ether,[7] was dissolved in a small amount of ethanol and combined with the sodium ethoxide solution. The mixture was heated on a steam bath for 15 min. and the excess ethanol was then removed by gentle heating at reduced pressure. A mixture of 2.62 g. (0.0084 mole) of iodoferrocene and 0.05 g. of freshly activated copper bronze was added and the reactants were mixed well. A 2-ft. air condenser was inserted and the tube was heated in a silicone bath at 150° (bath temperature) for 8 hr. The reaction residue and an orange sublimate that formed were combined and were extracted with 100 ml. of hot ethanol. The ethanol extracts were acidified with 100 ml. of 5% sulfuric acid solution and were subjected to steam distillation for approximately 1 hr. in the presence of several grams of powdered zinc.[17]

The distillate was collected, extracted with benzene, the benzene extracts were dried over Drierite, and the solvent was evaporated. The residue was dissolved in petroleum ether (b.p. 60–70°) and was chromatographed on alumina. A broad yellow foreband produced 0.55 g. of ferrocene, m.p. 170–173°. An orange trailing band produced 0.16 g. of crude diferrocenyl disulfide, m.p. 179–183°. One recrystallization from benzene–petroleum ether yielded orange crystals of the disulfide, m.p. 192–193° (reported m.p. 192°).[7] The infrared maxima (potassium bromide disk) of this product were identical to those published previously for diferrocenyl disulfide.[7]

The flask residue after cooling was extracted with benzene, the extracts were washed with water until the wash was neutral, the extracts were dried over Drierite, and the solvent was evaporated. There remained 2.50 g. of crude diferrocenyl sulfide, m.p. 152–153°. This product was dissolved in benzene–petroleum ether and chromatographed on alumina. A homogeneous band eluted, producing 2.14 g. of product, m.p. 155–156°. Recrystallization from *n*-heptane gave 2.00 g. (60% yield) of orange needles of diferrocenyl sulfide, m.p. 161.5–162°.

Anal. Calcd. for $C_{20}H_{18}Fe_2S$: C, 59.74; H, 4.51; Fe, 27.78; S, 7.97; mol. wt., 402. Found: C, 59.79; H, 4.59; Fe, 28.05; S, 8.22; mol. wt., 408.

The infrared spectrum of diferrocenyl sulfide (potassium bromide disk) exhibited bands at 3100, 1415, 1105, 1003, and 820 cm.$^{-1}$ characteristic of the ferrocenyl group, and other absorption bands at 1025 and 883 cm.$^{-1}$.

Ferrocenyl phenyl sulfide was prepared from 0.07 g. (0.003 g.-atom) of sodium, 0.35 g. (0.0032 mole) of benzenethiol, 0.936 g. (0.003 mole) of iodoferrocene, and 0.02 g. of copper bronze. The reaction mixture was heated at 158° for 2.5 hr. From the residue following steam distillation was obtained 0.67 g. (76% yield) of ferrocenyl phenyl sulfide, m.p. 110–111°. An analytical sample was prepared by chromatography of the product on alumina and subsequent recrystallization from petroleum ether; orange needles, m.p. 111.5–112°.

Anal. Calcd. for $C_{16}H_{14}FeS$: C, 65.31; H, 4.80; Fe, 18.98; S, 10.90; mol. wt., 294. Found: C, 65.12; H, 4.98; Fe, 18.90; S, 10.84; mol. wt., 288.

The infrared spectrum of ferrocenyl phenyl sulfide (potassium bromide disk) exhibited bands at 3100, 1418, 1108, 1002, and 820 cm.$^{-1}$ characteristic of the ferrocenyl group, bands at 1580, 1480, 745, and 690 cm.$^{-1}$ characteristic of the phenyl group, and other strong absorption bands at 1440, 1165, 1075, 890, and 830 cm.$^{-1}$

Ferrocenyl p-tolyl sulfide was prepared in 68% yield by a procedure identical to that described for ferrocenyl phenyl sulfide, except that *p*-toluenethiol was substituted for benzenethiol. The product was recrystallized from methanol, forming long yellow needles, m.p. 110.5–111°.

Anal. Calcd. for $C_{17}H_{16}FeS$: C, 66.25; H, 5.23; Fe, 18.12; S, 10.40; mol. wt., 308. Found: C, 66.23; H, 5.23; Fe, 18.28; S, 10.76; mol. wt., 315.

The infrared spectrum of ferrocenyl *p*-tolyl sulfide (potassium bromide disk) exhibited bands at 3100, 1411, 1103, 1006, and 816 cm.$^{-1}$ characteristic of the ferrocenyl group, bands at 1900, 1490, and 808 cm.$^{-1}$ characteristic of the *p*-tolyl group, and other strong absorption bands at 1182, 1165, 1083, 1023, 1018, 998, 890, 838, and 828 cm.$^{-1}$

Reaction of diferrocenylmercury and sulfur. A mixture of 1.14 g. (0.002 mole) of diferrocenylmercury and 0.16 g. of sulfur was thoroughly mixed and was added to a Schlenk tube under nitrogen. A loose-fitting plug of glass wool was inserted between the reactants and the upper portion of the tube. A 2-ft. air condenser was inserted and the tube was heated in a silicone bath at 160–180° for 18 hr. After cooling to room temperature, 0.20 g. of an orange sublimate was collected, m.p. 164–170°. The residue was extracted repeatedly with hot benzene, the solvent was evaporated, and the resulting residue plus the sublimate were chromatographed on alumina in benzene–petroleum ether solution. Elution with petroleum ether removed 0.16 g. of ferrocene, m.p. 173–174°. Continued elution with benzene produced 0.02 g. of an orange solid. This product was recrystallized from methanol, forming 0.01 g. of diferrocenyl disulfide, m.p. 185–187°. The infrared spectrum of this material (potassium bromide disk) was identical to the spectrum of diferrocenyl disulfide isolated above and with literature data.[7]

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(17) Under these conditions, any disulfide formed would be reduced to the thiol which in turn would distill with steam.[11] The diferrocenyl disulfide detected in the distillate probably resulted from distilled ferrocenethiol, since this thiol is known to oxidize readily in air to the disulfide.[7]

Indandiones. II. A Modified Dieckmann Reaction

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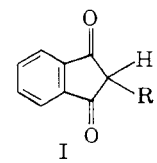
A new method affording excellent yields of arylindandiones (I) through the condensation of phthalide and aromatic aldehydes has been recently reported.[1] This reaction has now been recognized to proceed through the 3-(α-hydroxybenzyl)phthalide[1–3] *via* elimination of water to give the 2-arylindandione (I).[4]



I

In the Dieckmann reaction, unlike other carbonyl methylene condensations,[5,6] formed water

(1) S. L. Shapiro, K. Geiger, and L. Freedman, *J. Org. Chem.*, **25**, 1860 (1960).

(2) R. L. Horton and K. C. Murdock, *J. Org. Chem.*, **25**, 938 (1960).

(3) H. Zimmer and R. D. Barry, Am. Chem. Soc. Meeting, St. Louis, Mo., Abstr. (1961), p. 23N.

(4) See Scheme 1 of ref. 1.

(5) S. Patai and J. Zabicky, *J. Chem. Soc.*, 2030, 2038 (1960), and other references therein cited.

(6) D. N. Dhar and J. B. Lal, *Journ. and Proc. Inst. Chem.*, **31**, 297 (1959).

seriously affects yields and herein there is described its removal through the employment of esters as scavengers for water of reaction.

This study defines the parameters consistent with synthetic convenience and high conversions to indandiones. In Tables I–III, the scope of aromatic aldehyde, the variation of scavenger ester, and the effects of time and temperature are summarized.

With hindered esters such as isobutyl 2-ethylbutyrate, water removal, *via* saponification, is obtained at a rate[7] insufficient to eliminate side effects and good yields are not obtained.

TABLE I

VARIATION OF THE AROMATIC ALDEHYDE

[Constants: ester, ethyl propionate (3 equivalents); alkoxide, sodium methoxide (3 equivalents); time, 2 hours; temperature, 65°]

Aldehyde	Crude Yield of I, %	M.P.	M.P., Pure	Δ M.P.[a]
Benzaldehyde	100	135–142	148–149	10
p-Tolualdehyde	92	135–138	144–148	9.5
p-Fluorobenzaldehyde	100	114–117	116–117	1
p-Chlorobenzaldehyde	99	136–138	142–145	6.5
p-Bromobenzaldehyde	100	126–134	144–145	14.5
p-Iodobenzaldehyde	89	135–136	143–144	8
Anisaldehyde	100	148–154	152–154	2
α-Naphthaldehyde	97	207–211	217–218	8.5

[a] Δ M.P. is calculated by subtracting the center of the range of the pure melting point from the center of crude melting point range.

TABLE II[a]

VARIATION OF THE ESTER

[Constants: aldehyde, benzaldehyde[b1]; alkoxide, sodium methoxide (3 equivalents); time, 2 hours; temperature, 65°]

Ester	Crude Yield of I, %	M.P.	Δ M.P.
Methyl formate[c]	93.4	137–145	7.5
Ethyl acetate	87.5	116–140	20.5
Isopropyl acetate	91	139–144	7
Butyl acetate	82	140–147	5
Glycol diformate	83	135–143	9.5
Methyl propionate	100	144–149	2
Ethyl propionate	100	135–142	10
Isopropyl propionate	100	124–137	18
Ethyl butyrate	98	144–146	3.5
Methyl isobutyrate	96	137–144	8
Isobutyl 2-ethylbutyrate	53	114–134	24.5
Ethyl acetate[b2]	100	125–132	15
Methyl formate[b3,c]	96	147–150	4.5
Ethyl butyrate[b4]	95	208–211	8

[a] See Table I for definition of Δ M.P. and for m.p. of reference indandiones. [b1] Aldehyde varied where shown; [b2] *p*-chlorobenzaldehyde; [b3] *p*-anisaldehyde; [b4] α-naphthaldehyde. [c] Reaction temperature, 34°.

(7) M. S. Newman, *Steric Effects in Organic Chemistry*, Wiley, New York, 1956, p. 204 et seq.

TABLE III[a]

VARIATION OF TIME AND TEMPERATURE

[Constants: aldehyde, benzaldehyde; ester, ethyl propionate (3 equivalents); alkoxide, sodium methoxide (3 equivalents)]

Time, Hr.	Temperature	Crude Yield of I, %	M.P.	Δ M.P.
1	20	68	130–142	12.5
4	20	91	132–142	11.5
20	20	100	142–149	3
0.25	65	82	140–147	5
0.5	65	89	142–148	3.5
1	65	100	144–149	2
2	65	100	135–142	10
2[b]	65	10	75–105	
2[c]	65	85	139–145	6.5
2[d]	65	None		

[a] See footnote a of Table II. [b] One equivalent of ethyl propionate and one equivalent of sodium methoxide was used. [c] Two equivalents of ethyl propionate and two equivalents of sodium methoxide were used. [d] An additional three equivalents of water were added to reaction mixture.

The high yield with methyl formate where the reaction temperature was confined to 34° indicated further inspection of the role of time and temperature. From Table III it is seen that at 20° using ethyl propionate as a solvent, that a quantitative yield of I, R = phenyl is obtained after twenty hours, a substantial yield (91%) in four hours, with a drop-off to 68% in one hour. Alternatively, at 65° in the same system, a quantitative yield is obtained in one hour, with 82% and 89% yields with heating times of one quarter and one half hour, respectively. While the stoichiometry of the reaction calls for two equivalents of sodium methoxide, one to form the sodium salt of the product, and the other the sodium salt of the acid derived from the scavenger ester, it is preferable (see Table III) to use about three equivalents.

When water is deliberately added to the system, under conditions affording quantitative yield without water, no product is obtained.

As it serves in part as the solvent, about three equivalents of ester are preferred and under these conditions the following general alternatives are indicated—either conducting the reaction at room temperature overnight, or heating for one hour at 65°.

This work is being extended to evaluate aliphatic aldehydes, as well as other methylene carbonyl reactions and will be reported later.

EXPERIMENTAL[8]

α-Naphthylindandione. To a mixture of 146 g. (1 mole) of α-naphthaldehyde, 134 g. (1 mole) of phthalide, and 480 ml. of dried ethyl propionate, there was rapidly added 3 moles of sodium methoxide in 700 ml. of methanol. The reaction mixture was maintained at 65° with stirring for 2 hr. there-

(8) For a run typifying the standard Dieckmann procedure see 2-(*p*-bromophenyl)indandione in Ref. 1.

after. When cool, the volatiles were removed, the residue dissolved in 5.5 l. of water, the whole washed with ether, and filtered. Upon acidification to *p*H 2.0 the aqueous phase afforded the substantially pure product, 262 g. (96.5%), m.p. 207–211°.

On recrystallization (9 parts methyl ethyl ketone), there was obtained 217 g. (83%), m.p. 217–218°.

The runs cited in the tables were purified similarly to that described above with the variations involved being specifically shown in the tables.

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9-Ribityl Derivatives of Guanine and 8-Azaguanine[1a]

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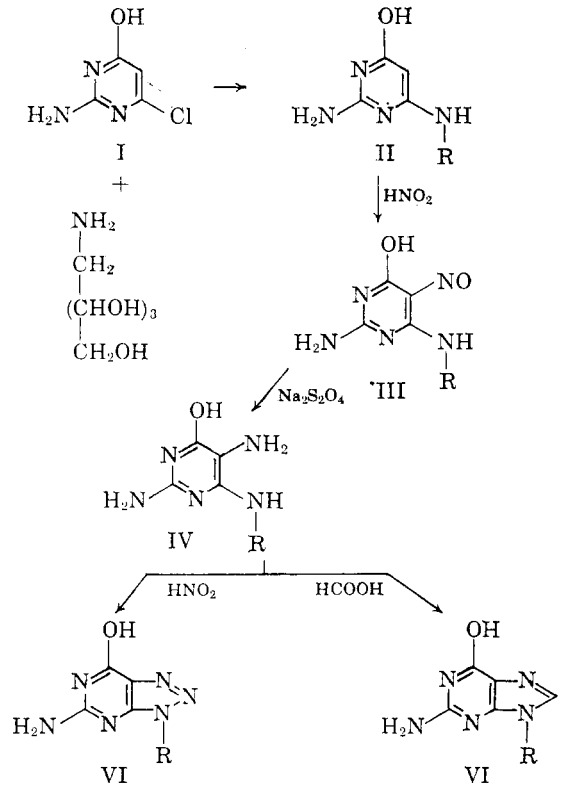
The biological transformation of a ribosyl derivative to the corresponding deoxyribosyl derivative might involve the intermediate formation of a ribityl derivative, rearrangement of which would then form the deoxy compound. Accordingly, 9-ribitylguanine was prepared as a possible biologically active intermediate, and an analog, 8-aza-9-ribitylguanine, was also prepared as a possible metabolic antagonist. During the course of this work, an enzyme requiring the vitamin B_{12} coenzyme has been observed to carry out a comparable intramolecular oxidation-reduction reaction on synthetic substrates—*e.g.*, cell-free extracts of *Aerobacter aerogenes* converted 1,2-propanediol and ethylene glycol to propionaldehyde and acetaldehyde, respectively.[2] These derivatives were synthesized through the indicated sequence of reactions (R = ribityl).

2 - Amino - 4,6 - dihydroxypyrimidine, prepared through the condensation of diethylmalonate and guanidine,[3] was treated with phosphorus oxychloride to form 2-amino-4,6-dichloropyrimidine.[4] Hydrolysis using one equivalent of sodium hydroxide in ethanol yielded 2-amino-4-chloro-6-hydroxypyrimidine[5] (I) which was subsequently condensed with ribitylamine[6] to form 2-amino-6-hydroxy-4-ribitylaminopyrimidine (II). Nitrosation of II



yielded the desired nitroso derivative III, which was then reduced with sodium hydrosulfite to produce an intermediate which proved to be difficult to isolate in a chemically pure state. Thus, the reduced reaction product, IV, was used directly without further purification to react with formic acid to form the 9-ribitylpurine V; or with nitrous acid to form the corresponding 8-aza-9-ribitylpurine VI.

9-Ribitylguanine possesses some activity in replacing purines as reversing agents for sulfonamide toxicity in *Lactobacillus arabinosus*, but it was ineffective in replacing guanine as a reversing agent for azaguanine toxicity. The ribityl derivative was not converted to the deoxyribosyl derivative by extracts of either *Escherichia coli* 9723 or *Lactobacillus leichmannii* ATCC 7830; however, these results do not preclude the possibility that a phosphorylated ribityl derivative might be an intermediate in the conversion of ribosyl to deoxyribosyl derivatives.

EXPERIMENTAL[7]

2-Amino-6-hydroxy-4-ribitylaminopyrimidine (II). A solution of 16.5 g. of 2-amino-4-chloro-6-hydroxypyrimidine and

(1)(a) After this manuscript had been accepted for publication an article appeared which described the syntheses of these analogs using a slightly different synthetic approach [J. Davoll and D. D. Evans, *J. Chem. Soc.*, 5041 (1960)]. (b) Predoctoral Fellow (CF-10,027) National Cancer Institute, United States Public Health Service.

(2) R. H. Abeles and H. A. Lee, Jr., *J. Biol. Chem.*, **236**, PC 1 (1961).

(3) A. Michael, *J. prakt. Chem.*, **49**, 35 (1894).

(4) E. Büttner, *Ber.*, **36**, 2227 (1903).

(5) H. S. Forrest, R. Hull, H. J. Rodda, and A. R. Todd, *J. Chem. Soc.*, 3 (1951).

(6) G. F. Maley and G. W. E. Plaut, *J. Biol. Chem.*, **234**, 641 (1959).

(7) All melting points are uncorrected. The authors are indebted to Mrs. J. Humphries for assistance with the microbial assays, and to J. D. Glass and C. Hedgcoth for the elemental analyses. Repeated attempts to obtain better nitrogen analyses failed; however, these results are in accord with those previously reported by other investigators[8] and are presumably due to the difficulty of burning these nitrogeneous compounds under the typical Dumas conditions. The ultraviolet spectra were determined using a Beckman DK-2 recording spectrophotometer.