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ONE-POT SYNTHESIS OF PURINYLPURINE-2,6-DIONES

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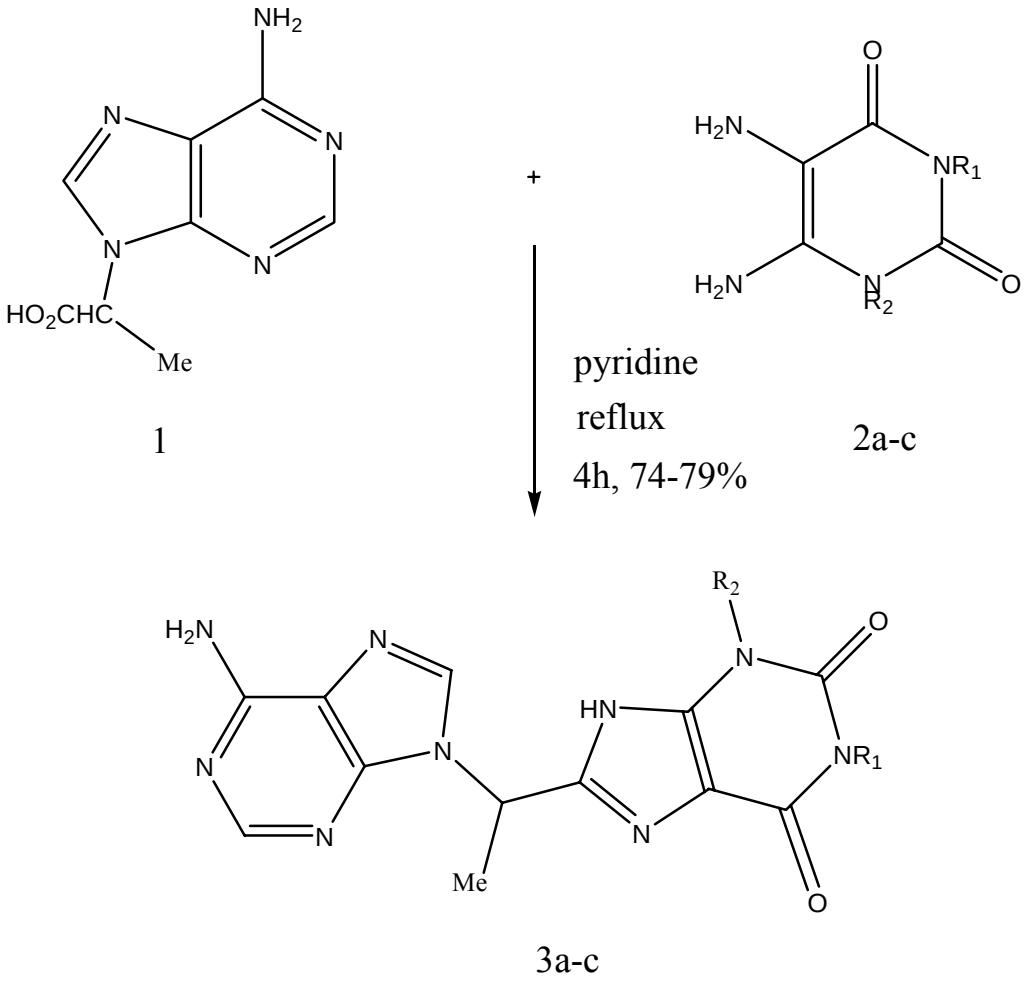
Abstract – Three new purinyl purine-2,6-diones have been synthesized in one-pot reaction.

Many optically active oligonucleotide derivatives with synthetic polymers have been reported[1-4] Such compounds have been prepared by reaction of α–nucleic acid base substituted propanoic acid with polyethylenimine, polyvinylamine, poly(vinyl alcohol) and polytrimethylenimine. Some of these analogues have shown antiviral activities.[5]

An α-nucleic acid base substituted propanoic acid is one of the simplest derivatives of α – nucleic acid base widely used as pendant group possessing an asymmetric center and acidic functional group. The carboxyl function present in such molecules is essential for optical resolution and grafting reaction. We have used the procedure of Mitsunobu *et al.*[6-7] for preparing (*R*)-2-(adenine-9-yl)propanoic acid **1**, the starting compound for present heterocyclic systems.

The ^{1}H and ^{13}C NMR spectra of the three compounds were measured at 300 MHz and 100 MHz respectively using Bruker (Avance) NMR instrument in $CDCl_3$ and the chemical shifts referenced to tetramethylsilane. Microanalysis was carried on a Carlo Erba 1108 instrument. Mass Spectra was taken on Jeol SX 102 spectrometer. All the chemicals used were of AR grade (Sigma, BDH, & E. Merck).



a: R_1=H, R_2=Me,. b: R_1=R_2=Me,. c: R_1=R_2=H

Scheme 1. Synthesis of purinylpurine-2,6-diones

General procedure for the synthesis of compounds (3a-3c)

A mixture of adenine (2.0 mmol) and triphenylphosphine (3.0 mmol) in THF (75 mL) was refluxed for 2 h. The reaction mixture was cooled to rt and diethyl azodicarboxylate (0.47 mL, 3.0 mmol) and (*S*)-ethyl lactate (0.48 mL, 4.0 mmol) were added dropwise. After reflux and usual work up involving acid hydrolysis, the desired compound **1,** $[\alpha]_D$ -46.1^0 (C 0.2, TFE-H_2O 1:1), in 72% yield was obtained by flash column chromatography on silica gel.

One pot condensation reaction between compound **1** (1.0 mmol) and **2a** (1.0 mmol) after reflux for 3-4 h afforded the desired product **3a** in 79 % yield after chromatographic separation on silica gel. The other two compounds in the series **3b** and **3c** were prepared by following the similar procedure in good yields. Compounds **2a-c** were prepared by literature methods[8] and chacterized by comparison with available

physicochemical data.

8-[1-(6-Aminopurin-9-yl)-ethyl]-3-methyl-3,9-dihydropurine-2,6-dione (3a)

Yield, 79 %, ^{1}H- NMR (300 MHz, $CDCl_3$) δ: 8 .06 (s, 1H, 2-H), 8.63 (s, 1H, 8-H), 5.12 (1H, CH), 1.88 (3H, C-CH_3), 2.72 (s, 3H, N-CH_3).^{13}C -NMR (100 MHz, $CDCl_3$) δ:166.9, 157.8, 155.5,154.7,151.9, 147.6,144.5, 135.9, 128.3, 54.6, 36.2, 20.7.m/z (FAB-MS) 327 (M^+). *Anal*. Calcd for $C_{13}H_{13}N_9O_2$: C, 47.70; H, 3.97; N, 38.53. Found: C,47.64; H, 3.94; N 38.56.

8-[1-(6-Aminopurin-9-yl)-ethyl]-1,3-methyl-3,9-dihydropurine-2,6-dione (3b)

Yield, 74 %,^{1}H- NMR (300 MHz, $CDCl_3$) δ: 8.04 (s, 1H, 2-H), 8.65 (s, 1H, 8-H), 5.09 (1H, CH), 1.86 (3H, C-CH_3), 2.68(s, 6H, 2N-CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 166.1, 157.7, 156.4, 154.6, 151.9, 147.7, 144.5,135.8, 128.3, 54.7, 36.6, 28.1, 20.9. m/z (FAB-MS) 341 (M^+). *Anal*. Calcd for $C_{14}H_{15}N_9O_2$: C, 49.26; H, 4.39; N, 36.95. Found: C, 49.21; H 4.37; N 36.91.

8-[1-(6-Aminopurin-9-yl)-ethyl]-3,9-dihydropurine-2,6-dione (3c)

Yield, 76 %, ^{1}H- NMR (300 MHz, $CDCl_3$) δ: 8.05 (s, 1H, 2-H), 8.66 (s, 1H, 8-H), 5.08 (1H, CH), 1.85 (3H, C-CH_3). ^{13}C-NMR (100 MHz, $CDCl_3$) δ: 167.1, 157.9, 154.8, 154.6, 151.8, 147.6, 144.6, 135.9, 128.4, 54.5, 20.8. m/z (FAB-MS) 313 (M^+). *Anal*. Calcd for $C_{12}H_{11}N_9O_2$:C, 46.00; H, 3.51; N, 40.25. Found: C, 46.05; H, 3.50; N, 40.21.

In summary, the heterocyclic compounds **3a-c** are being reported for the first time in literature. Such compounds can create great attention for chemists working in academics as well as industries for their diversified applications and uses.

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REFERENCES

1. C. G. Overberger and Y. J. Morishima, *Polym. Sci. Ploym. Chem. Ed*., 1980, **18**, 1247.
2. C. G. Overberger and S. J. Kikyotani, *Polym. Sci. Ploym. Chem. Ed*., 1983, **21**, 525, 541.
3. C. G. Overberger and C. X. Lu, J. *Polym. Sci. Ploym. Chem. Ed*., 1985, **23**, 1321.
4. C. C. Chen, Ph.D Dissertation, The University of Michigan, Ann Arbor, MI, **1985**.
5. J. Pitha, *Adv. Polym. Sci*., 1983, **50**, 1.

6. C. G. Overberger and J. Y. Chang, *Tetrahedron Lett*., 1989, **30**, 51.
7. O. Mitsunobu, *Synthesis*, 1981, **1**.
8. I. L. Finar, Organic Chemistry, 5th edn, (Longman Group Ltd, England) Vol. **2**, Ch. 16, p. 804, 805, 808, 809.