Cyclization of N^6-Substituted Adenines to Produce Compounds of the Pentaaza Steroid Type

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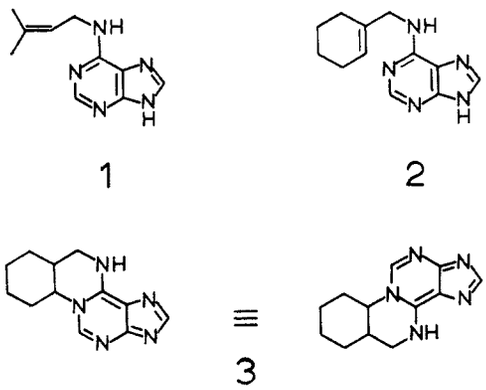
A new intramolecular cyclization ($N^6 \rightarrow 1$) of N^6-substituted adenines, that of conjugate addition to an α,β-unsaturated carbonyl system, has been used to prepare representative pentaaza analogs of "2-keto," "4-keto," and "6-keto steroids." For example, 6-(2-methoxy-1,4-dihydrobenzylamino)purine (**12**) and aqueous fluoroboric acid yielded 6a,7,8,9,10,10a,11,12-octahydro-10-oxo-3H-quinazolino[2,1-*i*]purin-6-ium fluoroborate (**13**), a "4-keto steroid" type. 6-(6-Methoxy-2,5-dihydrobenzylamino)purine (**14**) and trifluoroacetic acid in methanol gave 6a,7,10,10a,11,12-hexahydro-6a-methoxy-3H-quinazolino[2,1-*i*]purin-6-ium trifluoroacetate (**16**), a pentaaza steroid having an angular methoxyl group. 6-(4-Methoxy-2,5-dihydrobenzylamino) purine (**19**) and 6-(4-methoxy-6-methyl-2,5-dihydrobenzylamino)purine (**25**) underwent ring closure with hydrochloric acid, forming 6a,7,8,9,10,10a,11,12-octahydro-8-oxo-3H-quinazolino[2,1-*i*]purin-6-ium chloride (**20**) and 6a,7,8,9,10,10a,11,12-octahydro-6a-methyl-8-oxo-3H-quinazolino[2,1-*i*]purin-6-ium chloride (**27**), respectively, both examples of the "2-keto steroid" type. Acylation of adenine with 1-cyclohexenecarbonyl chloride resulted in 6a,7,8,9,10,10a,11,-12-octahydro-11-oxo-3H-quinazolino[2,1-*i*]purin-6-ium chloride (**29**), a "6-keto steroid" type. The ring-closure process was followed by ultraviolet and nmr spectra.

Among the examples of intramolecular cyclization of N^6-substituted adenines in which closure to either N-1 or N-7 is theoretically possible, only cyclization to N-1 has been observed.[1-12] The first report of a cyclized 6-substituted purine was by Johnson, Thomas, and Schaeffer,[1] who found that nitrous acid treatment of 6-hydrazino-9-β-D-ribofuranosylpurine gave 7-β-D-ribofuranosyltetrazolo[5,1-*i*]purine. More recently, Temple, Thorpe, Coburn, and Montgomery studied the equilibrium between 6-azidopurine and its tautomer tetrazolo[5,1-*i*]purine by infrared and nuclear magnetic resonance spectroscopy.[2] Treatment of 6-hydrazinopurine with diethoxymethyl acetate at room temperature yielded 9H-*s*-triazolo[3,4-*i*]purine, which upon heating at 180° in formamide underwent rearrangement to the isomeric 9H-*s*-triazolo[5,1-*i*]purine.[3] Attempted syntheses of the purin-6-yl analog of nitrogen mustard, N^6,N^6-bis(2-chloroethyl)adenine,[4-6] resulted in an ionic compound, the structure of which was shown to be the hydrochloride of 9-(2-chloroethyl)-7,8-dihydro-9H-imidazo[2,1-*i*]purine.[7] This ring closure is analogous to the facile cyclization of 6-(2-chloroethylthio)purine to 7,8-dihydrothiazolo[2,3-*i*]purine.[13] The reaction of alkyl- and aryl-substituted N-(purin-6-yl)-2-aminoethanol and N-(2-chloropurin-6-yl)-2-aminoethanol with thionyl chloride has also been investigated, and the only products isolated were the N-1 cyclic compounds (7,8-dihydro-9H-imidazo[2,1-*i*]-purine derivatives).[8] The rearrangement of N^6-glycyladenine to N-(purin-6-yl)glycine has been shown to proceed by a cyclic intermediate, 7,8-dihydro-8-oxo-3H-imidazo[2,1-*i*]purine, which can also be obtained by cyclization of N^6-chloroacetyladenine.[9]

The highly active cytokinin, 6-(3-methyl-2-butenylamino)purine **1**,[14,15] and its corresponding riboside, 6-(3-methyl-2-butenylamino)-9-β-D-ribofuranosylpurine,[10] undergo cyclization, $N_6 \rightarrow 1$, on treatment with strong acids[10-12,16,17] such as HCl, HBF_4, and CF_3COOH, and with electrophiles[11,17] such as I_2, Br_2, and NBS. It is instructive to note that, if the side-chain double bond, as in **1**, were contained in a cyclohexene ring **2**, then the product of cyclization, **3**, would be a pentaaza steroid with the purine moiety constituting rings C and D of such a system. Aza steroids are currently of considerable interest;[18-21] however, the only examples of pentaaza steroid types to date have resulted



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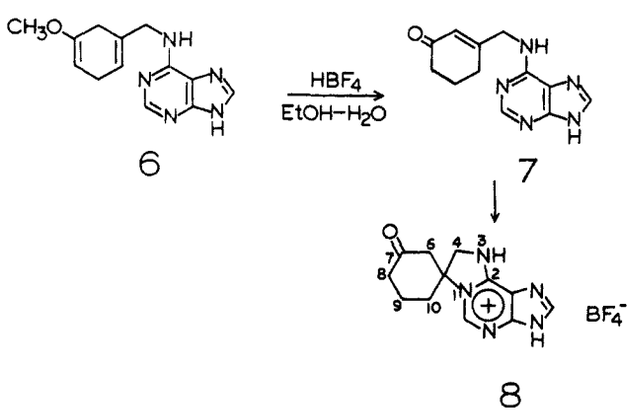
from multiple cyclization of 6-geranylaminopurine to 6a,7,8,9,10,10a,11,12-octahydro-6a,10,10-trimethylquinazolino[2,1-*i*]purine[22] and the synthesis of 4,5-dihydrobenzo[*f*]tetrazolo[5,1-*a*]phthalazine.[23] In view of the possibility of biological activity of steroidal purines, such as crossed steroid–purine antagonism, we decided to synthesize several representative pentaaza steroids related to adenine.

Our synthetic approach to pentaaza steroids involved preparation of the appropriate primary amines (containing ring A and sufficient functionality for cyclization), condensation of these with 6-chloropurine, and subsequent ring closure to the 1,N⁶-disubstituted adenines having a tetracyclic structure.

3-Methoxy-2,5-dihydrobenzylamine (**4**) was obtained by Birch reduction[24] of *m*-methoxybenzylamine (**5**) using sodium, ethanol, and ammonia. Under these conditions no benzyl–N cleavage occurs, which makes this reaction a valuable, general method for preparing dihydrobenzylamines of interest. 3-Methoxy-2,5-dihydrobenzylamine was condensed with 6-chloropurine to yield 6-(3-methoxy-2,5-dihydrobenzylamino)purine (**6**). It was hoped that **6**, with the enol ether as a ketone precursor, could lead to pentaaza analogs of testosterone or progesterone if cyclization could be effected at C-6 of the dihydrobenzene ring. However, treatment of **6** with aqueous fluoroboric acid yielded 7-oxo-3-aza-1-azoniaspiro[4.5]dec-1-eno[2,1-*i*]purine fluoroborate (**8**), probably through the intermediacy of 6-(3-oxo-1-cyclohexenylmethylamino)purine (**7**). Hydrolysis of the enol ether moiety proceeded with rearrangement[25] to give the α,β-unsaturated ketone **7**, which underwent acid-catalyzed conjugate addition to form **8**. The postulated intermediate **7** was obtained by an elimination reaction when deprotonation of **8** was attempted with sodium carbonate, and recyclization to **8** was observed under the stated acidic conditions. The structures of all cyclic compounds and their precursors were established by analysis of their ultraviolet absorption and nuclear magnetic resonance spectra. Details are provided in the Experimental Section. Ultraviolet spectra are particularly useful for determining the position or positions of substitution in alkylated adenines.[26] Whereas acidified alcohol solutions of N⁶-monosubstituted adenines show maxima typically in the range of 275–280 nm, 1,N⁶-disubstituted adenines exhibit maxima at considerably shorter wavelength (262–264 nm). The low solubility of adenine derivatives has presented some problems in nmr spectroscopy; however, usable spectra were obtained from solutions in deuterated dimethyl sulfoxide (DMSO-d_6). This solvent is particularly useful in that the difference in chemical shift between the signals observed for the 2 and 8 aromatic protons in a DMSO solution can be correlated with the substitution pattern of the purine ring.[27] In this respect, 1-substituted adenines generally show a substantially larger difference than do N⁶-substituted adenines.



Although the cyclization of **6** did not lead to a penta azasteroid, the conversion into **7** and **8** suggested that conjugate addition in appropriately designed substrates would offer a convenient route to pentaaza steroid analogs containing a ketone group at either the "2" or "4" position (steroid numbering). Birch reduction of *o*-methoxybenzylamine (**9**) afforded a mixture of 6-methoxy-2,5-dihydrobenzylamine (**10**) and 2-methoxy-1,4-dihydrobenzylamine (**11**). Compound **10** is the expected product, since reduction of benzene derivatives using Na–EtOH–NH_3 generally leads to α,δ-dihydrobenzene derivatives in which the hydrogen atoms add at positions carrying electron-withdrawing groups and avoid positions carrying electron-donating groups.[24] Isomers **10** and **11** were separated by distillation on a spinning-band column and condensed separately with 6-chloropurine, giving 6-(6-methoxy-2,5-dihydrobenzylamino)purine (**14**) and 6-(2-methoxy-1,4-dihydrobenzylamino)purine (**12**), respectively. Treatment of **12** with dilute aqueous fluoroboric acid gave the desired "4-keto steroid" analog, 6a,7,8,9,10,10a,11,12-octahydro-10-oxo-3H-quinazolino[2,1-*i*]purin-6-ium fluoroborate (**13**). Under the same conditions, **14** also underwent cyclization to a product assigned the structure 7-oxo-4-aza-2-azoniabicyclo[4.2.2]dec-2-eno[3,2-*i*]purine fluoborate (**15**). By contrast, under anhydrous conditions, **14** reacted with trifluoroacetic acid to give 6a,7,10,10a,11,12-hexahydro-6a-methoxy-3H-quinazolino[2,1-*i*]purin-6-ium trifluoroacetate (**16**), a pentaaza steroid with an angular methoxyl group. Compound **16** could be deprotonated to **17** (one possible tautomeric form is shown) without ring opening, in contrast to the ketonic cyclic salts, which showed varying tendencies to undergo reversal of the conjugate addition.

Birch reduction of *p*-methoxybenzylamine gave 4-methoxy-2,5-dihydrobenzylamine (**18**), which was condensed with 6-chloropurine, yielding 6-(4-methoxy-2,5-dihydrobenzylamino)purine (**19**). Treatment of **19** with fluoroboric acid did not readily effect cyclization; however, treatment with excess hydrochloric acid in aqueous ethanol did give rise to a "2-keto steroid" type, 6a,7,8,9,10,10a,11,12-octahydro-8-oxo-3H-quinazolino[2,1-*i*]purin-6-ium chloride (**20**), although in a somewhat low yield (34%). The lower yield of isolable product appears to be a consequence of the ease with which **20** undergoes a reverse reaction. Inclusion of the angular ("10-") methyl group was accomplished in an independent synthesis beginning with 4-methoxy-2-methylaniline (**21**). A Sandmeyer reaction of **21** with sodium cuprocyanide yielded 4-methoxy-2-methylben-

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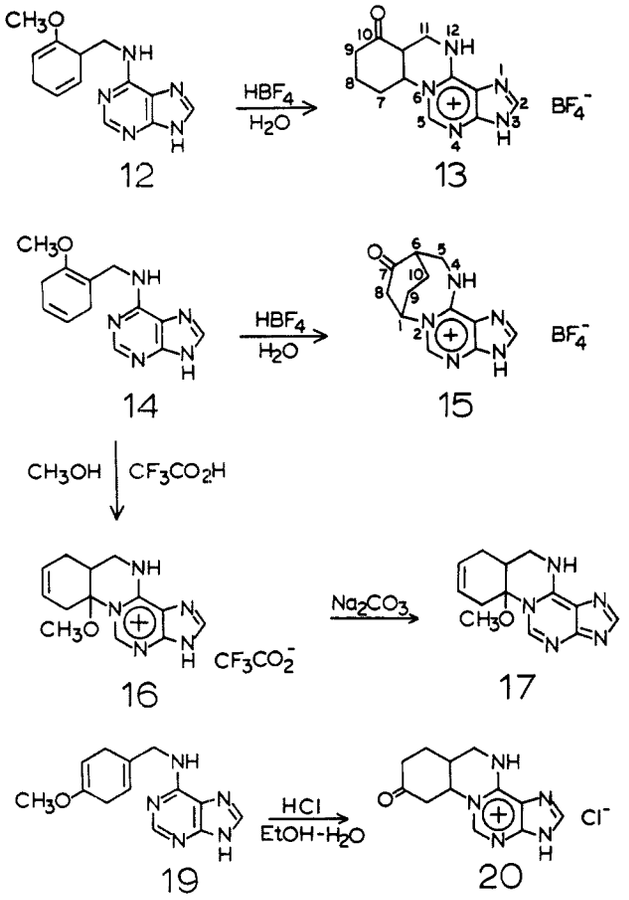
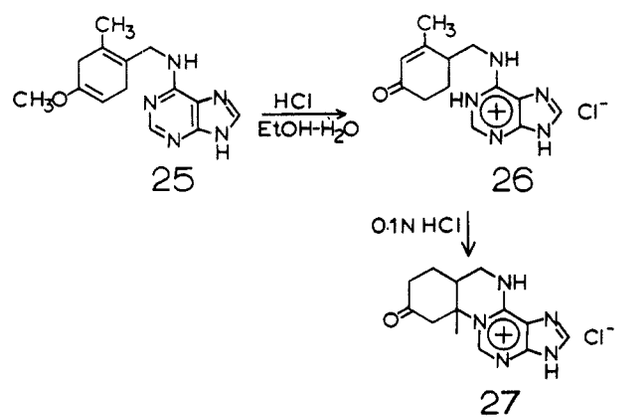
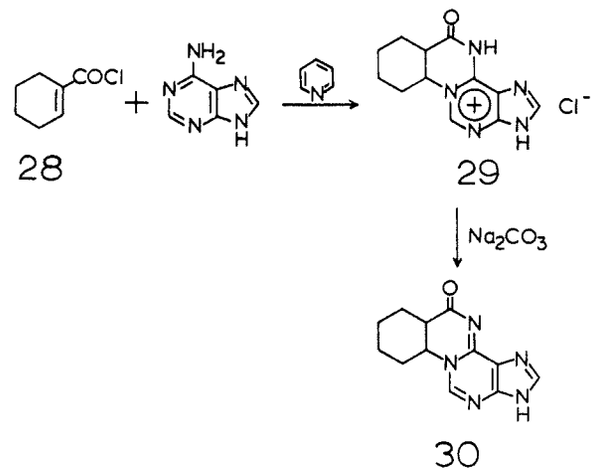


zonitrile (**22**), which was reduced with lithium aluminum hydride to the corresponding benzylamine **23**. Birch reduction of **23** gave 4-methoxy-6-methyl-2,5-dihydrobenzylamine (**24**), which was condensed with 6-chloropurine to yield 6-(4-methoxy-6-methyl-2,5-dihydrobenzylamino)purine (**25**). Treatment of **25** with hydrochloric acid in aqueous ethanol gave the hydrochloride salt of 6-(2-methyl-4-oxo-2-cyclohexenylmethylamino)purine (**26**). Ring closure of the intermediate salt **26** to 6a,7,8,9,10,10a,11,12-octahydro-6a-methyl-8-oxo-3H-quinazolino[2,1-*i*]purin-6-ium chloride (**27**) could be effected by dissolving it in dilute hydrochloric acid and allowing the solution to stand for several hours at 25°.



The reaction of adenine with 1-cyclohexenecarbonyl chloride **28** in pyridine resulted in 6a,7,8,9,10,10a,11,12-octahydro-11-oxo-3H-quinazolino[2,1-*i*]purin-6-ium chloride (**29**), a "6-keto steroid" type. This variation from the general method was suggested by the isolation of 7,8,9-trihydro-7,7-dimethyl-9-oxo-3H-pyrimido[2,1-*i*]purine and 7,8,9-trihydro-7-methyl-9-oxo-3H-pyrimido[2,1-*i*]purine from attempted acylations of adenine by 3-methyl-2-butenoic anhydride and crotonic anhydride, respectively.[28] The free base **30** (one tautomeric form is shown) of **29** was obtained by deprotonation with sodium carbonate.



In this investigation of synthetic routes leading to compounds having a pentaaza steroid structure *via* $N^6 \rightarrow 1$ cyclization of N^6-substituted adenines, the procedures involving intramolecular conjugate addition (of N-1) to an α,β-unsaturated carbonyl moiety in the N^6 side chain appear to be the most general and facile.

Experimental Section[29]

3-Methoxy-2,5-dihydrobenzylamine (**4**).—3-Methoxybenzylamine (29.1 g, 0.21 mol) was dissolved in 300 ml of ethanol, and *ca.* 1000 ml of ammonia was condensed into the solution. Sodium metal (29.2 g, 1.27 g-atoms) in small pieces was added to the stirred solution in 1 hr. Sodium ethoxide was decomposed by the cautious addition of 68.0 g (1.27 mol) of ammonium chloride. The ammonia was evaporated by means of a hot-water bath, and 600 ml of methylene chloride was added. The mixture was shaken with 600 ml of H_2O in a separatory funnel, the methylene chloride layer was drained, and the aqueous layer was extracted with two 300-ml portions of methylene chloride. The combined methylene chloride extracts were dried ($MgSO_4$), concentrated, and distilled, giving 24.2 g (82%) of the dihydrobenzylamine **4**: bp 84–85° (2 mm); $n^{20}D$ 1.5128; nmr ($CDCl_3$) τ 8.80 (s, 2, NH_2), 7.32 (m, 4, two sets $=CCH_2C=$), 6.87 (s, 2, $=CCH_2N$), 6.52 (s, 3, OCH_3), 5.44 (m, 1, $CH_3O-\underset{|}{C}=\underset{|}{C}-H$), and 4.47 ppm (m, 1, C=CH).

Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 68.87; H, 9.70; N, 9.99.

3-Methoxybenzylamine (**5**).—A solution of 25.0 g (0.17 mol) of 3-methoxybenzamide in 300 ml of warm anhydrous THF was added dropwise (1 hr) to a stirred refluxing suspension of 12.56 g (0.33 mol) of $LiAlH_4$ in 200 ml of THF. The mixture was stirred at reflux for 8 hr, cooled to ice-bath temperature, and decomposed by cautious dropwise addition of 12.5 ml of H_2O, 12.5 ml of 15% NaOH solution, and 37.5 ml of H_2O. The mixture was stirred for 30 min at room temperature and filtered, and the inorganic solid was washed thoroughly with warm THF. The combined THF filtrate and washings were dried (Na_2SO_4), concentrated *in vacuo*, and distilled, yielding 18.2 g (80%) of 3-

(28) J. J. McDonald and N. J. Leonard, unpublished observations.

(29) All melting points are corrected. Boiling points are uncorrected. Nmr spectra were obtained on a Varian Associates Model A-60 or A-100 spectrometer using tetramethylsilane as an internal standard. The uv spectra were recorded on a Cary Model 15 spectrophotometer in 95% EtOH, 0.1 *N* HCl in 95% EtOH, and 0.1 *N* NaOH in 95% EtOH as previously described.[26] We are indebted to Mr. J. Nemeth and his associates for the microanalyses.

methoxybenzylamine: bp 106–108° (5 mm) [lit.[30] bp 103–104° (6 mm)]; nmr ($CDCl_3$) τ 8.42 (s, 2, NH_2), 6.37 (s, 3, NH_2), 6.37 (s, 3, OCH_3), 6.33 (s, 2, $ArCH_2N$), and 2.7–3.4 ppm (m, 4, aromatic H).

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 69.62; H, 8.16; N, 9.91.

6-(3-Methoxy-2,5-dihydrobenzylamino)purine (6).—A mixture of 8.50 g (61 mmol) of 3-methoxy-2,5-dihydrobenzylamine, 9.42 g (61 mmol) of 6-chloropurine, and 8.7 ml (6.28 g, 62 mmol) of triethylamine in 100 ml of *n*-propyl alcohol was stirred at 65° for 10 hr. The solvent was removed *in vacuo*, and the residue was washed with water and acetone–ether, dried, and washed with warm methanol, giving 8.42 g (54%) of colorless microcrystals: mp 207–208° dec; uv $\lambda_{max}^{95\%\ EtOH}$ 268.5 (ϵ 18,200) and 210 nm (ϵ 22,100); (0.1 *N* HCl) 278 nm (ϵ 17,300); (0.1 *N* NaOH) 275.5 (ϵ 18,600) and 284 nm (sh, ϵ 13,800); nmr (NaOD–D_2O) τ 7.65 (m, 4, two sets $=CCH_2C=$), 6.83 (s, 3, OCH_3), 6.13 (s, 2, $=CCH_2N$), 5.77 (m, 1, $CH_3O-C=C-H$), 4.62 (m, 1, $C=CH$), and 1.83 and 2.03 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{13}H_{15}N_5O$: C, 60.68; H, 5.88; N, 27.22. Found: C, 60.63; H, 6.01; N, 27.12.

6-(3-Oxo-1-cyclohexenylmethylamino)purine (7).—To a stirred suspension of 0.515 g (2.0 mmol) of **6** in 24 ml of ethanol was added 1.0 ml of HBF_4 (50% aqueous). The resulting solution was heated at reflux for 10 min to effect cyclization. The acidic solution was neutralized by adding 15 ml of water containing 0.415 g (3.92 mmol) of Na_2CO_3. The cloudy solution was concentrated *in vacuo* to dryness, and the residue was triturated with 50 ml of hot ethanol and filtered. The ethanol filtrate was concentrated *in vacuo* to dryness, and the yellow solid was washed with 10 ml of water and dried, yielding 0.13 g of colorless solid, mp 225–229° dec. The aqueous washing was adjusted to pH 7 and cooled to 5°, giving a second crop, 0.12 g. The crude product was recrystallized from ethanol–hexane to yield 0.19 g (total) (39%) of the conjugated ketone **7**: mp 230–232° dec; uv $\lambda_{max}^{95\%\ EtOH}$ 267.5 (ϵ 17,600), 233 (ϵ 14,100), and 212 nm (ϵ 22,100); (0.1 *N* HCl) 278 (ϵ 16,100), 229 (sh, ϵ 14,400), and 213 nm (ϵ 17,500);[31] (0.1 *N* NaOH) 272.5 nm (ϵ 13,300); nmr (DMSO-d_6) τ 7.90–8.33 (m, 2, CCH_2C), 7.60–7.90 (m, 4, $COCH_2CCH_2C=$), 5.71 (d, 2, J = 5 Hz, $=CCH_2N-$), 4.33 (s, 1, $COCH=C$), and 2.00 and 1.93 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{12}H_{13}N_5O$: C, 59.25; H, 5.39; N, 28.79. Found: C, 58.57; H, 5.47; N, 28.62.

7-Oxo-3-aza-1-azoniaspiro[4.5]dec-1-eno[2,1-*i*]purine Fluoroborate (8).—To a stirred suspension of 0.515 g (2.0 mmol) of **6** in 24 ml of ethanol was added 1.0 ml of HBF_4 (50% aqueous). The resulting yellow solution was heated at reflux for 10 min. Ether (*ca.* 25 ml) was added to the warm solution, and stirring was continued while the mixture was allowed to cool. The precipitate was filtered, washed with ethanol–ether and ether, and dried to yield 0.35 g (53%) of the spiro ketone cyclic salt **8**: mp 217–219° dec; uv $\lambda_{max}^{95\%\ EtOH}$ 263.5 (ϵ 11,200), 232 (sh, ϵ 7400), and 214 nm (ϵ 20,600); (0.1 *N* HCl) 262.5 (ϵ 12,400) and 213.5 nm (ϵ 23,000); (0.1 *N* (NaOH) (unstable) 272 nm (ϵ 13,000); nmr (DMSO-d_6) τ 7.77–8.50 (m, 2, CCH_2C), 7.10–7.77 (m, 4, $COCH_2CCH_2CN^+$), 6.88 (AB quartet, 2, J = 13 Hz, $COCH_2CN^+$), 6.10 (AB quartet, 2, J = 11 Hz, CCH_2N), and 1.52 and 1.10 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{12}H_{14}BF_4N_5O$: C, 43.53; H, 4.26; N, 21.15. Found: C, 43.26; H, 4.35; N, 21.06.

2-Methoxybenzylamine (9) was prepared by the reduction of 2-methoxybenzamide with $LiAlH_4$. From 25.0 g (0.17 mol) of the amide there was obtained 17.06 g (75%) of the benzylamine **9**: bp 58–60° (0.35 mm) [lit.[32] bp 127–128° (30 mm)]; $n^{20}D$ 1.5494; nmr ($CDCl_3$) τ 8.58 (s, 2, NH_2), 6.25 (s, 5, $ArCH_2N$ and $ArOCH_3$), and 2.68–3.35 ppm (m, 4, aromatic H).

Anal. Calcd for $C_8H_{11}NO$: C, 70.04; H, 8.08; N, 10.21. Found: C, 70.02; H, 8.18; N, 10.07.

6-Methoxy-2,5-dihydrobenzylamine (10) and 2-methoxy-1,4-dihydrobenzylamine (11) were obtained as a mixture from the Birch reduction of **9** with sodium, ethanol, and ammonia (same procedure as for **4**). The crude product from 18.40 g of **9** was fractionally distilled using a small spinning-band column to give 7.32 g (39%) of pure **11** [bp 53–56° (1.15 mm); $n^{20}D$ 1.5034; nmr ($CDCl_3$) τ 9.00 (s, 2, NH_2), 7.00–7.40 (m, 4, $=CHCH_2CH=$ and $-CH_2N$), 6.53 (m, 1, $=CCHC=$), 6.48 (s, 3, OCH_3), 5.23 (t, 1, $J \cong 3$ Hz, $H-C=C-OCH_3$), and 4.00–4.65 ppm (m, 2, $H-C=C-H$)], 4.13 g (22%) of **11–10** mixture (about 1:2.2 by nmr integration), and 3.81 g (20%) of pure **10** [bp 61–62° (1.3 mm); $n^{20}D$ 1.5122; nmr ($CDCl_3$) τ 8.83 (s, 2, NH_2), 7.18 (m, 4, two sets $=CCH_2C=$), 6.70 (s, 2, $=CCH_2N$), 6.48 (s, 3, OCH_3), and 4.35 ppm (m, 2, $H-C=C-H$)].

Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found for **10**: C, 69.00; H, 9.54; N, 10.18.

6-(2-Methoxy-1,4-dihydrobenzylamino)purine (12).—2-Methoxy-1,4-dihydrobenzylamine (**11**, 5.04 g, 36.2 mmol) was condensed with 6-chloropurine by the procedure used in the preparation of **6** to yield 5.0 g (54%) of colorless microscopic needles, recrystallized from methanol for analysis: mp 214–215.5° dec; $\lambda_{max}^{95\%\ EtOH}$ 269.5 (ϵ 18,000) and 210 nm (ϵ 21,200); (0.1 *N* NaOH) 276 (ϵ 17,900) and 285 nm (sh, ϵ 13,200); nmr (DMSO-d_6) τ 7.13–7.40 (m, 2, $=CHCH_2CH=$), 6.50 (br, unresolved, 4, OCH_3 and $=CCHC=$), 6.00–6.40 (m, 2, CCH_2N), 5.25 (t, 1, J = 3.5 Hz, $CH_3O-C=C-H$), 4.25 (m, 2, $H-C=C-H$), 2.90–3.25 (m, 0.6, N^6-H partially exchanged), and 1.80 and 1.92 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{13}H_{15}N_5O$: C, 60.68; H, 5.88; N, 27.22. Found: C, 60.86; H, 6.15; N, 27.42.

6a,7,8,9,10,10a,11,12-Octahydro-10-oxo-3H-quinazolino[2,1-*i*]purin-6-ium Fluoroborate (13).—To a stirred suspension of 0.462 g (1.8 mmol) of **12** in 18 ml of H_2O was added 2.0 ml of 0.95 *M* HBF_4. The mixture was stirred for 2 hr at 25°, and the resulting solution was concentrated *in vacuo* to a pale yellow solid which was washed with acetone–ether and dried to yield 0.51 g (85%) of colorless microcrystals: softens *ca.* 172°, mp 225–235° dec; uv $\lambda_{max}^{95\%\ EtOH}$ 268 (ϵ 17,100) and 212 nm (ϵ 18,800); (0.1 *N* HCl) 264 (ϵ 13,400) and 212 nm (ϵ 17,200); (0.1 *N* NaOH) (unstable) 274 (ϵ 17,100) and 283 nm (sh, ϵ 14,300); nmr (DMSO-d_6) τ 7.15–8.60 (m, 4, CCH_2CH_2C), 6.35–7.15 (m, 2, CCH_2CO), 6.18 (AB quartet, 2, J = 10 Hz, CCH_2N), 4.16 (AB quartet, 2, J = 10 Hz, $COCHCHN^+$), and 1.10 and 1.46 ppm (br s, s, 2, purine H).

Anal. Calcd for $C_{12}H_{14}BF_4N_5O$: C, 43.53; H, 4.26; N, 21.15. Found: C, 43.78; H, 4.17; N, 21.01.

6-(6-Methoxy-2,5-dihydrobenzylamino)purine (14).—6-Methoxy-2,5-dihydrobenzylamine (**10**, 3.81 g, 27.4 mmol) was condensed with 6-chloropurine by the procedure used in the preparation of **6** to give 4.0 g (57%) of colorless microcrystals, recrystallized from methanol for analysis: mp 213–216° dec; $\lambda_{max}^{95\%\ EtOH}$ 270 (ϵ 18,800) and 210 nm (ϵ 21,400); (0.1 *N* HCl) 272 nm (br, ϵ 14,200); (0.1 *N* NaOH) 276 (ϵ 19,000) and 285 nm (sh, ϵ 13,900); nmr (DMSO-d_6) τ 7.20 (br, unresolved, 4, two sets $=CCH_2C=$), 6.43 (s, 3, OCH_3), 5.63 (d, 2, J = 6 Hz, $=CCH_2N$), 4.35 (s, 2, $H-C=C-H$), 2.72 (m, 0.7, N^6-H partially exchanged), and 1.75 and 1.87 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{13}H_{15}N_5O$: C, 60.68; H, 5.88; N, 27.22. Found: C, 60.46; H, 5.92; N, 27.37.

7-Oxo-4-aza-2-azoniabicyclo[4.2.2]dec-2-eno[3,2-*i*]purine Fluoroborate (15).—To a stirred suspension of 0.386 g (1.5 mmol) of **14** in 13 ml of H_2O was added 2.0 ml of 0.76 *M* HBF_4. The mixture was stirred for 3 hr at 25°, and the resulting solution was concentrated *in vacuo* to a colorless semisolid mass. The crude product was recrystallized from acetone–ether to yield 0.36 g (73%) of colorless microcrystals: mp 165–168° dec; uv $\lambda_{max}^{95\%\ EtOH}$ 267 (ϵ 17,000) and 212 nm (ϵ 18,100); (0.1 *N* HCl) 264.5 (ϵ 13,800) and 211 nm (ϵ 16,500); (0.1 *N* NaOH) (unstable) 275.5 (ϵ 17,200) and 284 nm (sh, ϵ 12,600); nmr (DMSO-d_6) τ 5.7–8.1 (m, *ca.* 8, CCH_2CH_2C, $COCH_2C$, and CCH_2N), 3.9–4.6 (m, COCH and CHN^+), 2.1 (v br, 0.6, N^6-H partially exchanged), and 1.14 and 1.46 ppm (br s, s, 2, purine H).

Anal. Calcd for $C_{12}H_{14}BF_4N_5O$: C, 43.53; H, 4.26; N, 21.15. Found: C, 43.49; H, 4.17; N, 20.80.

6a,7,10,10a,11,12-Hexahydro-6a-methoxy-3H-quinazolino-[2,1-*i*]purin-6-ium Trifluoroacetate (16).—To a stirred suspension of 0.515 g (2.0 mmol) of **14** in 20 ml of anhydrous methanol was added 0.264 g (2.3 mmol) of trifluoroacetic acid. The mixture was stirred at reflux for 1 hr, and the resulting solution

(30) C. W. Shoppee, *J. Chem. Soc.*, 696 (1932).

(31) An interesting feature of the ultraviolet spectrum of **7** is the shift to shorter wavelength observed for the conjugated ketone chromophore in going from neutral (233 nm) to acidic solution (229 nm), which is consistent with the location of positive charge nearby: *e.g.*, E. M. Kosower and D. C. Remy, *Tetrahedron*, **5**, 281 (1959); V. Georgian, *Chem. Ind.* (London), 930 (1954), 1480 (1957); C. A. Grob, A. Kaiser, and E. Renk, *ibid.*, 598 (1957).

(32) W. H. Carothers, C. F. Bickford, and G. J. Hurwitz, *J. Amer. Chem. Soc.*, **49**, 2908 (1927).

was concentrated *in vacuo* to a yellow oil which was crystallized from acetone–ether to yield 0.33 g (45%) of colorless microcrystals: mp 157–159° dec; uv $\lambda_{max}^{95\% EtOH}$ 266 (ε 12,000) and 228 nm (ε 5800); (0.1 *N* HCl) 263.5 nm (ε 13,200); (0.1 *N* NaOH) 281 (ε 14,400) and 273 nm (ε 14,900); nmr (DMSO-d_6) τ 6.70–8.05 (m, 4, $=CCH_2C$ and $=CCH_2C(OCH_3)N^+$), 6.58 (s, 3, OCH_3), 6.02–6.70 (m, CH and CCH_2N), 4.43 (AB quartet, 2, *J* = 11 Hz, H—C=C—H), and 1.31 and 1.46 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{15}H_{16}F_3N_5O_3$: C, 48.52; H, 4.34; N, 18.86. Found: C, 48.75; H, 4.48; N, 18.96.

6a,7,10,10a,11,12-Hexahydro-6a-methoxyquinazolino[2,1-*i*]purine (17).—To a stirred solution of 0.371 g (1.0 mmol) of **16** in 5 ml of H_2O was added 0.106 g (1.0 mmol) of solid Na_2CO_3. The solution was concentrated *in vacuo* to dryness, and the residue was extracted with acetone in a Soxhlet apparatus. The acetone extract was concentrated to yield 0.16 g (62%) of colorless microcrystals: mp 193–196° dec; uv $\lambda_{max}^{95\% EtOH}$ 278 (ε 14,000) and 231 nm (ε 19,500); (0.1 *N* HCl) 264.5 mμ (ε 14,000); (0.1 *N* NaOH) 281 (ε 14,600) and 273 nm (ε 15,100); nmr (DMSO-d_6) τ 6.9–8.1 [m, 4, $=CCH_2C$ and $=CCH_2C(OCH_3)N$], 6.68 (s, 3, OCH_3), 6.1–6.9 (m, 3, CH and CCH_2N), 4.34 (AB quartet, 2, *J* = 10 Hz, H—C=C—H), and 1.70 and 2.04 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{13}H_{15}N_5O$: C, 60.68; H, 5.88; N, 27.22. Found: C, 60.84; H, 5.66; N, 27.10.

4-Methoxy-2,5-dihydrobenzylamine (18).—*p*-Methoxybenzylamine (24.9 g, 0.18 mol) was reduced with sodium, ethanol, and ammonia (same procedure as for **4**) to yield 20.8 g (82%) of 4-methoxy-2,5-dihydrobenzylamine: bp 78–81° (1.5 mm); $n^{20}D$ 1.5110; nmr ($CDCl_3$) τ 8.87 (m, 2, NH_2), 7.25 (m, 4, two sets $=CCH_2C=$), 6.78 (s, 2, $=CCH_2N$), 6.28 (s, 3, OCH_3), 5.35 (m, 1, H—C=C—OCH_3), and 4.50 ppm (m, 1, H—C=C—).

Anal. Calcd for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 68.83; H, 9.57; N, 10.09.

6-(4-Methoxy-2,5-dihydrobenzylamino)purine (19).—4-Methoxy-2,5-dihydrobenzylamine (**18**, 10.23 g, 73.5 mmol) was condensed with 6-chloropurine by the procedure used in the preparation of **6** to yield 11.1 g (59%) of pale yellow microcrystals, recrystallized from methanol: mp 202–205° dec; uv $\lambda_{max}^{95\% EtOH}$ 268 (ε 18,400) and 211 nm (ε 19,300); (0.1 *N* HCl) 277 (ε 17,300) and 208.5 nm (ε 12,300); (0.1 *N* NaOH) 276 (ε 18,000) and 284 nm (sh, ε 13,200); nmr (DMSO-d_6) τ 7.30 (m, 4, two sets $=CCH_2C=$), 6.52 (s, 3, OCH_3), 5.85 (m, 2, $=CCH_2N$), 5.35 (m, 1, H—C=C—OCH_3), 4.45 (m, 1, H—C=C—), 2.35 (m, 0.6, N^6-H partially exchanged), and 1.80 and 1.88 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{13}H_{15}N_5O$: C, 60.68; H, 5.88; N, 27.22. Found: C, 60.46; H, 6.00; N, 27.39.

6a,7,8,9,10,10a,11,12-Octahydro-8-oxo-3H-quinazolino[2,1-*i*]purin-6-ium Chloride (20).—To a stirred suspension of 0.52 g (2.0 mmol) of **19** in 19 ml of ethanol was added 1.0 ml of 12 *M* HCl. The mixture was stirred for 15 min at 25° and for 30 min at reflux. The resulting solution was decolorized with charcoal and concentrated *in vacuo* to a pale yellow oil which was crystallized from 95% ethanol–ether to yield 0.19 g (34%) of colorless microcrystals: mp 227–228° dec; uv $\lambda_{max}^{95\% EtOH}$ 263.5 (ε 12,900) and 212 nm (ε 18,700); (0.1 *N* HCl) 262.5 (ε 13,900) and 212 nm (ε 20,400); (0.1 *N* NaOH) (unstable) 275 (ε 17,100) and 283 nm (sh, ε 13,000); nmr (DMSO-d_6) τ 7.58–8.30 (m, 4, $COCH_2CH_2C$), 6.86–7.38 (m, 3, $COCH_2CN^+$ and CH), 6.05 (AB quartet, 2, *J* = 12 Hz, CCH_2N), 4.86 (five-line m, 1, CHN^+), and 1.37 and 1.46 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{12}H_{14}ClN_5O$: C, 51.52; H, 5.04; N, 25.04. Calcd for $C_{12}H_{14}ClN_5O \cdot {}^1/_5C_2H_5OH$: C, 51.54; H, 5.31; N, 24.24. Found: C, 51.55; H, 5.37; N, 24.40.

4-Methoxy-2-methylbenzonitrile (22) was prepared by the Sandmeyer reaction from 4-methoxy-2-methylaniline (**21**, 54.87 g, 0.40 mol) and sodium cuprocyanide as in the preparation of 2-methylbenzonitrile.[33] The crude product was vacuum distilled: bp 82–83° (5 mm); yield 20.8 g (35%); $n^{20}D$ 1.5483; ir (neat) 2210 cm^{-1} (C≡N); nmr ($CDCl_3$) τ 7.52 (s, 3, $ArCH_3$), 6.16 (s, 3, $ArOCH_3$), and 2.45–3.40 ppm (m, 3, aromatic H).

Anal. Calcd for C_9H_9NO: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.68; H, 5.84; N, 9.52.

(33) H. T. Clarke and R. R. Read, "Organic Syntheses," Coll. Vol. I, John Wiley & Sons, Inc., New York, N. Y., 1941, p 514.

4-Methoxy-2-methylbenzylamine (23).—To a mechanically stirred suspension of 5.70 g (0.15 mol) of lithium aluminum hydride in 300 ml of ether was added a solution of 20.59 g (0.14 mol) of 4-methoxy-2-methylbenzonitrile in 200 ml of ether at a rate sufficient to produce a gentle reflux. After addition was complete, the mixture was stirred at reflux for 30 min, cooled, and decomposed by dropwise addition of 5.7 ml of H_2O, 5.7 ml of 15% NaOH, and 17.1 ml of H_2O. The mixture was stirred for 1 hr at 25° and filtered. The inorganic solid was washed thoroughly with ether, and the combined ether extracts were dried ($MgSO_4$), concentrated, and distilled: bp 82° (0.7 mm); yield 15.6 g (74%); $n^{20}D$ 1.5486 (lit.[34] $n^{28}D$ 1.546); nmr ($CDCl_3$) τ 8.77 (s, 2, NH_2), 7.73 (s, 3, $ArCH_3$), 6.29 (m, 5, $ArOCH_3$ and $ArCH_2N$), and 2.70–3.50 ppm (m, 3, aromatic H).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.66; N, 9.27. Found: C, 71.26; H, 8.54; N, 9.30.

4-Methoxy-6-methyl-2,5-dihydrobenzylamine (24).—4-Methoxy-2-methylbenzylamine (**23**, 15.3 g, 0.10 mol) was reduced with sodium, ethanol, and ammonia (same procedure as for **4**) to yield 13.8 g (89%) of a clear liquid: bp 68–70° (0.7 mm); $n^{20}D$ 1.5118; nmr ($CDCl_3$) τ 8.92 (s, 2, NH_2), 8.25 (s, 3, $=CCH_3$), 6.91–7.57 (m, 4, two sets $=CCH_2C=$), 6.73 (s, 2, $=CCH_2N$), 6.49 (s, 3, $=COCH_3$), and 5.23–5.56 ppm (m, 1, H—C=C—OCH_3).

Anal. Calcd for $C_9H_{15}NO$: C, 70.55; H, 9.87; N, 9.14. Found: C, 70.62; H, 9.98; N, 9.21.

6-(4-Methoxy-6-methyl-2,5-dihydrobenzylamino)purine (25).—4-Methoxy-6-methyl-2,5-dihydrobenzylamine (**24**, 4.96 g, 32.4 mmol) was condensed with 6-chloropurine by the procedure used in the preparation of **6** to yield 5.43 g (60%) of pale yellow microcrystals, recrystallized from methanol: mp 204–205° dec; uv $\lambda_{max}^{95\% EtOH}$ 270 (ε 19,300) and 211 nm (ε 21,700); (0.1 *N* HCl) 281 (ε 18,900) and 209 nm (ε 14,200); (0.1 *N* NaOH) 277 (ε 19,100) and 285 nm (sh, ε 14,000); nmr (DMSO-d_6) τ 8.20 (s, 3, $=CCH_3$), 6.95–7.45 (m, 4, two sets $=CCH_2C=$), 6.53 (s, 3, $=COCH_3$), 5.72 (m, 2, $=CCH_2N$), 5.35 (m, 1, H—C=C—OCH_3), 2.55 (m, 0.8, N^6-H partially exchanged), and 1.78 and 1.90 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{14}H_{17}N_5O$: C, 61.97; H, 6.32; N, 25.81. Found: C, 62.02; H, 6.41; N, 26.00.

6-(2-Methyl-4-oxo-2-cyclohexenylmethylamino)purine Hydrochloride (26).—To a stirred suspension of 0.271 g (1.0 mmol) of **25** in 9 ml of ethanol was added 1.0 ml of 12 *M* HCl. The mixture was stirred for 20 min at 25°, cooled to −20° for 1 hr, and filtered. The solid was washed with ethanol–ether and ether and dried to yield 0.22 g (75%) of colorless microcrystals: mp 217–218° dec; uv $\lambda_{max}^{95\% EtOH}$ 270 (ε 19,300), 232 (ε 12,200) and 213 nm (ε 22,600); (0.1 *N* HCl) 280.5 nm (ε 19,000); (0.1 *N* NaOH) 273.5 nm (ε 15,935); nmr (D_2O) τ 7.30–7.80 (m, 2, CCH_2C), 7.38 (s, 3, $=CCH_3$), 6.86–7.20 (m, 2, $COCH_2C$), 6.58 (m, 1, =CCH), 5.50 (m, 2, CCH_2N), 3.52 (s, 1, O=CCH=C), and 1.00 and 1.14 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{13}H_{16}ClN_5O$: C, 53.15; H, 5.49; N, 23.84. Found: C, 53.22; H, 5.48; N, 24.14.

6a,7,8,9,10,10a,11,12-Octahydro-6a-methyl-8-oxo-3H-quinazolino[2,1-*i*]purin-6-ium Chloride (27).—A solution of 0.22 g (0.75 mmol) of the intermediate salt **26** in 10.0 ml of 0.1 *N* HCl was allowed to stand for 8 hr at 25° and was concentrated *in vacuo* (20°) to a colorless solid which was triturated with 95% ethanol–ether, filtered, and dried to yield 0.20 g (91%) of colorless microcrystals: mp *ca.* 135° dec (hygroscopic); uv $\lambda_{max}^{95\% EtOH}$ 264.5 (ε 13,900) and 212 nm (ε 18,700); (0.1 *N* HCl) 265 (ε 13,000) and 212 nm (ε 17,700); (0.1 *N* NaOH) (unstable) 274.5 (ε 17,200) and 284 nm (sh, ε 13,600); nmr (D_2O) τ 7.75 (s, 3, CH_3CN^+), 6.44–7.92 (m, *ca.* 5, $O=CCH_2CH_2CH$), 6.08 (AB quartet, 2, *J* = 16 Hz, $O=CCH_2CN^+$), 5.34–5.88 (two overlapping quartets—AB portion of an ABX pattern, 2, $CHCH_2N$), and 0.93 and 1.25 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{13}H_{16}ClN_5O \cdot {}^1/_2H_2O$: C, 51.57; H, 5.66; N, 23.13. Found: C, 51.42; H, 5.93; N, 23.02.

6a,7,8,9,10,10a,11,12-Octahydro-11-oxo-3H-quinazolino[2,1-*i*]purin-6-ium Chloride (29).—A mixture of 1.35 g (10.0 mmol) of adenine and 2.89 g (20.0 mmol) of analytically pure 1-cyclo-

(34) S. H. S. Sharadamma, G. B. Maddi, S. N. Kulkarni, P. B. Sattur, and K. S. Norgund, *J. Karnatak Univ.*, **2**, 19 (1957); *Chem. Abstr.*, **53**, 9107i (1959).

hexenecarbonyl chloride, bp 53° (2.5 mm) (lit.[35] bp 203–204°), in 20 ml of dry pyridine was stirred at reflux for 6 hr. The resulting dark brown solution was concentrated *in vacuo* to a paste. A 30-ml portion of 95% ethanol was added, and the mixture was stirred for 30 min at reflux. The solvent was removed *in vacuo*, and the remaining semisolid was stirred for 1 hr at 25° with 50 ml of $CHCl_3$ and then filtered. The solid was washed with $CHCl_3$ and ether, dried, and recrystallized from ethanol with charcoal decolorization, giving 0.73 g (26%) of colorless microcrystals: mp 288–290° dec; uv $\lambda_{max}^{95\% EtOH}$ 320 (sh, ϵ 10,300), 309 (ϵ 12,700), 295.5 (ϵ 12,900), 288 (sh, ϵ 12,000), and 222 nm (ϵ 19,600); (0.1 *N* HCl) 285.5 (ϵ 15,900) and 220 nm (ϵ 29,600); (0.1 *N* NaOH) 315.5 (ϵ 24,800) and 242 nm (ϵ 17,900); nmr (DMSO-d_6) τ 7.55–9.15 (m, 8, cyclohexyl H), 6.27 (d, 1, J = 5 Hz, CHC=O), 4.60 (m, 1, CHN^+), and 0.71 and 1.04 ppm (2 s, 2, purine H).

Anal. Calcd for $C_{12}H_{14}ClN_5O$: C, 51.52; H, 5.04; N, 25.04. Found: C, 51.51; H, 5.16; N, 24.80.

3,6a,7,8,9,10,10a,11-Octahydro-11-oxoquinazolino[2,1-*i*]purine (30).—To a stirred solution of 0.280 g (1.0 mmol) of **29** in 5 ml of H_2O was added 0.053 g (0.50 mmol) of solid Na_2CO_3, giving an evolution of CO_2 and a precipitate within 1 min. The mixture was cooled to 5° and filtered. The solid was washed with cold H_2O and acetone–ether and dried to yield 0.18 g (74%) of colorless microcrystals: mp 267–268° dec; uv $\lambda_{max}^{95\% EtOH}$ 320 (sh, ϵ 15,700), 310 (ϵ 18,800), and 230 nm (ϵ 19,100); (0.1 *N* HCl) 286 (ϵ 15,900) and 220 nm (ϵ 29,400); (0.1 *N* NaOH) 316 (ϵ 25,100) and 243 nm (ϵ 18,100).

Anal. Calcd for $C_{12}H_{13}N_5O$: C, 59.25; H, 5.39; N, 28.79. Found: C, 59.24; H, 5.27; N, 28.91.

(35) J. Kenner and R. L. Wain, *Ber.*, **72**, 456 (1939).

Registry No.—**4**, 21882-99-5; **5**, 5071-96-5; **6**, 21883-01-2; **7**, 21883-02-3; **8**, 21899-62-7; **9**, 6850-57-3; **10**, 21883-04-5; **11**, 21883-05-6; **12**, 21883-06-7; **13**, 21899-63-8; **14**, 21883-07-8; **15**, 21899-64-9; **16**, 21883-08-9; **17**, 21883-09-0; **18**, 21883-10-3; **19**, 21883-11-4; **20**, 21883-12-5; **22**, 21883-13-6; **23**, 21883-14-7; **24**, 21883-15-8; **25**, 21883-16-9; **26**, 21883-17-0; **27**, 21883-18-1; **29**, 21883-19-2; **30**, 21883-20-5.

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Nucleophilic Displacement in 1,2:5,6-Di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-glucofuranose[1]

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Nucleophilic displacement of the *p*-tolylsulfonyloxy group in the 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-glucofuranose (I) has been successfully accomplished, using sodium azide and potassium thioacetate, to give the corresponding α-D-allofuranose derivatives (II and IV). Selective hydrolysis of 3-*S*-acetyl-1,2:5,6-di-*O*-isopropylidene-3-thio-α-D-allofuranose (IV) with 50% aqueous acetic acid affords 3-*S* acetyl-1,2-*O*-isopropylidene-3-thio-α-D-allofuranose (VI), which is acetylated to give 5,6-di-*O*-acetyl-3-*S*-acetyl-1,2-*O*-isopropylidene-3-thio-α-D-allofuranose (VII). Compound VII is desulfurized using Raney nickel in ethanol to give 5,6-di-*O*-acetyl-3-deoxy-1,2-*O*-isopropylidene-D-*ribo*-hexofuranose, which is deacetylated to give 3-deoxy-1,2-*O*-isopropylidene-D-*ribo*-hexofuranose (VIII) in an overall yield of 50% starting from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose.

The displacement of the *p*-tolylsulfonyloxy group in 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-glucofuranose (I) with ammonia[2] and hydrazine[2-6] occurs with inversion of configuration at C-3 to give D-allofuranose derivatives. The *p*-tolylsulfonyloxy group at C-3 as in I is reported[2-5] to be very resistant to nucleophiles other than the ones cited above.

We wish to report that nucleophilic displacement is feasible with azide and thiolacetate anions to give the corresponding 3-azido and 3-thioacetyl derivatives having the D-*allo* configuration. The displacement with thioacetate anion followed by desulfurization with Raney nickel has enabled us to synthesize the 3-deoxy-D-*ribo*-hexofuranose derivative in high yields.

In connection with other work in progress which required large quantities of 3-deoxy-1,2-*O*-isopropylidene-D-*ribo*-hexofuranose, the possibility of displacement of the *p*-tolylsulfonyloxy group in 1,2:5,6-di-*O*-isopropylidene-3-*O*-(*p*-tolylsulfonyl)-α-D-glucofuranose (I) was examined. Treatment of compound I at 115° in a current of nitrogen for 15 days in *N*,*N*-dimethylformamide (DMF) containing a slurry of sodium azide in water, so as to have DMF–water in the proportion of 19:1, affords a syrupy residue which exhibits strong absorptions at 2150 (azide) and at 1650 cm^{-1} suggestive of an olefin. Thin layer chromatographic examination of the syrupy product shows it to be composed of three main components, which are separated on a silica gel column to give a 53% yield of crystalline 3-azido-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (II), a 10% recovery of the starting material I, and a 12% yield of 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose. The infrared spectrum of compound II in Nujol shows a strong absorption at 2150 cm^{-1} (azide) and none for the tolylsulfonate group. The azide II, on reduction with Raney nickel, furnishes the known 3-amino-3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-allofuranose (III).

In a similar manner, compound I is heated at 115° in a current of nitrogen for 3 days in dry DMF containing potassium thioacetate to yield a syrupy residue which is acetylated in the usual manner. From this latter res-

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