[COMMUNICATION NO. 1673 FROM THE KODAK RESEARCH LABORATORIES]

β-Keto Acetals. I. Synthesis of Pyrazoles and Pyrimidines and the Steric Inhibition of Resonance in 5-Alkyl-1-*p*-nitrophenylpyrazoles

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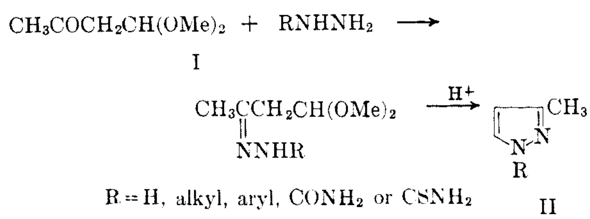
β-Ketobutyracetal (4,4-dimethoxy-2-butanone) and its analogs react readily with hydrazines and semicarbazides to produce pyrazoles, and with guanidine, urea, and thiourea to yield pyrimidines. The reaction with hydrazines can be carried out in two steps, when necessary, to produce an isomerically pure product. Other existing pyrazole syntheses cannot be so controlled. The two isomeric β-keto acetals prepared from the product of the Claisen condensation between ethyl formate and 2-butanone have been identified *via* the pyrazoles formed from the acetals with *p*-nitrophenylhydrazine. The structures of the 1-*p*-nitrophenylpyrazoles were determined *via* their ultraviolet spectra. Steric inhibition of resonance in the 5-alkyl-1-*p*-nitrophenylpyrazoles is shown by a marked hypsochromic shift of λ_{max} in the ultraviolet spectra, whereas an alkyl group in the 4-position of the pyrazole ring has the expected mildly bathochromic effect.

Recent developments[1] of convenient methods of β-keto acetal synthesis have aroused considerable interest[2,3] in these compounds as intermediates of real value in organic synthesis, particularly for perfumes and drugs.

In the past, three different types of compounds have been used for the synthesis of the heterocycles to be reported here; these are: (a) 2-chlorovinyl ketones[4,5] which are unstable and are lachrymators and vesicants, (b) ethynyl ketones[6] which are strong lachrymators and sternutators, and (c) sodium formyl ketones. The last-named, although rather easily accessible,[7] are hygroscopic compounds of poor stability which must usually be prepared just prior to use. The β-keto acetals prepared from them in good yield have none of these disadvantages; furthermore, they are unique in their ability to yield isomerically pure products (*i.e.*, exclusively 1,3-isomers) by reaction, for example, in the following manner:



R = H, alkyl, aryl, $CONH_2$ or $CSNH_2$

Arylhydrazines react with β-ketobutyracetal (4,4-dimethoxy-2-butanone) (I) in the presence of acidic catalysts to produce exclusively the 1-aryl-3-methylpyrazoles. Sodium formylacetone is reported to give a mixture of the 3- and 5-methyl isomers,[8] as does β-ketobutyracetal when a basic catalyst is used. In the absence of added acid or base, the intermediate arylhydrazone can be isolated and subsequently converted to the pyrazole by treatment with acid or with heat alone.

With certain higher acetals, complications are encountered, as in the case of the acetal derived from 2-butanone, which consists of a mixture of the two products, III and IV, which are difficult to separate completely.[9]

$CH_3COCH(CH_3)CH(OCH_3)_2$ (III) $CH_3CH_2COCH_2CH(OCH_3)_2$ (IV)

$CH_3CH_2COCH(CH_3)CH(OCH_3)_2$ (VIII)

By fractional distillation in an efficient column, the isomers were separated into two distinct fractions; the lower-boiling one tentatively was selected as having the branched structure (III). Confirmation of this was found by conversion of each isomeric acetal into the 1-*p*-nitrophenylpyrazoles and comparison of the ultraviolet spectra of the latter with the spectra of closely related homologs of definite structure.

The straight-chain acetal (IV), unlike β-ketobutyracetal, quite unexpectedly produced two isomeric pyrazoles, the 3-ethyl- (V) and 5-ethyl-1-*p*-nitrophenylpyrazole (VI), whereas from III, only a single isomer, *i.e.*, 3,4-dimethyl-1-*p*-nitrophenylpyrazole (VII), was isolated. Attempts to avoid formation of VI by use of the two-step method met with difficulty in the isolation of the hydrazones, and were not pursued further. The acetal derived from diethyl ketone, *i.e.*, 1,1-dimethoxy-2-methyl-3-pentanone (VIII), also yielded two derivatives:

(1) Hata, Yamada, Iwao, Kato, Sugimoto, and Inouye, *J. Pharm. Soc. Japan*, **69**, 477 (1949); *Chem. Abstr.*, **44**, 3455 (1950).

(2) Nesmeyanov, Kochetkov, and Rybinskaya, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 395 (1951); *Chem. Abstr.*, **46**, 3007 (1952).

(3) Franke, Kraft, Tietjen, and Weber, *Chem. Ber.*, **86**, 797 (1953).

(4) Kochetkov, Nesmeyanov, and Semenov, *Izvest. Akad. Nauk SSSR, Otdel. Khim. Nauk*, 87 (1952); *Chem. Abstr.*, **47**, 2167 (1953).

(5) Nesmeyanov and Kochetkov, *Doklady Akad. Nauk SSSR*, **77**, 65 (1951); *Chem. Abstr.*, **46**, 497 (1952).

(6) Bowden and Jones, *J. Chem. Soc.*, 953 (1946).

(7) Von Auwers and Hollmann, *Ber.*, **59**, 1282 (1926).

(8) Claisen and Roosen, *Ber.*, **24**, 1889 (1891).

(9) Royals and Brannock, *J. Am. Chem. Soc.*, **76**, 1180 (1954).

3-ethyl-4-methyl- (IX) and 5-ethyl-4-methyl-1-*p*-nitrophenylpyrazole (X).

The ultraviolet spectrum of the higher-melting pyrazole (V) from IV was practically identical with that of 3-methyl-1-*p*-nitrophenylpyrazole, thus indicating it to be the 3-ethyl compound. Likewise, the spectrum of the supposed VII coincided nicely with that of the higher-melting and predominating isomer (IX) from VIII. As further discussion will show, the most positive evidence for the identity of IX as the 3-ethyl-4-methyl compound lies in its high value of λ_{max}, and with this granted, there is no doubt that VII is indeed 3,4-dimethyl-1-*p*-nitrophenylpyrazole.

The lower-melting 5-ethylpyrazole (VI) from IV showed a surprisingly large hypsochromic shift and reduced intensity (λ_{max} 299 mμ; log ϵ 4.03), as compared with the 3-ethyl compound (λ_{max} 323 mμ; log ϵ 4.23). This effect most certainly must be attributed to a steric inhibition of resonance caused by interference of the 5-ethyl group with the phenyl ring, with a resulting decrease in the coplanarity of the molecule. A similar effect, but not so large, has been reported in the case of 2-ethyl- and 2-methylbiphenyl.[10] Likewise, the 5-ethyl-4-methyl compound (X) (λ_{max} 306 mμ; log ϵ 4.03) shows a similar and still larger effect compared with the 3-ethyl-4-methyl isomer (IX) (λ_{max} 335 mμ; log ϵ 4.28); this enhanced inhibition is undoubtedly due to the crowding of the 5-ethyl group by the 4-methyl group, pushing it still closer to the sphere of the phenyl ring. Further confirmation of the steric effect of an alkyl group in the 5-position of the pyrazole ring was found in the known 3,5-dimethyl-1-*p*-nitrophenylpyrazole (λ_{max} 311 mμ; log ϵ 4.07). Here, the effect of the 5-methyl group is somewhat less than that of ethyl; this again corresponds to the results in the biphenyl series.

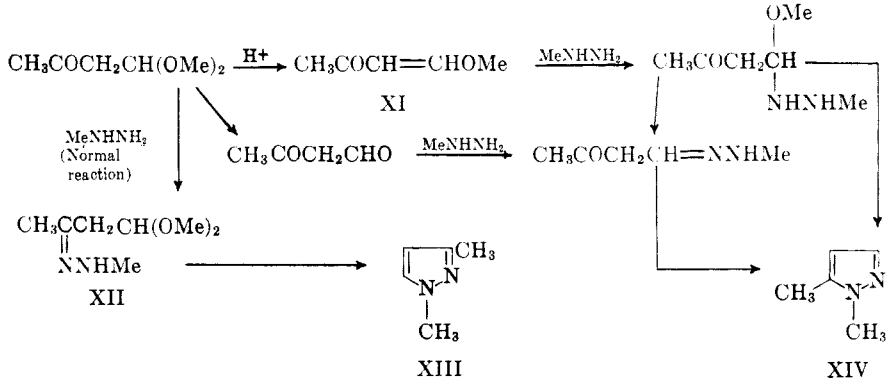
The hypsochromic shift of λ_{max} in the ultraviolet spectra is noticeably greater with these compounds than in the corresponding biphenyl series, where λ_{max} is reduced from 249 mμ to 233 mμ by one *o*-ethyl substitution. This is not unexpected, in view of the generally shorter bond length of C—N, compared with C—C. On the other hand, the different geometry of the 6–5 *versus* the 6–6 ring system would tend to have the opposite effect, that of moving the ethyl group further from the sphere of the phenyl ring.

A methyl group in the 4-position of the pyrazole ring exerts the normal bathochromic effect of this auxochromic group, and the same is probably true of substitution in the 3-position, although no proof was possible with the present compounds. On the other hand, substitution on the side chain (*e.g.*, methyl to ethyl) has no effect on λ_{max}.

All other data accumulated, *e.g.*, the secondary maxima in the ultraviolet, the infrared spectra, melting points, and solubilities, fall in line with the relationships established by the ultraviolet spectra; thus, there is every reason to believe that the above structural assignments are correct.

The steric effect of a substituent in the 5-position of the pyrazole ring in the 1-phenylpyrazoles has its counterpart in *ortho* substitution of the phenyl ring, as exemplified in 1-(2,6-dichloro-4-nitrophenyl)-3-methylpyrazole. Here the effect on the ultraviolet spectrum of two *ortho* substituents in the phenyl ring (λ_{max} 297 mμ; log ϵ 3.72) is, as expected, considerably greater than that due to the lone ethyl group in 5-ethyl-4-methyl-1-*p*-nitrophenylpyrazole (X).

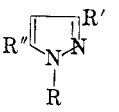
Alkylhydrazines differ somewhat from the arylhydrazines in their reactions with β-ketobutyracetal; for example, methylhydrazine sulfate yields a mixture of 1,3- and 1,5-dimethylpyrazole (XIII and XIV). This may be due to a slower rate of reaction of the alkylhydrazines so that the following can occur. The formation of XI from β-ketobutyracetal has been found to occur readily under acid catalysis.



Von Auwers and Hollmann[7] also obtained a mixture of the two dimethylpyrazoles with sodium formylacetone ($CH_3COCH{=}CHONa$), and attempted, without success, to avoid formation of XIV by use of the ether (XI) or the corresponding benzoate. This difficulty has been readily circumvented by means of the acetal, with which condensation of the free methylhydrazine took place normally at room temperature, to yield the hydrazone

(10) Braude, Sondheimer, and Forbes, *Nature*, **173**, 117 (1954).

TABLE I
PYRAZOLES FROM β-KETOBUTYRACETAL[a]



R	R′	R″	Method of Synthesis	Yield, %	M.P., °C. B.P., °C.	Mm.	n_D^{25}	Analyses Calc'd C	H	N	Found C	H	N
C_6H_5	CH_3	H	A	70	250–253	760							
C_6H_5	CH_3	H	B[b]	52	120–122	9	1.5875	75.9	6.4	17.7	75.6	6.7	17.0
C_6H_5	H	CH_3											
C_6H_5	CH_3	H	C[c]	47	35.5–36.5		1.5873						
p-$NO_2C_6H_4$	CH_3	H	A	68	165.5								
			D[d]	78	165.5								
p-$NH_2C_6H_4$	CH_3	H	[e]	94	98			69.3	6.4	24.3	69.6	6.1	24.0
$CONH_2$	CH_3	H	A	85	123.5–124.5[f]			48.0	5.6	33.6	48.2	5.5	33.5
			D[g]	37	122.5–124								
$CSNH_2$	CH_3	H	A	53.5	132.5–133.5			42.6	5.0	29.7	43.6	5.4	29.0[h]
			D[i]	23									
H	CH_3	H	A	86	200–202	760	1.4955						
CH_3	CH_3	H	A	68	141–150	760	1.4713–1.4745						
CH_3	H	CH_3											
CH_3	CH_3	H	D (details given)	61	143–145		1.4734						

[a] John Cawley, of the Research Laboratories of Distillation Products Industries, obtained a pyrazole of m.p. 128° from the reaction of β-ketobutyracetal and 2,4-dinitrophenylhydrazine in alcohol and concentrated hydrochloric acid [b] Crystallization of the distillate from ligroin gave the 1,3-isomer, m.p. 35–36° [Knorr, *Ann.*, **238**, 203 (1887)]. Treatment with methyl iodide gave the *methiodide* of the 1,5-isomer, m.p. 256.5° [Stoermer, *Ber.*, **40**, 484 (1907)]. [c] The intermediate phenylhydrazone, m.p. 67–68°. [d] The intermediate *p*-nitrophenylhydrazone, m.p. 133–134°. [e] By reduction of the nitro compound in a Parr shaker at 40 p.s.i., using Raney nickel catalyst. [f] This has a double melting point, with partial melting at 94–96°; the reported value [von Auwers and Daniel, *J. prakt. Chem.*, **110**, 235 (1925)] of 127–128° was never observed. [g] The intermediate semicarbazone, m.p. 131–133°. [h] Repeated recrystallization from ethanol or benzene failed to give an analytically pure compound. [i] The intermediate *thiosemicarbazone*, m.p. 122–123°.

(XII). Cyclization then also proceeded normally in the presence of aqueous acid to give 1,3-dimethylpyrazole in 61% yield. The nature of the products in these reactions was determined by the picrates.

There has been considerable confusion in the literature concerning the identity of the two isomeric dimethylpyrazoles just mentioned. The most recent article in which an attempt was made to assign correct structures[11] has the isomer producing a picrate of m.p. 172°, identified as 1,5-dimethylpyrazole (the picrate of the second isomer melts at 136°). This is incorrect, for there is little doubt that the product of the two-step reaction, which yields the higher-melting picrate, is 1,3-dimethylpyrazole.

Semicarbazide and *thiosemicarbazide* give the expected homogeneous products (II, R = $CONH_2$ and $CSNH_2$). *Aminoguanidine*, reacting as a hydrazine, readily yielded the bis(guanylhydrazone), but, unlike the analogous case of acetylacetone,[12] the product was not readily converted to the pyrazole [II, R = C(=NH)NH_2]. A similar difference in ease of cyclization has been noted between the anils of acetylacetone and acetylacetaldehyde. *Guanidine*, *urea*, and *thiourea* react with β-keto acetals to produce pyrimidines; for example, guanidine and β-ketobutyracetal give 2-amino-4-methylpyrimidine, a key intermediate in the synthesis of sulfamerazine. There are three possible methods of effecting this reaction: (1) by acid catalysis (36% yield);[13] (2) by basic catalysis (70% yield); and (3) by azeotropic distillation of water from the reaction in xylene between the keto acetal and guanidine carbonate (96% yield). Of the various methods[14] available for the synthesis of 2-amino-4-methylpyrimidine, the last-named would appear to be the most convenient.

β-Ketobutyracetal also reacts with aniline to produce an anil, $CH_3COCH{=}CHNHC_6H_5$, of a type useful in quinoline-type syntheses.[15]

EXPERIMENTAL

PYRAZOLES

These were prepared by one or more of the following general procedures, although slight modifications were necessary, on occasion, for certain of the compounds. Physical properties and other data are recorded in Table I.

(11) Von Auwers and Hollmann, *Ber.*, **59**, 601 (1926).

(12) Thiele and Draille, *Ann.*, **302**, 293 (1898).

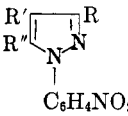
(13) This yield is not typical for the acid-catalyzed reaction, but was obtained in a small-scale experiment performed as described in the Experimental section. Dr. Charles Benton, of the Research Laboratories of Distillation Products Industries, has obtained yields of 78% in this reaction, using a sulfuric acid catalyst.

(14) (a) Okeda and Teraishi, Japanese Patent 179,747; *Chem. Abstr.*, **46**, 1595 (1952); Okeda, Teraishi, and Hinoki, Japanese Patent 2883; *Chem. Abstr.*, **47**, 2778 (1953); (b) Ishikawa and Kano, *J. Pharm. Soc. Japan*, **71**, 80 (1951); *Chem. Abstr.*, **45**, 8536 (1951); (c) Andersag and Mauss, U. S. Patent 2,570,087; *Chem. Abstr.*, **46**, 5093 (1952); (d) Prevost, German Patent 812,315; *Chem. Abstr.*, **47**, 1195 (1953); (e) Tabuchi and Maemoto, Japanese Patent 181,370; *Chem. Abstr.*, **46**, 9621 (1952).

(15) Johnson, Woroch, and Mathews, *J. Am. Chem. Soc.*, **69**, 570 (1947).

TABLE II

1-*p*-NITROPHENYLPYRAZOLES



β-Ketoacetal Precursor	No. in Text	R	R′	R″	M.P., °C.	Analysis Calc'd C	Calc'd H	Calc'd N	Found C	Found H	Found N	Ultraviolet Absorption, λ_{max} (log ε) in MeOH	
4,4-Dimethoxy-2-butanone		CH_3	H	H	165.5[a]							323 (4.25)	227 (3.88)
1,1-Dimethoxy-3-pentanone	V	C_2H_5	H	H	121	60.8	5.1	19.35	60.8	5.1	19.6	323 (4.23)	224 (3.89)
1,1-Dimethoxy-3-pentanone	VI	H	H	C_2H_5	112	60.8	5.1	19.35	61.1	5.2	19.6	299 (4.03)	216 (3.98)
4,4-Dimethoxy-3-methyl-2-butanone	VII	CH_3	CH_3	H	160	60.8	5.1	19.35	61.2	5.3	19.1	335 (4.25)	232 (3.84)
1,1-Dimethoxy-2-methyl-3-pentanone	IX	C_2H_5	CH_3	H	138	62.3	5.7	18.2	62.2	5.9	18.2	335 (4.28)	232 (3.89)
	X	H	CH_3	C_2H_5	77–78.5	62.3	5.7	18.2	62.3	5.8	18.5	306 (4.03)	217 (4.05)[b]
Pentan-2,4-dione		CH_3	H	CH_3	101–102.5[c]							311 (4.07)	220 (4.04)
1-(2,6-Dichloro-4-nitrophenyl)-3-methylpyrazole[d]					145–146	44.2	2.6	15.4	44.6	2.9	15.8	297 (3.72)	

[a] Lit. value 166° [Knorr, *Ann.*, **279**, 221 (1894)]. [b] This is a shoulder on a higher peak at λ_{max} 205 mμ (log ε 4.14). [c] Lit. value 102° [Morgan and Drew, *J. Chem. Soc.*, **119**, 620 (1921)]. [d] The author is indebted to A. Loria, of these laboratories, for the sample of 2,6-dichloro-4-nitrophenylhydrazine used.

A. By acid catalysis. An aqueous solution of equivalent amounts of the β-keto acetal and an acid salt of the hydrazine derivative (with the aryl hydrazines, 50% aqueous ethanol is preferable) was heated briefly on a steam-bath and allowed to cool. (In the reaction with semicarbazide hydrochloride to form 3-methylpyrazole-1-carbonamide, the temperature was kept below 45° to avoid decomposition to 3-methylpyrazole.) Solid products were separated by filtration, while liquids and low-melting solids were extracted with ether, dried, and distilled. The more water-soluble products, like 3-methylpyrazole, were forced out of the water layer with potassium hydroxide.

B. By base catalysis. A methanol solution containing equivalent amounts of the β-keto acetal and the hydrazine derivative was heated with sodium methoxide under reflux for two hours. The solution was diluted with benzene, filtered, washed with water, and distilled.

C. By the hydrazone and heat. The intermediate hydrazone was readily obtained by heating equivalent amounts of the β-keto acetal and the free base in alcohol. The hydrazone, after isolation, was heated under nitrogen until methanol ceased to distill, and the product was isolated in the usual way.

D. By the hydrazone and acid. Treatment of the hydrazone in ethanol with a few drops of hydrochloric acid and brief heating sufficed to form the pyrazole which was isolated as in *A*.

PYRAZOLES FROM ACETALS DERIVED FROM 2-BUTANONE

The crude reaction product from 2-butanone[1] was treated with methanolic sodium methoxide, thereby converting any β-ketovinyl ethers to the β-keto acetals. Fractional distillation of the product yielded two distinct fractions which were subsequently identified by their pyrazole derivatives as follows:

(1) 4,4-Dimethoxy-3-methyl-2-butanone, b.p. 59–61° (9 mm.); n_D^{25} 1.4167.

(2) 1,1-Dimethoxy-3-pentanone, b.p. 69° (11 mm.); n_D^{25} 1.4184.

Each fraction was treated with *p*-nitrophenylhydrazine hydrochloride as in procedure *A*, and the resulting 1-*p*-nitrophenylpyrazoles were separated by fractional recrystallization from ethanol to give three of the four possible isomers. These are shown in Table II, along with homologous compounds prepared in a similar fashion.

1,3-Dimethylpyrazole. The usual method of pyrazole synthesis (procedure *A*) gave a 68% yield of a mixture of the 1,3- and 1,5-dimethylpyrazoles, b.p. 141–150°; n_D^{25} 1.4717–1.4749. The crude picrates (m.p. 125–146°) obtained from this mixture were separated by fractional crystallization into those of the 1,5-compound (m.p. 132°) and the 1,3-isomer (m.p. 171°). The pure 1,3-dimethylpyrazole was obtained as follows:

Methylhydrazine (3 g.) was added, dropwise, with cooling, to 8.6 g. of 4,4-dimethoxy-2-butanone. The mixture was allowed to warm to 40°, and was heated on the steam-bath for ten minutes to complete formation of the methylhydrazone. To 5.5 g. of the crude hydrazone in 5 ml. of water was added 5.3 g. of 6 *N* hydrochloric acid (solution then strongly acid), and the solution was heated for 20 minutes on the steam-bath. Addition of 2.4 g. of 50% aqueous sodium hydroxide produced the pyrazole which was isolated as before. The over-all yield of 1,3-dimethylpyrazole was 61%, b.p. 143–145°; n_D^{25} 1.4734. The crude picrate (from ether) melted at 157–165° and, after a single recrystallization, gave the pure 1,3-dimethylpyrazole picrate, m.p. 170–171°.

Butan-1,3-dione-bis(guanylhydrazone). A solution of 26.4 g. of aminoguanidine sulfate, 13.2 g. of 4,4-dimethoxy-2-butanone, and 3.5 ml. of 6 *N* sulfuric acid in 40 ml. of water was heated on the steam-bath for one hour. The product, butan-1,3-dione-bis(guanylhydrazone) sulfate, was obtained in a 20.8-g. (70%) yield. Recrystallization from water yielded a pure product of m.p. 197.5° (dec.).

Anal. Calc'd for $C_6H_{14}N_8 \cdot H_2SO_4$: C, 24.3; H, 5.4; N, 37.8; S, 10.8. Found: C, 24.3; H, 5.8; N, 36.3; S, 10.5.

The same product was obtained when one-half the above amount of aminoguanidine sulfate was used. Attempts to cyclize this product to the pyrazole, or to obtain the pyrazole directly, by the usual methods, were unsuccessful.

2-AMINO-4-METHYLPYRIMIDINE

A. By action of heat. A mixture of 13.2 g. of 4,4-dimethoxy-2-butanone, 9.0 g. of guanidine carbonate, and 50 ml. of

xylene was heated under reflux using a water separator until the water-methanol phase was completely removed (2–3 hours). The solution was filtered and allowed to cool, yielding 10.5 g. (96%) of pale tan crystals of 2-amino-4-methylpyrimidine[16]; m.p. 156.5–157.5°.

B. By alkaline catalysis. A mixture of 3.2 g. of guanidine hydrochloride, 3.6 g. (100% excess) of sodium methoxide, and 25 ml. of dry methanol was warmed for a few minutes and filtered. To the filtrate was added 4.4 g. of 4,4-dimethoxy-2-butanone, and the solution was boiled under reflux for ten minutes, and then most of the methanol was allowed to distill. The residue was extracted with 100 ml. of benzene, using Nuchar to give 2.2 g. (61%) of colorless needles; m.p. 156–156.5°.

C. By acid catalysis. When equivalent amounts of guanidine hydrochloride and 4,4-dimethoxy-2-butanone were heated in the minimum of water for one-half hour, an impure product, m.p. 153–158°, was obtained in but 36% yield.

4-Methyl-2-pyrimidinol. To a solution of 18 g. of urea in 200 ml. of ethanol was added 40 g. of β-ketobutyracetal, followed by the gradual addition of 60 ml. of concentrated hydrochloric acid. After 20 hours, the golden yellow crystals of hydrochloride were filtered and washed with alcohol. Yield, 35 g. (79%); m.p. 240° in a preheated bath. The literature[17] reports 241°.

Anal. Calc'd for $C_5H_7ClN_2O$: N, 19.1. Found: N, 19.3.

4-Methyl-2-pyrimidinethiol. In a similar manner, using thiourea, 29.6 g. (91%) of the bright yellow hydrochloride was produced. It was found difficult to obtain a pure sample of this product by recrystallization, since, in solution, it very soon forms a highly insoluble polymer. By dissolving it in water at 25° and reprecipitating with one-third volume of concentrated hydrochloric acid, a sample of m.p. 259° (preheated bath) was obtained.

Anal. Calc'd for $C_5H_7ClN_2S$: C, 37.0; H, 4.3; N, 17.2. Found: C, 36.4; H, 4.3; N, 18.0.

4-Phenylamino-3-buten-2-one. A mixture of 26.4 g. of 4,4-dimethoxy-2-butanone and 18.6 g. of aniline was heated first on the steam-bath, and then gently with a free flame until methanol ceased to distill. Distillation *in vacuo* gave 13.7 g. of crude product, b.p. 85–115° (0.3 mm.), which solidified in the receiver. Trituration with ether yielded 10.8 g. (34% yield) of nearly colorless solid of m.p. 85–87°. Further purification by recrystallization from dilute alcohol yielded the pure anil[18]; m.p. 91.5–92.5°.

Acknowledgment. The author is indebted to three members of these laboratories for the data furnished by their groups: D. Ketchum (microanalysis); D. W. Stewart (infrared spectra); and E. E. Richardson (ultraviolet spectra).

Note added in proof: An excellent review article has just appeared which describes numerous reactions of β-ketobutyracetal [Franke and Kraft, *Agnew. Chem.*, **67**, 395 (1955)].

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(16) Jensen, Falkenberg, Thorsteinsson, and Lauridsen, *Dansk. Tids. Farm.*, **16**, 141 (1942); *Chem. Abstr.*, **38**, 3263 (1944).

(17) Matsukawa and Ohta, *J. Pharm. Soc. Japan*, **69**, 489 (1949); *Chem. Abstr.*, **44**, 3455 (1950).

(18) Thielepape, *Ber.*, **55**, 127 (1922); [see also Bowden, Braude, Jones, and Weedon, *J. Chem. Soc.*, 45 (1946)].