Anal. Calcd for $C_{10}H_{15}N$: C, 80.48; H, 10.13; N, 9.38. Found: C, 80.48; H, 10.06; N, 9.26.

3-Prenyl-3-cyanocyclohexene (2c) has bp (Kugelrohr) 100–150 °C (5 torr): IR (CCl_4) 2225 cm^{-1}; NMR (CCl_4) δ 6.05–5.30 (m, 2), 5.40–5.05 (t, 1, J = 8 Hz with fine splitting from methyl groups), 2.40–2.10 (br d, 2, $RCH_2CH{=}C(CH_3)_2$, J = 8 Hz), 2.20–1.50 (m, 12, broad singlets centered at 1.80 and 1.67 for two methyl groups); mass spectrum (70 eV) m/e (rel intensity) 175 (9), 108 (7), 107 (75), 106 (9), 80 (11), 79 (9), 69 (100), 41 (45).

Anal. Calcd for $C_{12}H_{17}N$: C, 82.23; H, 9.78; N, 7.99. Found: C, 82.09; H, 9.70; N, 7.95.

Methyl 3-methylcyclohexene-3-carboxylate has bp 90–92 °C (32 torr): IR (CCl_4) 1733 cm^{-1}; NMR (CCl_4) δ 5.65–5.50 (m, 2), 3.60 (s, 3, OCH_3), 2.30–1.30 (m, 6), 1.20 (s, 3, CH_3); mass spectrum (70 eV) m/e (rel intensity) 154 (9.6), 121 (10), 94 (11), 93 (100), 92 (14).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.25; H, 9.25.

Methyl 3-Methylcyclopentene-3-carboxylate (5). To a solution prepared from 4.40 g (18 mmol) of triphenylmethane and 200 mg (25 mmol) of lithium hydryde in 45 mL of dry THF was added a solution of 2.00 g (16.8 mmol) of cyclopentene carboxylic acid in 10 mL of THF. The mixture was heated at reflux until evolution of H_2 ceased (20 min) then cooled in an ice–salt bath while 10 mL of 1.8 M n-butyllithium in hexane (18 mmol) was added (syringe). The resulting deep red mixture was heated at 35 °C for 1 h, cooled to 0 °C, quenched with 3 mL of methyl iodide, and stirred at 30 °C for 3 h. After the usual extraction the acidic product was taken up in ether and treated with an ethereal solution of diazomethane to give (after solvent removal) 1.64 g of oil from which 1.12 g (48%) of **5** was separated by preparative TLC (silica gel): IR (CCl_4) 1735 cm^{-1}; NMR (CCl_4) δ 5.80–5.50 (m, 2), 3.63 (s, 3, OCH_3), 2.52–2.20 (m, 3), 1.92–1.45 (m, 1), 1.27 (s, 3, CH_3); mass spectrum (70 eV) m/e (rel intensity) 140 (4.9), 81 (100).

Anal. Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.42; H, 8.86.

Dimeric product 6[8] (TLC isolation) has: IR (CCl_4) 1735, 1725 cm^{-1}; NMR (CCl_4) δ 5.75–5.20 (m, 2), 3.58 (s, 3, OCH_3), 3.53 (s, 3, OCH_3), 2.60–1.35 (m, 11), 1.20 (s, 3, CH_3); mass spectrum (70 eV) m/e 266 (1), 234 (6), 208 (8), 207 (52), 206 (23), 193 (8), 175 (17), 147 (17), 146 (100), 145 (13), 133 (15), 126 (52), 125 (17).

Methyl 1-methyl-2(*N,N*-diisopropyl)aminocyclopentane carboxylate (7) (TLC isolation) has: IR (CCl_4) 1725, 1714 cm^{-1}; NMR (CCl_4) δ 3.56 (s, 3, OCH_3), 3.20–2.60 (m, 3), 2.30–1.30 (m, 6), 1.18 (s, 3, CH_3), 0.96 (d, 12, J = 6.5 Hz); mass spectrum (70 eV) m/e (rel intensity) 242 (3.2), 241 (21), 226 (26), 198 (17), 141 (13), 140 (100), 98 (67).

Anal. Calcd for $C_{14}H_{27}O_2N$: C, 69.66; H, 11.28; N, 5.80. Found: C, 69.86; H, 11.11; N, 5.92.

Registry No.—**1**, 1855-63-6; 1 anion, 68317-67-9; **2a**, 68317-68-0; **2b**, 68317-69-1; **2c**, 68317-70-4; **3a**, 68317-71-5; **3b**, 68317-72-6; **5**, 68317-73-7; **6**, 68317-74-8; **7**, 68317-75-9; methyl 3-methylcyclohexene-3-carboxylate, 68317-76-0; cyclopentenecarboxylic acid, 1560-11-8; 1-methyl-2-cyclopentene carboxylic acid, 68317-77-1.

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(8) An insufficient quantity of **6** was isolated for complete characterization by combustion analysis.
(9) NMR spectra were recorded with a Perkin-Elmer R-32 (90 MHz) spectrometer using Me_4Si as an internal standard. Mass spectra were recorded using a Hitachi RMU-6 mass spectrometer. Elemental analyses were determined by Bernhardt Microanalytisches Laboratorium, Elbach über Engelskirchen, West Germany.

Improved Synthesis of 3,4-Dihydroxyphenylpyruvic Acid[1]

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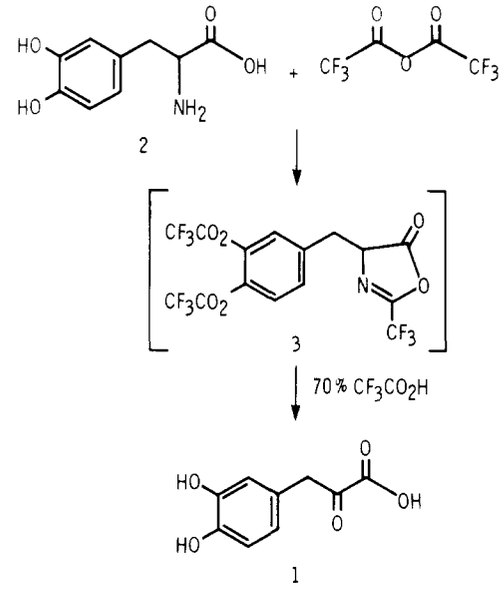
Several lines of research[2,3] in our laboratory prompted an investigation of a more facile synthesis of 3,4-dihydroxyphenylpyruvic acid (**1**). Since a previously reported synthetic procedure[4,5] proved to be unsatisfactory in our hands, we attempted to exploit Weygand's observation[6] that the hydrolysis of trifluoromethyloxazolones produced pyruvic acids. Another attractive feature of this approach is the fact that oxazolones are readily available from α-amino acids which in turn can be obtained commercially with various isotopic labels. Isotopically labeled phenylpyruvic acids are not commercially available.

We have found that hydrolysis of the putative trifluoromethyloxazolone intermediate (**3**) in 70% aqueous trifluoroacetic acid at room temperature produced **1** in 87% yield. The product (**1**) precipitated as it was formed and was isolated by filtration. This procedure avoids conditions known to be detrimental to the stability of **1**, i.e., exposure to base and oxygen, especially when it is in solution. Undistilled **3** contains incompletely reacted amino acid which eventually contaminates the product with the *N*-trifluoroacetyl derivative of **2** if the distillation step is omitted. An overall yield of 69% of **1**



from **2** was realized. The crystalline solid (**1**) is quite stable when stored at 4 °C but slowly decomposes at room temperature.

Experimental Section

Melting points were determined on a Fisher-Johns block. Mass spectra were obtained with an LKB 9000 mass spectrometer while NMR were recorded on a Varian Associates A-60 NMR spectrometer using tetramethylsilane as an internal standard.

3,4-Dihydroxyphenylpyruvic Acid (1). A slurry of L-3,4-dihydroxyphenylalanine (**2**) (5 g, 2.5 mmol) in trifluoroacetic anhydride (26.3 g, 12.5 mmol) was stirred until completely dissolved. After the solution was refluxed for 24 h (bath temperature 85 °C), trifluoroacetic acid was removed by distillation and the residue vacuum distilled on a short path apparatus (140 °C (3 mm)) to give a light yellow oil. The distillate was taken up in 70% aqueous trifluoroacetic acid and allowed to stand at room temperature for 24 h. The resulting slurry was cooled to 4 °C and filtered, washing twice with 10 mL of cold H_2O. The filtrate (2.8 g of **1**) could be recrystallized from water

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for analytical samples, mp 190–192 °C dec (lit.[4] mp 192–193 °C), after drying in vacuo over P_2O_5. Mother liquors were combined, the solvent removed, and the residue recrystallized from 70% aqueous trifluoroacetic acid to give an additional 0.6 g of **1**, mp 187–192 °C dec. The pure compound (**1**) showed: mass spectrum (20 eV) *m/e* 196 (M^+, 38%), 150 (17%), 123 (100%), 122 (9%), 105 (3%), 94 (3%), 77 (10%); NMR (10% D_2O in $(CD_3)_2CO$) δ 6.45 (s, 1 H, β-H), 6.87 (d, J = 8 Hz, 1 H, H_5), 7.20 (dd, J = 8, 2 Hz, 1 H, H_6), 7.45 (d, J = 2 Hz, 1 H, H_2) (enol form); UV (MeOH) λ_{max} 307 nm (mixture of enol and keto tautomers).

Registry No.—1 keto form, 4228-66-4; 1 enol form, 68307-79-9; 2, 59-92-7; 3, 68307-80-2.

References and Notes

(1) This research was supported by National Science Foundation (GM 17957) and National Institutes of Health (5-TO1-HL-05672) grants.
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Pteridines. 46. Unequivocal Synthesis of 2,4-Diamino-6(5*H*)-pteridinone (4-Amino-4-deoxyxanthopterin) and Xanthopterin from 5,7-Diaminofurazano[3,4-*d*]pyrimidine[1,2]

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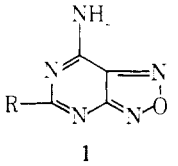
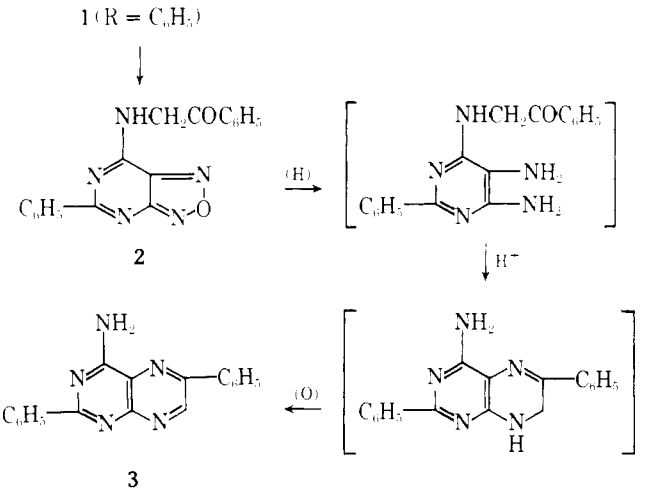
7-Aminofurazano[3,4-*d*]pyrimidines (**1**), which are readily prepared by lead tetraacetate oxidation of 4,6-diamino-5-



1

nitrosopyrimidines,[3] represent latent 4,5,6-triaminopyrimidines of considerable synthetic versatility. The 7-amino substituent (particularly when acylated) is remarkably reactive toward nucleophilic displacement reactions,[3,4] and the substituent thus introduced can be modified (e.g., by acylation) without incident. Reductive cleavage of the N–O–N linkage then generates a strongly nucleophilic 5-amino grouping which cyclizes with the newly introduced (and perhaps modified) adjacent substituent. The 6-amino group remaining from the reductive cleavage reaction is extruded as a substituent on the new fused heterocycle. In this way furazano[3,4-*d*]pyrimidines have been exploited as intermediates for the synthesis of adenines,[3,5] 4-aminopyrrolo[3,2-*d*]pyrimidines,[6] 4-amino-7-azapteridines,[7] and (in a few limited cases) 4-aminopteridines.[7] An example of the latter transformation is the unequivocal synthesis of 2,6-diphenyl-4-aminopteridine (**3**) from 5-phenyl-7-(benzoylmethylamino)-furazano[3,4-*d*]pyrimidine (**2**), prepared from 5-phenyl-7-aminofurazano[3,4-*d*]pyrimidine (**1**, R = C_6H_5) and aminoacetophenone, by reductive cleavage of the furazan ring, acid-catalyzed cyclization, and oxidation.

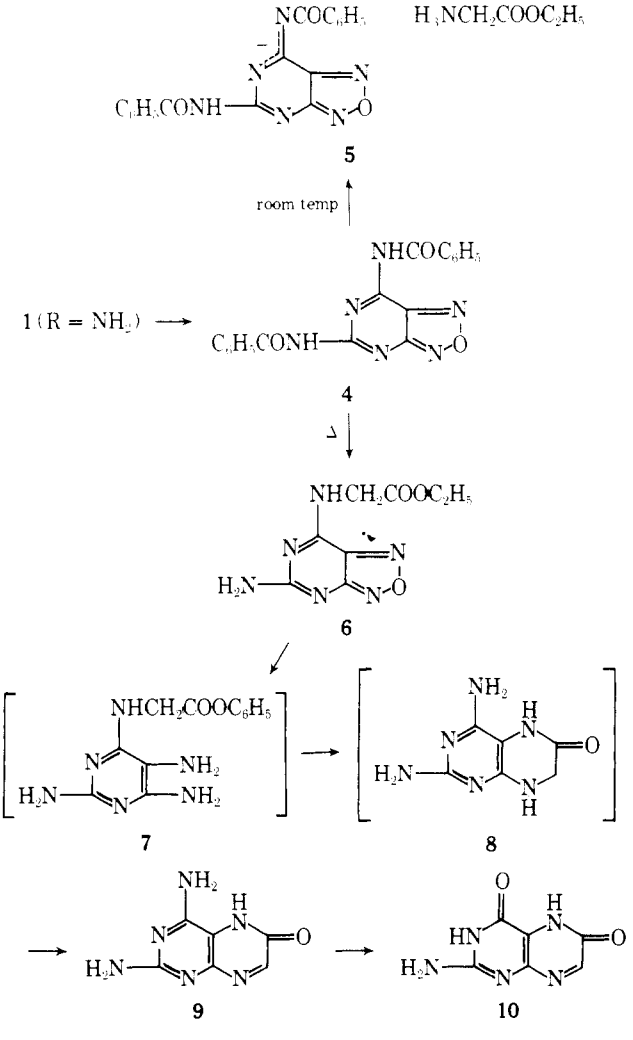
The present note describes an extension of this general synthetic method to the unequivocal synthesis of 4-amino-



2 **3**

4-deoxyxanthopterin (2,4-diamino-6(5*H*)-pteridinone) (**9**) and, by hydrolysis of the latter, a new synthesis of the naturally occurring insect pigment and antitumor agent xanthopterin (**10**).[8]

Fusion of 5,7-diaminofurazano[3,4-*d*]pyrimidine (**1**, R = NH_2) with benzoic anhydride at 200 °C gave 5,7-bis(benzoylamino)furazano[3,4-*d*]pyrimidine (**4**) in 91% yield. Although reaction of the latter intermediate with ethyl glycinate in THF at room temperature resulted only in the formation of a salt (**5**), heating a mixture of **4** and ethyl glycinate at 110 °C for 5 min resulted both in displacement of the 7-benzoylamino substituent and in aminolytic cleavage of the 5-benzoyl grouping to give 5-amino-7-(carbethoxymethylamino)fura-



5 **4** **6** **7** **8** **9** **10**

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