9 H), 0.17 (s, 6 H); $^{13}C$ NMR ($CDCl_3$) δ 129.12, 128.16, 127.24, 124.60, 92.62, 89.94, 89.21, 82.00, 34.68, 30.87, 29.48, 26.16, 25.96, 22.57, 22.20, 20.14, 16.84, 14.01, –4.52; IR (KBr) 3080, 2980, 2950, 2880, 2160, 1615, 1510, 1485, 1480, 1460, 1380, 1260, 900, 840, 830, 820, 780, 700 $cm^{-1}$; UV (methanol) $\lambda_{max}$ 248 nm; MS, *m/e* 432 ($M^+$, 1.4), 375 ($M^+$ – *tert*-butyl, 3.5), 348 ($M^+$ – DMB, 2.4), 291 ($M^+$ – *tert*-butyl – DMB, 13.5), 207 ($M^+$ – *tert*-butyl – 2DMB, 7.2), 73 ($C_3H_9Si^+$, 100). Anal. Calcd for $C_{28}H_{44}Si$: C, 83.26; H, 10.26. Found: C, 83.19; H, 10.22. **9**: $^1H$ NMR ($CDCl_3$) δ 7.19 (s, 5 H), 1.36 (s, 6 H), 1.14 (s, 6 H), 1.02 (s, 6 H), 1.00 (s, 6 H), 0.91 (s, 9 H), 0.06 (s, 6 H); $^{13}C$ NMR ($CDCl_3$) δ 140.25, 131.06, 127.90, 125.84, 106.21, 84.13, 82.00, 78.62, 32.97, 31.90, 28.67, 26.14, 23.78, 20.55, 19.19, 19.04, 16.65, –4.37; IR (KBr) 3080, 3030, 2980, 2960, 2880, 2170, 1620, 1510, 1490, 1480, 1460, 1390, 1375, 1260, 1120, 845, 830, 820, 780, 770, 730, 710, 680 $cm^{-1}$; UV (methanol) $\lambda_{max}$ 250 nm (sh); MS, *m/e* 432 ($M^+$, 2.1), 375 ($M^+$ – *tert*-butyl, 20.9), 348 ($M^+$ – DMB, 33.0), 291 ($M^+$ – *tert*-butyl – DMB, 81.1), 207 ($M^+$ – *tert*-butyl – 2DMB, 100), 73 ($C_3H_9Si^+$, 90.9). Anal. Calcd for $C_{28}H_{44}Si$: C, 83.26; H, 10.26. Found: C, 83.29; H, 10.17.

**Irradiation of 1 with DMB/AcCN.** Deaerated 4 mM DMB/AcCN (1:1 molar ratio) solution of **1** was irradiated with 350-nm UV light in a Rayonet photochemical reactor Model RPR-208. A 20-mL Pyrex ampule was used as a reaction vessel for three freeze–pump–thaw degassing cycles. After the irradiation, the solvent was evaporated in vacuo and the photoadducts **5** and **10** were isolated in 4% and 14% yields, respectively, by preparative thin-layer chromatography using *n*-hexane/diethyl ether (2:1, v/v) followed by column chromatography using *n*-hexane/diethyl ether (20:1, v/v) as eluents. Highly pure photoadduct **10** was obtained from reverse-phase HPLC using a μ-Bondpak $C_{18}$ column and a $MeOH/H_2O/THF$ (10:1:1, v/v/v) solvent system. **10**: $^1H$ NMR ($CDCl_3$) δ 7.35 (s, 5 H), 7.32 (s, 5 H), 1.9–1.4 (m, 3 H), 1.41 (s, 6 H), 1.08 (s, 6 H); $^{13}C$ NMR ($CDCl_3$) δ 139.59, 132.55, 132.08, 129.27, 128.97, 128.85, 127.08, 122.99, 118.14, 88.10, 86.23, 78.99, 76.41, 30.38, 26.70, 21.32, 21.18, 21.08, 17.89, 13.57; IR (KBr) 3060, 3010, 2930, 2240, 1600, 1490, 1380, 1360, 1110, 755, 700, 690 $cm^{-1}$; UV (methanol) $\lambda_{max}$ 248 nm; MS, *m/e* 363 ($M^+$, 21.9), 279 ($M^+$ – DMB, 16.4), 226 ($M^+$ – DMB – AcCN, 97.3). Anal. Calcd for $C_{27}H_{25}N$: C, 89.22; H, 6.93; N, 3.82. Found: C, 89.17; H, 7.11; N, 3.71.

**Quantum Yield Measurements.** Samples for quantum yield determination were degassed and sealed in Pyrex ampules. DMB solutions of samples (3 mL) were pipetted into ampules, degassed through three cycles of the freeze–pump–thaw method with cooling in liquid nitrogen, and sealed. Azulene concentrations were 0–2.5 × $10^{-4}$ M, and the concentration of **1** was $10^{-4}$ M. The samples were irradiated with a Hanovia 450-W medium-pressure mercury arc lamp (Type 679A36) in a merrgy-go-round apparatus. Mercury emission line of 366 nm was isolated by Corning glass filters 0-52 and 7-37. Ferrioxalate actinometry was used to monitor the intensity of the light absorbed. Quantitative analysis was carried out by HPLC utilizing a Radialpak Si column and *n*-hexane as a solvent.

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**Registry No.** **1**, 20264-56-6; **3**, 17814-74-3; **4**, 113860-44-9; **5**, 106507-59-9; **7**, 113860-46-1; **8**, 113860-47-2; **9**, 113860-48-3; **10**, 113860-49-4; DMB, 563-79-1; AcCN, 107-13-1; $C_6H_5C{\equiv}CBr$, 932-87-6; $HC{\equiv}CC{\equiv}CSi(CH_3)_2C_4H_9$-*t*, 113860-45-0.

# Synthesis of C-Nucleoside Analogue of (*S*)-9-(2,3-Dihydroxypropyl)adenine and Related Acyclonucleosides

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Synthesis of C-nucleoside analogue of (*S*)-9-(2,3-dihydroxypropyl)adenine [(*S*)-DHPA] and related compounds is described. 3-Amino-4-[2,3-(isopropylidenedioxy)-1-propyl]pyrazole (**6**) was prepared in six steps from 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**) by routes involving Wittig reaction, sodium borohydride reduction, formylation, and the cyclocondensation with thiosemicarbazide followed by the alkaline hydrolysis of 3-amino-2-thiocarbamoylpyrazole **9**. Cyclization of **6** with *N*-cyanoformimidate, followed by the removal of protecting group yielded 4-amino-8-(2,3-dihydroxy-1-propyl)pyrazolo[1,5-*a*]-1,3,5-triazine (**11**), the C-nucleoside analogue of (*S*)-DHPA. The guanine analogue **15** was synthesized by cyclizing **6** with *N*-(ethoxycarbonyl)-*S*-methylisothiourea followed by the deblocking of isopropylidene group. Analogous sequence of reactions of **6** with ethoxycarbonyl isothiocyanate and the subsequent desulfurization of **21** gave the inosine analogue **23**. Synthesis of 8-(2,3-dihydroxy-1-propyl)-4-thioxo-3,4-dihydropyrazolo[1,5-*a*]-1,3,5-triazine (**17**) from **9** is also reported.

The acyclonucleosides have been the subject of intense research for the past 10 years. Their chemistry and biology has been the subject of a recent review.[1] Acyclovir, the first clinically useful antiherpes (herpes type-2) agent, has inspired continuing research in this area. The usefulness of acyclovir originates from the drug's selective inhibitory activities on several virally induced enzymes such as thymidine kinase and DNA polymerase.[2]

A number of acyclonucleosides have been synthesized as potential antiviral agents.[1] Among them, (*S*)-9-(2,3-dihydroxypropyl)adenine [(*S*)-DHPA] (Figure 1) seems to be an interesting compound. It possesses broad-spectrum antiviral activities on DNA and RNA viruses as well as plant viruses.[3] It is interesting to note that only the *S* enantiomer exhibits antiviral activity. Recently, De Clercq, Holy, and co-workers reported selective broad-spectrum antiviral activities of a (*S*)-DHPA analogue, (*S*)-9-[3-hydroxy-2-(phosphonomethoxy)propyl]adenine [(*S*)-HPMPA][4] (Figure 1). Again, only the *S* isomer exhibited antiviral activity, whereas the *R* enantiomer is markedly less active. During the toxicological studies of (*S*)-DHPA, it was found that the compound inhibited spermatogenesis in mice. Moreover, the testicular dysfunction generated

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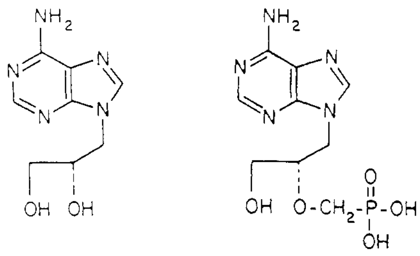
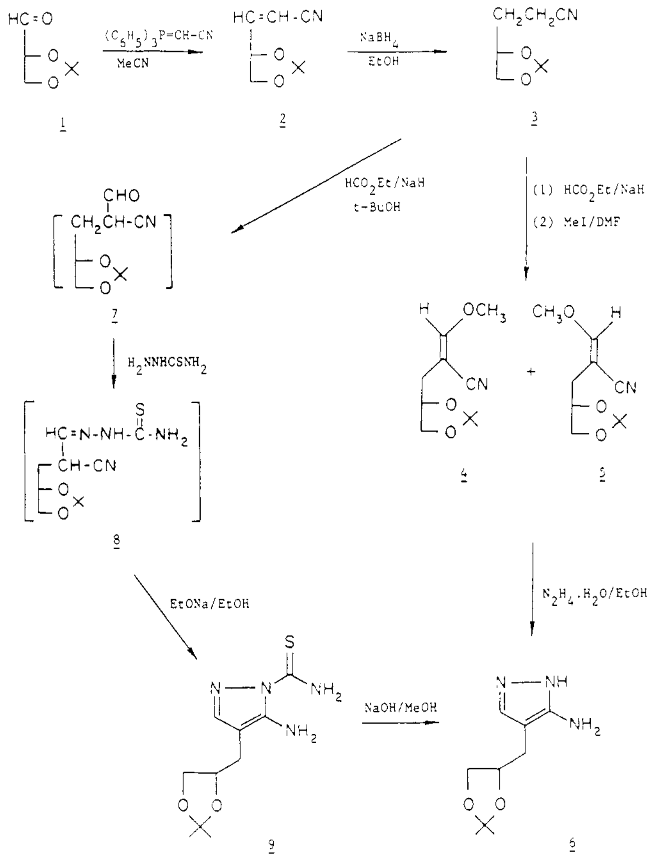


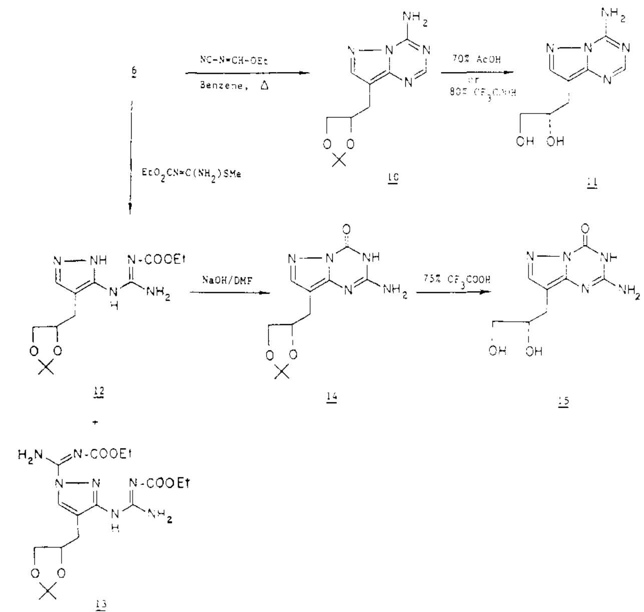
(S)-DHPA (S)-HPMPA

**Figure 1.**

**Scheme I**



**Scheme II**



by (*S*)-DHPA was fully reversible.[5] Therefore, it was of interest to synthesize the C-nucleoside analogues of (*S*)-DHPA as antiviral as well as antifertility agents for males.

## Results and Discussion

In order to obtain the necessary starting material **3**, glyceraldehyde derivative **1**[6-8] was reacted with (cyanomethylene)triphenylphosphorane to yield a mixture of cis and trans isomers **2** in a ratio of 1:4, which was selectively reduced with sodium borohydride to **3** (Scheme I). Initially, **3** was formylated with ethyl formate by using the method reported earlier[9] to form the aldehyde enolate, which was methylated by methyl iodide to give a mixture of the cis and trans isomers **4** and **5**. This mixture was chromatographically separated and the structural assignments for the compounds **4** and **5** were made on the basis of $^1$H NMR spectroscopy. The isomer with the more deshielded olefinic proton was assigned the *E* configuration **5** in which the olefinic hydrogen and the cyano group are cis oriented. The counterpart was assigned the *Z* configuration **4**.[10] The mixture of **4** and **5** was treated with hydrazine in refluxing ethanol[11] to yield the desired 3-aminopyrazole derivative **6** (27% yield). In view of the fact that the 3-aminopyrazole **6** was obtained in poor yield, an alternate approach was employed for the synthesis of **6** from **7**. The 2-formylpropionitrile **7** was condensed with thiosemicarbazide under acidic condition[12] to afford thiosemicarbazone **8**. The thiosemicarbazone **8**, without isolation, was treated with sodium ethoxide to yield 2-(thiocarbamoyl)-3-aminopyrazole derivative **9**, which was hydrolyzed with sodium hydroxide to give an improved yield (77%) of **6**. It was advantageous to use this procedure because **9** could be isolated as a crystalline compound. Furthermore, **9** can be used as a starting material for the synthesis of the 6-mercaptopurine analogue **17**.

The C-nucleoside analogue of (*S*)-DHPA, **11** was prepared by reacting **6** and *N*-cyanoformimidate[13,14] to yield **10**, followed by deblocking the isopropylidene group with 80% trifluoroacetic acid or 70% acetic acid (Scheme II). The guanine analogue **15** was also prepared from **6**. Reaction of *N*-(ethoxycarbonyl)-*S*-methylisothiourea with **6** gave a mixture of three compounds on TLC. On cooling the mixture a white solid precipitated, which was found to be **14** (4% yield). The two other components in the filtrate were separated and found to be **12** and **13** on the basis of spectral characteristics.[15,16] The guanine analogue **14** was obtained in much higher yield by the treatment of **12** with sodium hydroxide. The final product **15** was

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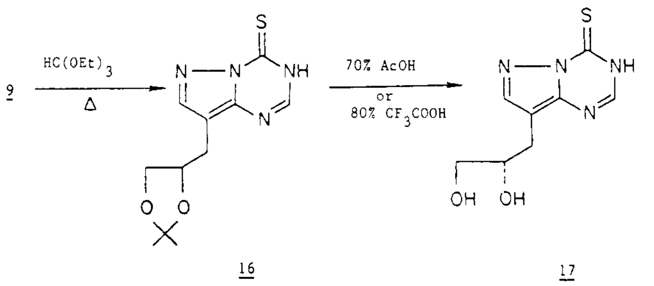
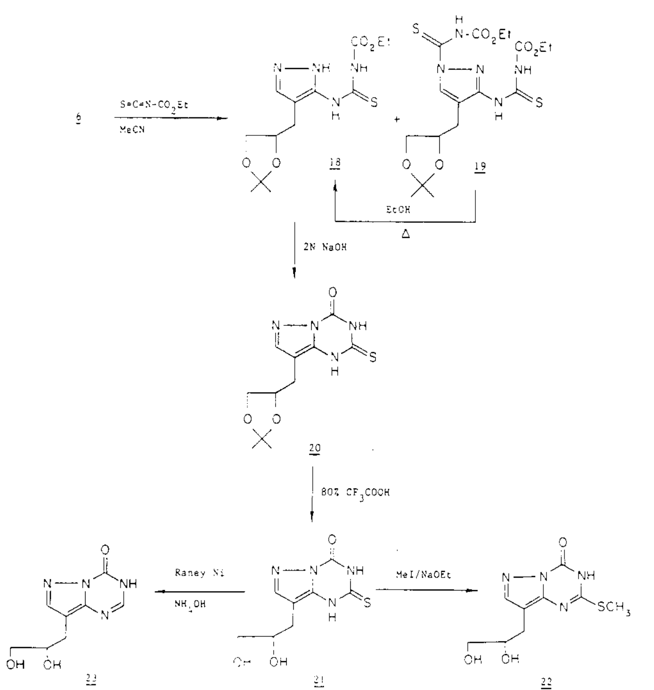
**Scheme III**



**Scheme IV**



readily obtained by deprotecting the isopropylidene group with trifluoroacetic acid.

In order to synthesize 6-mercaptopurine analogue **17**, **9** was reacted with triethyl orthoformate according to the reported procedure[12] to give **16**, which was then treated with 80% trifluoroacetic acid to afford the desired compound **17** in good yield (74%) (Scheme III).

The inosine analogue **23** was also prepared from the 3-aminopyrazole derivative **6** according to the procedure previously described.[11] From the reaction of **6** and ethoxycarbonyl isothiocyanate, a mixture of **18** and **19** was obtained (Scheme IV). However, in contrast to the stability of **13**, the thiourea derivative **19** (yellow) was found to undergo conversion to **18** (colorless) in refluxing ethanol.[15,16] The cyclization of **18** to **20** was readily achieved with 2 N NaOH. The inosine analogue **23** was then obtained from **20** by acid treatment followed by desulfurization with Raney nickel.[15]

Since (*S*)-DHPA was found to be a potent inhibitor of *S*-adenosylhomocysteinase,[17] compound **11** was tested in the system. However, **11** was found to be a poor inhibitor ($K_I$ = 334 nM). Other biological testings are in progress and will be reported elsewhere.

## Experimental Section

Melting points were determined on a Thomas Hoover capillary apparatus and are uncorrected. $^1$H NMR spectra were recorded on a JEOL FX 90Q Fourier transform spectrometer or a Bruker AM 250 NMR spectrometer for the 90- and 250-MHz $^1$H NMR spectra, respectively, using $Me_4Si$ as internal standard; chemical shifts are reported in parts per million ($\delta$) and signals are quoted as s (singlet), d (doublet), t (triplet), q (quintet), or m (multiplet). UV spectra were obtained on a Bausch and Lomb Spectronic 2000 spectrometer. IR spectra were taken on a Perkin-Elmer 684 spectrophotometer. Optical rotations were measured on a Perkin-Elmer 141 polarimeter. TLC was performed on Uniplates (silica gel) purchased from Analtech Co. Elemental analyses were performed by Atlantic Microlab Inc., Atlanta, GA.

**3-(2,2-Dimethyl-1,3-dioxolan-4-yl)acrylonitrile (2).** A mixture of 2,3-*O*-isopropylidene-D-glyceraldehyde (**1**)[6-8] (32.5 g, 250 mmol) and (cyanomethylene)triphenylphosphorane (82.7g, 275 mmol) in dry MeCN (750 mL, dried over 4A molecular sieves), was refluxed for 2 h.[9] The solvent was removed by distillation in vacuo, and the residue was dissolved in $Et_2O$ (275 mL). The $Ph_3PO$ separated on cooling. The mixture was filtered, and the filtrate was concentrated to a syrup. The syrup was purified by vacuum flash chromatography on silica gel column (17 × 8.5 cm) using hexanes–ethyl acetate (4:1) as the eluent. Fractions were monitored by TLC and compound **2** was obtained as a colorless liquid 23.0 g (61%) after the evaporation of appropriate fractions: IR (neat) 2230 (CN) and 1640 cm$^{-1}$ (C=C); $^1$H NMR ($CDCl_3$) $\delta$ 1.38 (s, 3 H, $CH_3$), 1.44 (s, 3 H, $CH_3$), 3.59–3.75 (m, 1 H, H-2′), 4.11–4.35 (m, 1 H, H-2′), 4.5–4.77 (m, ~0.8 H, H-1′ of trans isomer), 4.8–5.12 (m, ~0.2 H, H-1′ of cis isomer), 5.47 (dd, $J$ = 11.21, 1.00 Hz, ~0.2 H, H-2 of cis isomer), 5.71 (dd, $J$ = 16.04, 1.76 Hz, ~0.8 H, H-2 of trans isomer), 6.50 (dd, $J$ = 11.21, 8.01 Hz, ~0.2 H, H-3 of cis), 6.71 (dd, $J$ = 16.04, 4.61 Hz, ~0.8 H, H-3 of trans). Thus, the complex of olefinic signals that integrated for one proton each at $\delta$ 5.37–5.8 and 6.35–6.83 indicated a mixture of cis and trans isomers in a ratio of 1:4.

Anal. Calcd for $C_8H_{11}NO_2$: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.63; H, 7.25; N, 9.08.

**3-(2,2-Dimethyl-1,3-dioxolan-4-yl)propionitrile (3).** To a well stirred suspension of $NaBH_4$ (5.67 g, 150 mmol) in absolute EtOH (60 mL) was added dropwide a solution of **2** (23.0g, 150 mmol) in absolute EtOH (60 mL) during 1 h. The mixture was stirred at 0–5 °C for 1 h and then at room temperature for 0.5 h. The solvent was removed by distillation under reduced pressure. The residue was stirred with $CHCl_3$ (250 mL) for 0.5 h and filtered. The filter cake as washed with $CHCl_3$ (50 mL). The filtrate and the washings were combined and washed with water until the washings became neutral. The $CHCl_3$ layer was dried ($Na_2SO_4$) and filtered. Concentration of the filtrate yielded a pale yellow syrup, which was purified by flash chromatography on silica gel column (15 × 8 cm) using hexanes–ethyl acetate (4:1) as the eluent. After the evaporation of the solvent from appropriate fractions, **3** was obtained as a colorless liquid (15 g, 64%): IR (neat) 2250 cm$^{-1}$ (CN); $^1$H NMR ($CDCl_3$) $\delta$ 1.34 (s, 3 H, $CH_3$), 1.40 (s, 3 H, $CH_3$), 1.66–2.04, (m, 2 H, H-3) 2.5 (t, $J$ = 7.2 Hz, 2 H, H-2), 3.44–3.72 (m, 1 H, H-4), 3.95–4.35 (m, 2 H, H-5).

Anal. Calcd for $C_8H_{13}NO_2$: C, 61.91; H, 8.44; N, 9.03. Found: C, 61.85; H, 8.47; N, 8.97.

**(*Z*)- and (*E*)-2-[(2,2-Dimethyl-1,3-dioxolan-4-yl)-methyl]-3-methoxyacrylonitrile (4 and 5).** To a well-stirred suspension of NaH (3 g, 50% in mineral oil) in absolute $Et_2O$ (60 mL) was added absolute EtOH (0.4 mL), followed by a mixture of **3** (9 g, 58 mmol), $HCO_2Et$ (20 mL, dried over 4A molecular sieves) and absolute EtOH (0.4 mL) in anhydrous $Et_2O$ (30 mL).[9] The mixture was stirred at room temperature for 12 h, and the solvents were removed by distillation under reduced pressure (<30 °C). The residue was dissolved in DMF (75 mL), and then MeI (16.4 g, 116 mmol) was added dropwise during 0.5 h. The mixture was stirred at room temperature for 12 h and then poured into ice–water mixture (500 L). The aqueous solution was then extracted with $CHCl_3$ (75 mL × 4). The combined organic extracts were washed with water, dried ($Na_2SO_4$), and evaporated in vacuo to yield a syrup. TLC (hexanes–ethyl acetate, 4:1) of the product showed the presence of at least four components. ($R_f$ 0.40, 0.34, 0.31, and 0.13). The major two components with low $R_f$ were separated by column chromatography on silica gel (7.5 × 5 cm) using hexanes–ethyl acetate (8:1) as the eluent. The IR and $^1$H NMR spectra of these separated fractions indicated that the compound with $R_f$ 0.31 on TLC is the *Z* isomer,[10] (0.7 g, 6%) **4**:

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IR (neat) 2215 (CN) and 1645 cm$^{-1}$ (C=C); $^1$H NMR ($CDCl_3$) δ 1.35 (s, 3 H, $CH_3$), 1.43 (s, 3 H, $CH_3$), 2.16–2.68 (m, 2 H, H-1′), 3.62 (dd, J = 7.2, 9 Hz, 1 H, H-2′), 3.84 (s, 3 H, $OCH_3$) 3.96–4.36 (m, 2 H, H-2′ and -3′), 6.87 (s, 1 H, H-3).

Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 60.96; H, 7.71; N, 7.05.

The compound with $R_f$ 0.13 on TLC was found to be the *E* isomer **5** (0.8 g, 7%): IR (neat) 2220 (CN) and 1650 cm$^{-1}$ (C=C); $^1$H NMR ($CDCl_3$) δ 1.35 (s, 3 H, $CH_3$), 1.42 (s, 3 H, $CH_3$), 2.3 (d, 2 H, H-1′), 3.62 (dd, J = 5.4, 9 Hz, 1 H, H-2′), 3.85 (s, 3 H, $OCH_3$), 3.95–4.38 (m, 2 H, H-3′), 6.67 (s, 1 H, H-3).

Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.89; H, 7.67; N, 7.10. Found: C, 60.99; H, 7.68; N, 7.04.

**3-Amino-4-[2,3-(isopropylidenedioxy)-1-propyl]pyrazole (6). Method A. From the (*Z*)- and (*E*)-3-Methoxyacrylonitriles 4 and 5.** A solution of hydrazine hydrate (1.25 g, 25 mmol) in absolute EtOH (5 mL) was added dropwise to a solution of a mixture of **4** and **5** (0.98 g, 5 mmol) in absolute EtOH (10 mL). The mixture was refluxed for 36 h and cooled. After neutralization of the mixture with 1 N HCl, it was extracted with $CHCl_3$ (50 mL × 3), and the $CHCl_3$ extract was dried ($Na_2SO_4$) and evaporated in vacuo to a brownish syrup. TLC on silica gel ($CHCl_3$–MeOH, 10:1) showed the presence of at least three components, of which the compound with $R_f$ 0.53 was found to be identical with the product obtained by the hydrolysis of thiocarbamoyl derivative **9**. Compound **6** was isolated after preparative TLC of the reaction mixture on silica gel plates (20 × 20 cm) using $CHCl_3$–MeOH (10:1) as solvent system (0.28 g, 27% yield): UV $\lambda_{max}$(pH 1) 245 nm and $\lambda_{max}$(pH 8) 231 nm.

Anal. Calcd for $C_9H_{15}N_3O_2{\cdot}0.5H_2O$: C, 52.43; H, 7.70; N, 20.39. Found: C, 52.11; H, 7.45; N, 20.17.

**Method B. By the Hydrolysis of 2-(Thiocarbamoyl)pyrazole 9.** To a solution of **9** (5.6 g; 22 mmol) in MeOH (80 mL) was added 2 N NaOH in MeOH (40 mL) at once, and the mixture was heated at 50–60 °C for 2 h. After cooling, the reaction mixture was neutralized with acetic acid. Solvents were distilled off, and the residue was triturated with $CHCl_3$ (100 mL). The mixture was filtered, and the filtrate was concentrated to small volume. This was further purified by vacuum flash chromatography on a silica gel column (7.5 × 6 cm) using $CHCl_3$–MeOH (10:1) as solvent system. Evaporation of the appropriate fractions yielded 3-aminopyrazole **6** as a syrupy liquid, 3.3 g (77%): UV $\lambda_{max}$(pH 1) 244 nm (ε 6700) and $\lambda_{max}$(pH 8) 231 nm (ε 4560); IR (neat) 3330 and 3220 cm$^{-1}$ ($NH_2$); $^1$H NMR ($CDCl_3$) δ 1.35 (s, 3 H, $CH_3$), 1.40 (s, 3 H, $CH_3$), 2.38–2.82 (m, 2 H, H-1′), 3.58 (dd, J = 7.3, 7.6 Hz, 1 H, H-3′), 4.0 (dd, J = 6.0, 7.6 Hz, 1 H, H-3′), 4.1–4.4 (m, 1 H, H-2′), 5.14 (br s, 3 H, NH and $NH_2$, exchangeable), 7.14 (s, 1 H, H-5).

**3-(2,2-Dimethyl-1,3-dioxolan-4-yl)-2-formylpropionitrile (7).** To a well-stirred suspension of NaH (7.16 g, 60% in mineral oil) in anhydrous $Et_2O$ (150 mL) was added *t*-BuOH (2.5 mL), followed immediately by a mixture of **3** (19.5 g, 125 mmol), $HCO_2Et$ (40 mL, dried over 4A molecular sieves), and *t*-BuOH (2.5 mL) in anhydrous $Et_2O$ (70 mL). The mixture was stirred at room temperature for 15 h. To the resulting slurry was added water (250 mL), and the organic layer was separated. The aqueous layer was washed with $Et_2O$ (200 mL). The combined etheral solution was dried ($Na_2SO_4$) and concentrated in vacuo to recover the unreacted nitrile derivative **3**. The aqueous solution was acidified to pH 6–7 by using dilute AcOH and then extracted with ethyl acetate (100 mL × 5). Ethyl acetate extracts were combined, dried ($Na_2SO_4$), and concentrated in vacuo below 40 °C. Crude **7** obtained as a pale yellow syrup (11.0 g, 48%) was used in the next reaction without purification.

**3-Amino-4-[2,3-(isopropylidenedioxy)-1-propyl]-2-(thiocarbamoyl)pyrazole (9).** A mixture of 2-formylpropionitrile **7** (14.66 g, 80 mmol), thiosemicarbazide (10.21 g, 112 mmol), AcOH (14 mL), water (70 mL), and EtOH (240 mL) was heated at 75–80 °C for 1.5 h. The solvents were removed by distillation in vacuo below 50 °C. The resulting syrup was triturated with water (200 mL). The aqueous layer was separated by decantation. The gummy residue was dried in vacuo for 24 h and dissolved in absolute EtOH (200 mL). The resulting solution was treated dropwise with 1 M NaOEt solution in EtOH until alkaline to litmus and stirred for 30 min. The reaction mixture was then acidified with AcOH, and the solvents were evaporated in vacuo below 40 °C. The syrupy residue on trituration with hexanes yielded a crystalline solid (10.5 g, 51%). Recrystallization from EtOH at 40–50 °C yielded analytically pure **9**: mp 111–113 °C; UV $\lambda_{max}$(pH 2) 240 (ε 9900) and 272 nm (14700), $\lambda_{max}$(pH 7) 240 (ε 11200) and 274 nm (14900); IR (KBr) 3420 and 3300 cm$^{-1}$ ($NH_2$); $^1$H NMR ($Me_2SO$-$d_6$) δ 1.26 (s, 3 H, $CH_3$), 1.32 (s, 3 H, $CH_3$), 2.51 (d, J = 6.15 Hz, 2 H, H-1′), 3.49 (dd, J = 7.91, 6.74 Hz, 1 H, H-3′), 3.94 (dd, J = 7.91, 6.74 Hz, 1 H, H-3′), 4.2 (q, J = 6.4 Hz, 1 H, H-2′), 7.30 (s, 1 H, H-5), 9.08 (br s, 1 H, $NH_2$), exchangeable) 9.45 (br s, 1 H, $NH_2$ exchangeable).

Anal. Calcd for $C_{10}H_{16}O_2N_4S$: C, 46.86; H, 6.29; N, 21.86; S, 12.51. Found: C, 46.83; H, 6.29; N, 21.82; S, 12.46.

**4-Amino-8-[2,3-(isopropylidenedioxy)-1-propyl]pyrazolo[1,5-*a*]-1,3,5-triazine (10).** To a warm solution of *N*-cyanoformimidate (3.9 g, 40 mmol) in $C_6H_6$ (50 mL) was slowly added a solution of aminopyrazole **6** (3.95 g, 20 mmol) in $C_6H_6$ (100 mL). The mixture was heated at reflux for 6 h and cooled. Solvents were removed by evaporation in vacuo, and the resulting syrupy residue was stirred with $CHCl_3$ (100 mL) for 1 h. $CHCl_3$ extract was washed with water (15 mL), dried ($Na_2SO_4$), and concentrated under reduced pressure. Pale yellow crystalline solid obtained was recrystallized from hexanes–ethyl acetate to yield 2.0 g (40%) of **10**: mp 184–185 °C; UV $\lambda_{max}$(pH 1) 223 (ε 11900) and 256 nm (6100), $\lambda_{max}$(pH 8) 274 nm (ε 11000), $\lambda_{max}$(pH 13) 274 nm (ε 11500); IR (KBr) 3280 and 3100 cm$^{-1}$ ($NH_2$); $^1$H NMR ($Me_2SO$-$d_6$, 250 MHz) δ 1.26 (s, 3 H, $CH_3$), 1.32 (s, 3 H, $CH_3$), 2.82 (dd, J = 6.9, 14.3 Hz, 1 H, H-1′), 2.88 (dd, J = 5.95, 14.3 Hz, 1 H, H-1′), 3.60 (dd, J = 6.0, 8.1 Hz, 1 H, H-3′), 3.93 (dd, J = 6.1, 8.1 Hz, 1 H, H-3′), 4.34 (q, J = 6.4 Hz, 1 H, H-2′), 8.04 (s, 1 H, H-2), 8.06 (s, 1 H, H-7), 8.31 (br s, 1 H, NH, exchangeable), 8.63 (br s, 1 H, NH, exchangeable).

Anal. Calcd for $C_{11}H_{15}N_5O_2$: C, 53.00; H, 6.07; N, 28.10. Found: C, 52.95; H, 6.08; N, 28.06.

**4-Amino-8-(2,3-dihydroxy-1-propyl)pyrazolo[1,5-*a*]-1,3,5-triazine (11).** A solution of **10** (1.70 g, 6.8 mmol) in 80% $CF_3COOH$ (27 mL) was stirred at room temperature for 10 min. Excess of acid was removed by distillation in vacuo. The residue was coevaporated with EtOH (10 mL) several times. The syrup obtained was dissolved in 0.1 N NaOH solution (50 mL) and stirred at 70 °C for 15–20 min. The mixture was concentrated in vacuo, and the residue was dissolved in 50% EtOH (50 mL). The solution was neutralized with weak acid resin. After filtration, the filtrate was concentrated in vacuo, and the residue was coevaporated with EtOH (10 mL) several times to yield a colorless solid (1.2 g, 84%). Recrystallization from EtOH gave colorless crystals: mp 170–172 °C; $[\alpha]_D$ −24.3° (*c* 1, $H_2O$); UV $\lambda_{max}$(pH 1) 222 (ε 14000) and 257 nm (6200), $\lambda_{max}$(pH 8) 274 nm (ε 8700), $\lambda_{max}$(pH 13) 274 nm (ε 11500); IR (KBr) 3100–3400 cm$^{-1}$ (broad, $NH_2$, OH); $^1$H NMR ($Me_2SO$-$d_6$, 250 MHz) δ 2.58 (dd, J = 7.5, 14.5 Hz, 1 H, H-1′), 2.83 (dd, J = 5.0, 14.5 Hz, 1 H, H-1′), 3.24–3.39 (m, 2 H, H-3′), 3.65–3.78 (m, 1 H, H-2′), 4.57 (t, J = 5.7 Hz, 1 H, OH-3′, exchangeable), 4.69 (d, J = 5.05 Hz, 1 H, OH-2′, exchangeable), 8.01 (s, 1 H, H-2), 8.03 (s, 1 H, H-7), 8.25 (br s, 1 H, NH, exchangeable), 8.56 (br s, 1 H, NH, exchangeable).

Anal. Calcd for $C_8H_{11}N_5O_2$: C, 45.93; H, 5.30; N, 33.48. Found: C, 45.84; H, 5.35; N, 33.45.

Deblocking of **10** with 70% AcOH at 100 °C for 2 h also yielded **11**, in 73% yield.

**3-[*N*″-(Ethoxycarbonyl)guanidino]-4-[2,3-(isopropylidenedioxy)-1-propyl]-1*H*-pyrazole (12) and 1-[*N*′-(Ethoxycarbonyl)amidino]-3-[*N*″-ethoxycarbonyl)guanidino]-4-[2,3-(isopropylidenedioxy)-1-propyl]pyrazole (13).** To a solution of aminopyrazole **6** (3.75 g, 19 mmol) in boiling anhydrous $Et_2O$ (80 mL) was added, dropwise, a solution of *N*-(ethoxycarbonyl)-*S*-methylisothiourea[16] (6.16 g, 38 mmol) in $CH_2Cl_2$ (20 mL). The mixture was heated at reflux for 24 h and cooled to 20 °C. The fine precipitate obtained was collected by filtration. TLC (hexanes–ethyl acetate, 2:1) of the filtrate indicated the presence of three components [$R_f$ 0.93 (*N*-carbethoxy-*S*-methylisothiourea), 0.67 (minor), 0.21 (major)]. These three compounds were separated by vacuum flash chromatography on silica gel column (8 × 3.5 cm) using hexanes–ethyl acetate (1:1) as the eluent. After the evaporation of appropriate fraction, the less polar compound (0.7 g, 9%) was obtained as a syrup, which on trituration with hexanes yielded a colorless solid, identified as **13** by UV and NMR spectral characteristics: UV $\lambda_{max}$(pH 1)

293 nm (ε 19970), $\lambda_{max}$(pH 8) 222 (ε 11900) and 290 nm (27000), $\lambda_{max}$(pH 13) 284 nm (ε 21630); $^1$H NMR ($Me_2SO$-$d_6$) δ 1.21 (t, $J$ = 7.03 Hz, 6 H, 2 × $CO_2CH_2CH_3$), 1.26 (s, 3 H, $CH_3$), 1.32 (s, 3 H, $CH_3$), 2.63 (d, $J$ = 6.16 Hz, 2 H, H-1′), 3.43–3.67 (m, 1 H, H-3′), 3.75–4.4 (m, 6 H, H-2′, H-3′ and 2 × $CO_2CH_2CH_3$), 8.13 (s, 1 H, H-5), 8.37 (br s, 2 H, $NH_2$, exchangeable), 8.93 (br s, 2 H, $NH_2$, exchangeable), 10.2 (br s, 1 H, NH, exchangeable).

The more polar compound **12** was obtained as colorless crystals, 3.53 g (60%): UV $\lambda_{max}$(pH 1) 243 nm (ε 6230), $\lambda_{max}$(pH 8) 246 nm (ε 18580), $\lambda_{max}$(pH 13) 264 nm (ε 9830); $^1$H NMR ($Me_2SO$-$d_6$) δ 1.14 (t, $J$ = 7.03 Hz, 3 H, $CO_2CH_2CH_3$), 1.24 (s, 3 H, $CH_3$), 1.29 (s, 3 H, $CH_3$), 2.62 (d, $J$ = 6.15 Hz, 2 H, H-1′), 3.48 (m, 1 H, H-3′), 3.73–4.3 (m, 4 H, $CO_2CH_2CH_3$, H-2′ and -3′), 7.53 (s, 1 H, H-5), 8.23 (br s, 2 H, $NH_2$, exchangeable).

Attempts to prepare analytical sample of **12**, by recrystallization (hexanes–benzene) or by preparative TLC (hexanes–ethyl acetate, 2:1) resulted in the cyclization to yield **14**.

The white precipitate (0.15 g, 4%) obtained in the above reaction was identified as **14** by mp, TLC, and $^1$H NMR spectral characteristics with the authentic sample of **14** prepared by the base-catalyzed cyclization of **12** as described in the next reaction.

**2-Amino-8-[2,3-(isopropylidenedioxy)-1-propyl]-4-oxo-3,4-dihydropyrazolo[1,5-*a*]-1,3,5-triazine (14).** The aminopyrazole derivative **12** (3.11 g, 10 mmol) was dissolved in DMF (132 mL), and then the solution was treated with 1 N NaOH solution (18 mL). The mixture was stirred at room temperature for 5 h and neutralized with 1 N HCl. Solvents were evaporated in vacuo (<40 °C), and the residue was triturated with water. The colorless solid obtained was collected by filtration and dried (2.0 g, 75%). Recrystallization from EtOH gave pure **14**: mp 263–265 °C; UV $\lambda_{max}$(pH 1) 251 nm (ε 9890), $\lambda_{max}$(pH 8) 270 nm (ε 9700), $\lambda_{max}$ (pH 13) 265 nm (ε 10100); $^1$H NMR ($Me_2SO$-$d_6$) δ 1.25 (s, 3 H, $CH_3$), 1.32 (s, 3 H, $CH_3$), 2.4–2.85 (m, 2 H, H-1′), 3.56 (dd, $J$ = 7.92, 6.59 Hz, 1 H, H-3′), 3.89 (dd, $J$ = 7.92, 6.15 Hz, 1 H, H-3′), 4.24 (q, $J$ = 6.15 Hz, 1 H, H-2′), 6.63 (br s, 2 H, $NH_2$, exchangeable), 7.71 (s, 1 H, H-7), 11.2 (br s, 1 H, NH, exchangeable).

Anal. Calcd for $C_{11}H_{15}N_5O_3{\cdot}0.5H_2O$: C, 48.17; H, 5.88; N, 25.53. Found: C, 48.62; H, 5.74; N, 25.77.

**2-Amino-8-(2,3-dihydroxy-1-propyl)-4-oxo-3,4-dihydropyrazolo[1,5-*a*]-1,3,5-triazine (15).** A solution of **14** (1.8 g, 6.8 mmol) in 75% aqueous $CF_3COOH$ (27 mL) was stirred at room temperature for 5 min and then concentrated to a syrup in vacuo (>35 °C). The residue was coevaporated with EtOH (10 mL) several times. Solid obtained was triturated with cold water (5 mL), collected by filtration, and dried. Recrystallization from hot water yielded 1.2 g (78%) of **15** as colorless crystals: mp 259–261 °C; $[\alpha]_D$ −33.6° ($c$ 1, $Me_2SO$); UV $\lambda_{max}$ (pH 2) 250 nm (ε 9100), $\lambda_{max}$(pH 7.5) 268 nm (ε 10900), $\lambda_{max}$(pH 12) 266 nm (ε 11000); $^1$H NMR ($Me_2SO$-$d_6$) δ 2.2–2.75 (m, 2 H, H-1′), 3.29 (d, $J$ = 5.28 Hz, 2 H, H-3′), 3.4–3.7 (m, 1 H, H-2′), 4.3–4.9 (br m, 2 H, OH-2′ and -3′, exchangeable), 6.63 (br s, 2 H, $NH_2$, exchangeable), 7.69 (s, 1 H, H-7).

Anal. Calcd for $C_8H_{11}N_5O_3$: C, 42.56; H, 4.91; N, 31.27. Found: C, 42.52; H, 4.94; N, 31.06.

**8-[2,3-(Isopropylidenedioxy)-1-propyl]-4-thioxo-3,4-dihydropyrazolo[1,5-*a*]-1,3,5-triazine (16).** A mixture of **9** (1.03 g, 4 mmol) and $HC(OEt)_3$ (15 mL) was heated at 100–105 °C for 2 h and cooled. The precipitate obtained was filtered, washed with EtOH (5 mL), and dried. Recrystallization from $C_6H_6$-MeOH yielded the analytical sample, 0.46 g (43%): mp 248–250 °C; UV $\lambda_{max}$(pH 2) 278 nm (ε 24400), $\lambda_{max}$(pH 6) 276 (ε 19250) and 311 nm (9900), $\lambda_{max}$(pH 12) 274 (ε 14430) and 312 nm (10730); IR (KBr) 3100 cm$^{-1}$ (NH); $^1$H NMR ($Me_2SO$-$d_6$) δ 1.25 (s, 3 H, $CH_3$), 1.31 (s, 3 H, $CH_3$), 2.83 (d, $J$ = 6.4 Hz, 2 H, H-1′), 3.57 (dd, $J$ = 8.5, 7.11 Hz, 1 H, H-3′), 3.93 (dd, $J$ = 8.5, 7.11 Hz, 1 H, H-3′), 4.33 (q, $J$ = 7.1 Hz, 1 H, H-2′), 7.8 (s, 1 H, H-2), 8.19 (s, 1 H, H-7).

Anal. Calcd for $C_{11}H_{14}N_4O_2S$: C, 49.61; H, 5.30; N, 21.04; S, 12.04. Found: C, 49.51; H, 5.31; N, 21.00; S, 12.09.

**8-(2,3-Dihydroxy-1-propyl)-4-thixo-3,4-dihydropyrazolo-[1,5-*a*]-1,3,5-triazine (17).** A solution of **16** (1.81 g, 6.8 mmol) in 80% $CF_3COOH$ (27 mL) was stirred at room temperature for 10 min and then evaporated to dryness in vacuo. The residue was coevaporated with EtOH (10 mL) for several times to remove residual $CF_3COOH$. The solid obtained was then crystallized from MeOH–$H_2O$ to yield 1.14 g (74%) of **17** as a white solid: mp 208–210 °C; $[\alpha]_D$ −22.2° ($c$ 1, $H_2O$); UV $\lambda_{max}$(pH 2) 278 nm, $\lambda_{max}$(pH 7) 277 (ε 20500) and 312 nm (9840), $\lambda_{max}$ (pH 12) 275 (ε 15200) and 322 nm (11100); $^1$H NMR ($Me_2SO$-$d_6$) δ 2.4–3.0 (m, 2 H, H-1′), 3.31 (d, $J$ = 5.47 Hz, 2 H, H-3′), 3.5–3.85 (m, 1 H, H-2′), 4.1–5.2 (br m, 2 H, OH-2′ and -3′, exchangeable), 7.96 (s, 1 H, H-2), 8.16 (s, 1 H, H-7).

Anal. Calcd for $C_8H_{10}N_4O_2S$: C, 42.47; H, 4.45; N, 24.76; S, 14.17. Found: C, 42.40; H, 4.45; N, 24.70; S, 14.09.

Compound **17** could also be obtained in 49% yield by deblocking **16** with 70% AcOH at 100 °C for 2 h.

***N*-(Ethoxycarbonyl)-*N′*-[4-[2,3-(isopropylidenedioxy)-1-propyl]pyrazol-3-yl]thiourea (18).** To a cold solution of aminopyrazole **6** (3.94 g, 20 mmol) in dry $CH_3CN$ (20 mL) was added a solution of ethoxycarbonyl isothiocyanate (3 g, 23 mmol) in $CH_3CN$ (10 mL), and the mixture was stirred at room temperature for 2 h. The solvents were removed in vacuo below 40 °C. TLC ($CHCl_3$–MeOH, 10:1) of the residue showed the presence of two major compounds. The residue was dissolved in EtOH (50 mL) and refluxed for 1 h. During this time the less polar compound ($R_f$ 0.82) was converted into more polar derivative ($R_f$ 0.62). On evaporation of the solvents, the colorless syrup obtained was chromatographed on silica gel column (10 × 6.5 cm) by using $CHCl_3$–MeOH (30:1) as the eluent. Evaporation of appropriate fractions yielded **18** as a colorless solid (3.0 g, 46%). Recrystallization from hexanes–ethyl acetate yielded analytically pure sample: mp 140–142 °C; IR (KBr) 3280, 3220, 3160 (NH) and 1725 cm$^{-1}$ (CO); $^1$H NMR ($CDCl_3$) δ 1.2–1.46 (m, 9 H, $CH_3$), 2.73 (d, $J$ = 5.56 Hz, 2 H, H-1′), 3.58 (t, $J$ = 7.62 Hz, 1 H, H-3′), 3.39–4.45 (m, 4 H, $CH_2$ and H-2′ and -3′), 7.46 (s, 1 H, H-5), 8.74 (br s, 1 H, NH, exchangeable), 11.45 (br s, 1 H, NH, exchangeable).

Anal. Calcd for $C_{13}H_{20}N_4O_4S$: C, 47.55; H, 6.14; N, 17.06; S, 9.76. Found: C, 47.62; H, 6.16; N, 17.05; S, 9.71.

**8-[2,3-(Isopropylidenedioxy)-1-propyl]-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrazolo[1,5-*a*]-1,3,5-triazine (20).** A solution *N*-carbethoxythiourea **18** (2.28 g, 7 mmol) in 2 N NaOH (15 mL) was stirred at room temperature for 3 h. The resulting solution was acidified with 10% AcOH to pH 7 and cooled. The precipitated solid was separated by filtration, dried, and recrystallized from $C_6H_6$–MeOH to afford 1.2 g (61%) of analytically pure **20**: UV $\lambda_{max}$(pH 1) 250 (ε 10410) and 290 nm (19300), $\lambda_{max}$(pH 7) 232 (ε 9800) and 305 nm (19850), $\lambda_{max}$(pH 12) 251 (ε 19480) and 292 nm (19300); $^1$H NMR ($Me_2SO$-$d_6$) δ 1.25 (s, 3 H, $CH_3$), 1.33 (s, 3 H, $CH_3$), 2.3–2.85 (m, 2 H, H-1′), 3.55 (dd, $J$ = 7.91, 6.74 Hz, 1 H, H-3′), 3.87 (dd, $J$ = 7.91, 5.81 Hz, 1 H, H-3′), 4.23 (q, $J$ = 6.4 Hz, 1 H, H-2′), 7.59 (s, 1 H, H-7), 10.8 (br s, 1 H, NH, exchangeable).

Anal. Calcd for $C_{11}H_{13}N_4O_3SNa{\cdot}H_2O$: C, 40.99; H, 4.69; N, 17.38; S, 9.95. Found: C, 41.14; H, 4.66; N, 17.33; S, 9.91.

**8-(2,3-Dihydroxy-1-propyl)-4-oxo-2-thioxo-1,2,3,4-tetrahydropyrazolo[1,5-*a*]-1,3,5-triazine (21).** A solution of **20** (0.94 g, 33 mmol) in 75% aqueous $CF_3COOH$ (13 mL) was stirred at room temperature for 10 min and concentrated to a syrup, in vacuo (35 °C). The residue was coevaporated several times with EtOH (10 mL). The solid obtained was recrystallized from hot water to yield 0.62 g (78%) of **21** as colorless crystals: mp 232–234 °C; $[\alpha]_D$ −32.9° ($c$ 1, $Me_2SO$); UV $\lambda_{max}$(pH 1) 250 (ε 10830) and 290 nm (20180), $\lambda_{max}$(pH 7) 245 (ε 8490) and 293 nm (21340), $\lambda_{max}$(pH 12) 250 (ε 21840) and 292 nm (16310); $^1$H NMR ($Me_2SO$-$d_6$) δ 2.2–2.84 (m, 2 H, H-1′), 2.9–3.4 (m, 2 H, H-3′), 3.4–3.75 (m, 1 H, H-2′), 4.1–5.0 (br m, 2 H, OH-2′ and -3′, exchangeable), 7.78 (s, 1 H, H-7), 12.65 (br s, 1 H, NH, exchangeable).

Anal. Calcd for $C_8H_{10}N_4O_3S$: C, 39.67; H, 4.61; N, 23.13; S, 13.23. Found: C, 39.60; H, 4.20; N, 23.10; S, 13.14.

**8-(2,3-Dihydroxy-1-propyl)-2-(methylthio)-4-oxo-3,4-dihydropyrazolo[1,5-*a*]-1,3,5-triazine (22).** Compound **21** (340 mg, 1.4 mmol) was dissolved in MeOH (6 mL) containing NaOMe (2.8 mmol), and then MeI (0.4 mL) was added. After the mixture was stirred for 0.5 h, the sodium salt separated was filtered, dissolved in minimum quantity of water, and acidified with 5% AcOH. The precipitated product was filtered, and recrystallization from MeOH afforded 0.23 g (64%) of the analytically pure product: mp 223–225 °C; $[\alpha]_D$ −34.9° ($c$ 1, $Me_2SO$); UV $\lambda_{max}$(pH 1) 243 nm (ε 3670), $\lambda_{max}$(pH 6) 245 nm (ε 5200), $\lambda_{max}$(pH 12) 255 nm (ε 7300); $^1$H NMR ($Me_2SO$-$d_6$) δ 2.3–2.9 (m, 2 H, H-1′), 2.55 (s, 3 H, $CH_3$), 3.31 (2 H, d, $J$ = 5.28 Hz, H-3′), 3.5–3.85 (m, 1 H, H-2′), 4.05–4.8 (br m, 2 H, OH-2′ and -3′, exchangeable), 7.89 (s, 1 H, H-7), 12.7 (br s, 1 H, NH, exchangeable).

Anal. Calcd for $C_9H_{12}N_4O_3S$: C, 42.18; H, 4.72; N, 21.86; S, 12.51. Found: C, 42.09; H, 4.74; N, 21.81; S, 12.60.

**8-(2,3-Dihydroxy-1-propyl)-4-oxo-3,4-dihydropyrazolo-[1,5-*a*]-1,3,5-triazine (23).** Raney nickel (1.4 g) was added to a solution of compound **21** (0.21 g, 1 mmol) in 3% $NH_4OH$ solution (10 mL). The suspension was heated at reflux for 1.5 h. The catalyst was separated by filtration of the hot suspension and washed with hot water (4 mL). The filtrate and the washings were combined, evaporated to 2 mL, and then acidified with 10% AcOH. The precipitated product was collected by filtration, dried, and recrystallized from MeOH to afford 0.15 g (71%) of analytically pure 4-oxopyrazolotriazine **23**: mp 225–227 °C; $[\alpha]_D$ −35.6° (*c* 1, $Me_2SO$); UV $\lambda_{max}$(pH 1) 265 nm ($\epsilon$ 8900), $\lambda_{max}$(pH 8) 265 nm ($\epsilon$ 9900), $\lambda_{max}$(pH 12) 271 nm ($\epsilon$ 9780); $^1H$ NMR ($Me_2SO$-$d_6$) $\delta$ 2.3–2.95 (m, 2 H, H-1′), 3.31 (d, $J$ = 5.49 Hz, 2 H, H-3′), 3.5–3.85 (m, 1 H, H-2′), 4.2–5.2 (br m, 2 H, OH-2′ and -3′, exchangeable), 7.95 (s, 1 H, H-2), 7.97 (s, 1 H, H-7).

Anal. Calcd for $C_8H_{10}N_4O_3$: C, 45.71; H, 4.80; N, 26.66. Found: C, 45.63; H, 4.83; N, 26.57.

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# Studies in the Cyclopropoarene Series: On the Polarity of Alkylidenecycloproparenes

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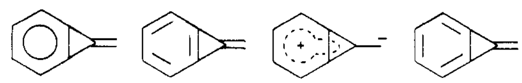
Permanent dipole moments of the alkylidenecycloproparenes **4–6**, **8–10**, and **14** fall in the range 0.4–2.6 D. The data confirm polarity in these compounds to an extent that is dependent upon the nature of the substituents attached to the exocyclic double bond. The experimentally determined values compare well with those computed for suitable model compounds at the 3-21G level. Fulvalene **14** with a cycloheptatrienylidene substituent is notable; the dipole of 1.2 D is in the *same* direction as the cyclopentadienylidene analogue **10** (2.6 D) and has the cycloproparenyl moiety as the positively charged component.

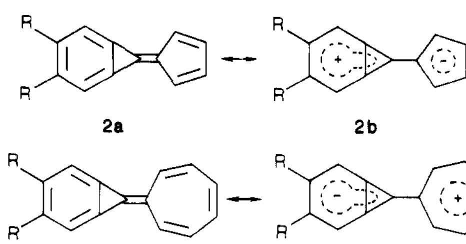
Strained organic molecules have attracted organic chemists for more than a century because of their unusual properties.[1] The strained ortho-bridged aromatics[2] and the cross-conjugated systems represented by the fulvenes[3] and radialenes[4] are interesting classes of compound in this context. The recently reported and surprisingly stable alkylidenecycloproparenes, e.g. **1**,[5] combine the structural



**1a** **1b** **1c** **1d**

features of these groups into a single molecule. Thus the ortho-fused **1a** may be regarded simultaneously as a benzannulated methylenecyclopropene (**1b**), a benzannulated triafulvene (**1b** ↔ **1c**), and an unusual radialene (**1d**).[6] A similar consideration of the cyclopentadienylidene homologue **2** shows that the "electron-sink" should stabilize charge separation further, cf. **2b**, when compared with **1c**. By comparison the electron-donating ability of the cycloheptatrienylidene moiety, coupled with the known stability of the cycloproparenyl anion,[5,7] could neutralize or even reverse the polarity in fulvalene **3** to favor **3b**. Thus the cycloproparenylidene substructure in these molecules is of particular interest as an ambiphile capable of stabilizing both positive and negative charge.

We now provide details of the synthesis of the new alkylidenecycloproparenes **5**, **7**, and **9**, the hitherto unknown[8] calicene derivatives **10** and **11**, and to the best of our knowledge the first examples of triaheptafulvalenes, namely compounds **12–15**. Dipole moment measurements[9,10] have been carried out on **4–6**, **8–10**, and **14** as representative examples of compounds currently available and the results compare well with ab initio molecular orbital calculations performed at the 3-21G level for suitable model systems.




**2a** **2b** **3a** **3b**

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