C, 36.57; H, 2.64; N, 21.47.

Fractions 9 and 10 contained 1.35 g of the proposed 1,2-dihydroxymethylimidazole.

From chromatography of the 6 g of less soluble material from the second extraction of the original reaction mixture only 0.3 g of 1,2-dihydroxymethylimidazole and 0.34 g of 2,4,5-trihydroxymethylimidazole were obtained and the remainder of the material from the column remained unresolved.

Action of Water on 1-Imidazolemethanol. 1-Imidazolemethanol (0.5 g) was digested repeatedly with water. After the final evaporation of water, the residue, a syrup (0.3625 g), was dissolved in acetone and chromatographed, yielding 0.1834 g of imidazole (identified by ir), mp 79–85°.

Acknowledgment. Grateful acknowledgment is made to The American Association of University Women for the Ida M. Green Postdoctoral Fellowship which has supported this research.

Registry No.—**1**, 288-32-4; **2**, 51505-76-1; **3**, 54986-29-7; **4**, 3724-26-3; **5**, 54986-27-5; **6**, 54986-28-6; formaldehyde, 50-00-0.

References and Notes

(1) L. J. Saidel and R. L. Carino, *Fed. Proc.*, **25**, 796 (1966).
(2) C. J. Martin and M. A. Marini, *J. Biol. Chem.*, **242**, 5736 (1967).
(3) P. Dunlop, M. A. Marini, H. M. Fales, E. Sokoloski, and C. J. Martin, *Bioorg. Chem.*, **2**, 235–247 (1973).
(4) R. C. Kallen and W. P. Jencks, *J. Biol. Chem.*, **241**, 5864 (1966).
(5) R. G. Jones, *J. Am. Chem. Soc.*, **71**, 383 (1949).
(6) J. M. Bobbitt, "Thin-Layer Chromatography", Reinhold, New York, N.Y. 1963, pp 44–46.
(7) P. E. Iversen and H. Lund, *Acta Chem. Scand.*, **20**, 2649–2657 (1966).

A New Synthesis of 3-Substituted 1-Methylnaphthalenes via Ring Expansion of 1-Methylindenes[1]

J. Samuel Gillespie, Jr.,* Satya Prakash Acharya, and Dwight A. Shamblee

Virginia Institute for Scientific Research, Richmond, Virginia 23229

Received January 15, 1975

Specifically substituted 3-aryl-1-methylnaphthalenes and their derivatives can be synthesized by a convenient and productive reaction sequence,[2] which, however, is suitable for 3-aryl substitution only. A different approach, now reported, was required for the preparation of naphthalenes with other 3 substituents.

Since specifically substituted 1-methylindenes could be prepared easily from 3-arylbutanoic acids, ring expansion to the title compounds offered a convenient route. Parham and his group[3] obtained only 2-chloro-1-methylnaphthalene from attempts to prepare 3-chloro-1-methylnaphthalene by treating 1-methylindene with potassium *tert*-butoxide and chloroform, and they doubted the stability of the indene. Others[4–8] showed that 1-methylindene is stable under neutral or mild acidic conditions at room temperature and that it isomerized rapidly to 3-methylindene in base. We confirmed the stability of 4,6-dichloro-1-methylindene (**6b**) at room temperature under acidic conditions and isomerized it to 5,7-dichloro-3-methylindene (**8b**) by exposure to a small amount of pyridine.[9]

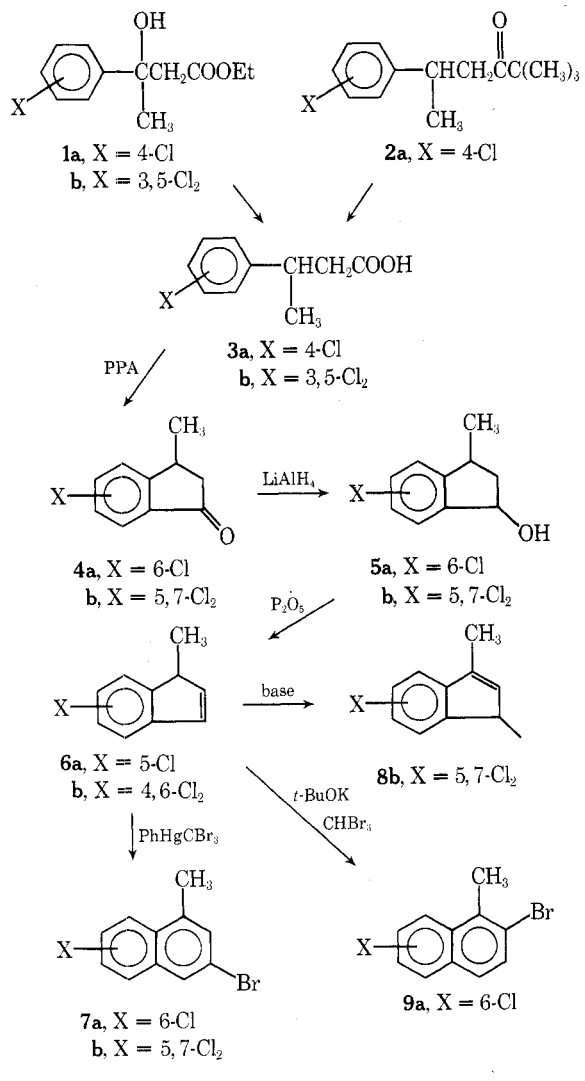
Carried out under neutral conditions, e.g., by carbene generation from phenyl(tribromomethyl)mercury,[10] ring expansion yielded the desired 3-bromo-1-methylnaphthalenes; e.g., 4,6-dichloro-1-methylindene (**6b**) gave 3-bromo-5,7-dichloro-1-methylnaphthalene (**7b**) (Scheme I

Table I
3-Substituted 1-Methylnaphthalenes and Precursors[a]

Compd	Method[b]	Yield, %	Mp or bp, °C (mm)	Solvent of crystn	Molecular formula
1b	*c*	85	105 (0.2)		$C_{12}H_{14}Cl_2O_3$
2a	*d*	97	77 (0.5)		$C_{14}H_{19}ClO$
3a	*d*	88	90–93	MeOH–petroleum ether	$C_{10}H_{11}ClO_2$
	A	87			
3b	A	83	100–103	Petroleum ether	$C_{10}H_{10}Cl_2O_2$
4a	B	74	65 (0.07)		$C_{10}H_9ClO$
4b	B	86	59–61	Petroleum ether	$C_{10}H_8Cl_2O$
5a	*e*	100	78–79	Et_2O–petroleum ether	$C_{10}H_{11}ClO$
6a[f]	C	80	60 (1)		$C_{10}H_9Cl$
6b	C	90	65 (0.02)		$C_{10}H_8Cl_2$
7a	E	40	56–57	MeOH	$C_{11}H_8BrCl$
7b	E	55	169–171	Acetone	$C_{11}H_7BrCl_2$
9a	F	16	53–54	MeOH	$C_{11}H_8BrCl$

[a] Satisfactory analytical data (±0.4% for C, H, Cl, etc.) were reported for all compounds listed in the table. [b] The capital letter refers to the general procedure described in the Experimental Section. [c] Prepared by Reformatsky reaction.[12] [d] Prepared according to ref 2. [e] Prepared by reduction of **4a** with $LiAlH_4$.[13] [f] NMR (CCl_4) δ 7.12 (3 H, broad m, phenyl), 6.58 (1 H, d of d, J_{12} = 2 Hz, =CH), 6.40 (1 H, d of d, J_{23} = 6 Hz, =CH), 3.33 (1 H, broad q, J_{1CH3} = 8 Hz, CH_3CH), 1.23 (3 H, d, J_{13} = 2 Hz, CH_3).

Scheme I



and Table I), which showed only meta couplings in NMR. Repetition of the method of Parham et al.[2] with 5-chloro-1-methylindene (**6a**) gave the expected product from the rearranged indene, 2-bromo-6-chloro-1-methylnaphthalene (**9a**).

We developed a new method to prepare phenyl(tribromomethyl)mercury by mixing phenylmercuric chloride, sodium hydride, and bromoform in benzene and initiating the reaction with methanol. Although the yields by this method were somewhat lower than those reported by Seyferth,[11] it is a very convenient procedure.

Experimental Section

Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Boiling points are also uncorrected. NMR spectra were obtained on a Varian A-60 spectrometer. Microanalyses were performed by Microanalysis, Inc., Wilmington, Del.

A. 3-Arylbutanoic Acids (3). A mixture of 1 (0.2 mol), red phosphorus (1 mol), and HI (57%, 240 g) was refluxed for 18 hr and then cooled and diluted with an equal volume of water. The aqueous layer was decanted, and the red gum was extracted with dilute NaOH. The extract was filtered and acidified. The oil that separated was extracted with Et_2O. The ethereal solution was dried (Na_2SO_4), ether was removed, and the product was crystallized. This procedure is based on the work of Spring.[14]

B. 3-Methylindanones (4). **3** (0.01 mol) was added, with good agitation, to hot (115°) polyphosphoric acid (250 g). The reaction mixture was stirred at this temperature for 30 min, cooled, and poured into ice–water. The product was extracted with ether. The ethereal solution was washed with $NaHCO_3$ and dried (Na_2SO_4), and ether was removed.

C. 1-Methylindenes (6). **5** (1 mol) was heated to 100° with stirring. P_2O_5 (5 g) was added quickly in one lot, and the mixture was immediately distilled under vacuum. The receiving flask was cooled with a Dry Ice–acetone bath, so that the product and water were collected together. The distillate was dissolved in ether and dried (Na_2SO_4) and ether was removed.

D. Phenyl(tribromomethyl)mercury. NaH (13 g of 56% dispersion in oil, washed with benzene), phenylmercuric chloride (50 g), bromoform (80 g), and benzene (800 ml) were mixed with rapid stirring and cooled in ice–water. The reaction was initiated with MeOH (0.5 ml), and the rate was maintained if necessary by additional drops of MeOH. After 1 hr the cooling bath was removed. As the reaction progressed, the thick white reaction mixture changed into a thin gray slurry. The mixture was stirred at room temperature overnight. Benzene was removed from the filtered solution using rotary evaporation with a bath temperature of 40° and cooling the trap in a Dry Ice–acetone bath. The heavy white solid residue was washed with petroleum ether and dried in air, yield 50 g. On melting it decomposed at about 120° and was sufficiently pure for use.

E. 3-Bromo-1-methylnaphthalenes (7). A mixture of **6** (0.3 mol), phenyl(tribromomethyl)mercury (0.4 mol), and benzene (600 ml) was refluxed for 4 hr. The solid dissolved at first, and then a precipitate appeared. Benzene was evaporated from the cooled, fil-

tered solution, and the residue was extracted with boiling acetone, from which on cooling the product crystallized.

F. 2-Bromo-6-chloro-1-methylnaphthalene (9a). K (1 g) was dissolved in *t*-BuOH (25 ml), and the solution was cooled in ice–water. **6a** (4 g) was added followed by bromoform (8 g). The solution was stirred in the cold for 2 hr and diluted with water. The precipitated solid was collected, yield 1 g.

Acknowledgments. The authors wish to thank Dr. William J. Welstead, Jr., and Mr. Ashby F. Johnson, A. H. Robins Company, Inc., Richmond, Va., for NMR spectra.

Registry No.—**1a,** 21133-98-2; **1b,** 55058-75-8; **2a,** 55058-76-9; **3a,** 5292-23-9; **3b,** 55058-77-0; **4a,** 54795-05-0; **4b,** 55058-78-1; **5a,** 55058-79-2; **5b,** 55058-80-5; **6a,** 55058-81-6; **6b,** 55058-82-7; **7a,** 55058-83-8; **7b,** 55058-84-9; **8b,** 55058-85-0; **9a,** 55058-86-1.

References and Notes

(1) The work described in this paper was performed under Contract DADA-17-72-C-2078 with the U.S. Army Medical Research and Development Command. This is Contribution No. 1281 from the Army Research Program on Malaria.
(2) J. S. Gillespie, Jr., S. P. Acharya, D. A. Shamblee, and R. E. Davis, *Tetrahedron*, **31**, 3 (1975).
(3) W. E. Parham, H. E. Reiff, and P. Swartzentruber, *J. Am. Chem. Soc.*, **78**, 1437 (1956).
(4) T. L. Yarboro, C. Karr, Jr., and P. A. Estep, *J. Chem. Eng. Data*, **6**, 421 (1961).
(5) G. Bergson and A. Weidler, *Acta Chem. Scand.*, **17**, 862 (1963).
(6) A. Wiedler, *Acta Chem. Scand.*, **17**, 2724 (1963).
(7) A. Weidler and G. Bergson, *Acta Chem. Scand.*, **18**, 1487 (1964).
(8) H. Christol, F. Plenat, and C. F. Huebner, *Bull. Soc. Chim. Fr.*, 1640 (1964).
(9) The isomerization was followed by NMR. For 4,6-dichloro-1-methylindene (**6b**) in $CDCl_3$: δ 7.27 (2 H, s, phenyl), 6.88 (1 H, d of d, J_{12} = 2 Hz, =CH), 6.52 (1 H, d of d, J_{23} = 6 Hz, =CH), 3.53 (1 H, broad q, $J_{1\,CH_3}$ = 8 Hz, CH_3CH), 1.28 (3 H, d, J_{13} = 2 Hz, CH_3). For 5,7-dichloro-3-methylindene (**8b**) in $CDCl_3$ with a trace of C_6D_5N: δ 7.17 (2 H, s, phenyl), 6.23 (1 H, m, J_{12} = 2, J_{13} = 2 Hz, =CH), 3.20 (2 H, m, J_{2CH_3} = 2 Hz, CH_2), 2.03 (3 H, m, CH_3).
(10) D. Seyferth, *Acc. Chem. Res.*, **5**, 65 (1972).
(11) D. Seyferth and R. L. Lambert, Jr., *J. Organomet. Chem.*, **16**, 21 (1969).
(12) R. L. Shriner, *Org. React.*, **1**, 1 (1942).
(13) W. G. Brown, *Org. React.*, **6**, 474 (1951).
(14) F. S. Spring, *J. Chem. Soc.*, 1332 (1934).

Ylidenemalononitriles in Thiophene Ring Annelations

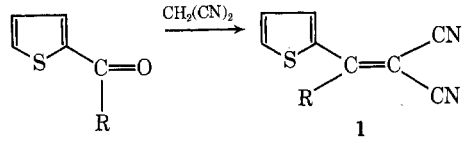
S. W. Schneller* and D. R. Moore

Department of Chemistry, University of South Florida, Tampa, Florida 33620

Received December 24, 1974

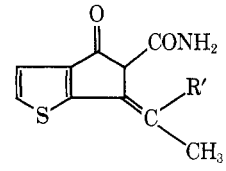
Synthetic methods available for the construction of rings fused to heterocyclic molecules are limited owing to the vulnerability of the heteroatom to the well-established conditions of carbocyclic chemistry. Acid-mediated cyclizations of ylidenemalononitriles[1,2] to form fused keto amides appeared to present a valuable potential for this problem. This has now proven successful in the thiophene series.

The thiophene ylidenemalononitriles (1) were readily obtained by a Knoevenagel reaction between the corresponding precursor[3] and malononitrile.

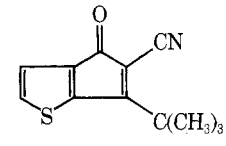


1

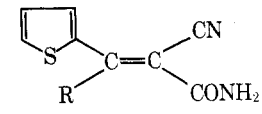
Treatment of **1** (R = C_2H_5) and **1** (R = *i*-C_3H_7) with polyphosphoric acid produced the ring-cyclized products **2**. The structural assignments for **2** were based on spectral data. The ir spectrum (KBr) of **2** (R′ = H) has NH absorption at 3.00 and 3.15 μ, ketone carbonyl at 5.91 μ, and



2



3



4

amide carbonyl at 6.02 μ, while **2** (R′ = CH_3) has similar peaks at 2.98, 3.14, 5.90, and 6.02 μ which is in agreement with similar ring systems in the benzene series.[6] The NMR spectrum (DMSO-d_6) also supports structure **2** by displaying a simple two-proton thiophene absorption with doublets at δ 7.19 (J = 5 Hz) and 7.70 (J = 5 Hz), methine (proton α to amide and ketone carbonyls) absorption at δ 4.32, vinyl quartet absorption (for **2**, R′ = H) at δ 5.75 (J = 7 Hz), and methyl singlets at δ 1.80 and 1.97 for **2** (R′ = CH_3) and a methyl doublet at δ 1.93 (J = 7 Hz) for **2** (R′ = H). The above data is clearly in accord with the bicyclic systems **2** possessing the exocyclic double bond.[7]

On the other hand, when **1** (R = *t*-C_4H_9) was subjected to polyphosphoric acid the anticipated endocyclic fused system (**3**) resulted. The structural assignment for **3** was based on the ir spectrum (KBr) (nitrile absorption at 4.52 μ and a carbonyl band at 5.80 μ) and the NMR spectrum (DMSO-d_6) [two-proton thiophene doublets at δ 7.20 (J = 5 Hz) and 7.62 (J = 5 Hz) and a nine-proton methyl singlet at δ 1.54]. Thus far it has not been possible to hydrolyze the nitrile functionality of **3** to the corresponding carboxamido group.

To complete the series, **1** (R = H and CH_3) was studied under the cyclization conditions and found to yield only (by TLC) **4**. Confirmation of the product formation was obtained when products identical (by melting point and TLC) with **4** were realized from the reactions of thiophenecarboxaldehyde and methyl 2-thienyl ketone with cyanoacetamide.[1,8]

These results suggest that the fusion of a functionalized five-membered ring to a thiophene ring is possible via ylidenemalononitriles which possess at least a secondary γ carbon.[9] If the γ carbon possesses at least one hydrogen the exocyclic products (**2**) are realized as a means of relieving the steric strain which would result with the endocyclic isomer. When the γ carbon is quaternary, the endocyclic isomer (**3**) is the only structure possible and it forms, but in considerably diminished yields compared to **2**.

Experimental Section[10]

Preparation of the Ylidenemalononitriles. A solution of 0.3 mol of the carbonyl agent,[3] 0.5 mol of malononitrile, 12.0 g of ammonium acetate, and 24 ml of glacial acetic acid in 200 ml of toluene was refluxed with the aid of a Dean-Stark trap until the amount of water collected in the trap remained constant (4–24 hr, the sterically hindered ketones requiring the longer reflux time). Following the reflux period, the solution was cooled and decanted from a malononitrile polymer. The polymeric gum was washed with toluene (50 ml) and the combined toluene fractions were washed with water (2 × 50 ml), dried over anhydrous magnesium sulfate, and concentrated to yield the crude product, whose properties are listed in Table I. In the case of **1** (R = *i*-C_3H_7) and **1** (R = *t*-C_4H_9) it was necessary to remove the unreacted ketone (via vacuum distillation) from the crude product mixture to realize the desired ylidenemalononitrile.

Treatment of Ylidenemalononitriles (1) with Polyphosphoric Acid. After 200 g of polyphosphoric acid was warmed to the temperature required for reaction, 2.0 g of **1** was added slowly