## Syntheses of Kinetin-analogs. I\*

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The discovery of kinetin<sup>1)</sup>, 6-(2-furfuryl)aminopurine (isolated from autoclaved

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Dotanicu, L. P. Botanicu, M. H. Von
1) C. O. Miller, F. Skoog, F. S. Okumura, M. H. Von
Saltza and F. M. Strong, J. Am. Chem. Soc., 77, 1392, 2662 (1955); 78, 1375 (1956).

TABLE I SYNTHESES OF 6-SUBSTITUTED PURINES

	Temp. (°C) and time (hr.) of run	Yield (%)	M. p. (°C)	Analysis						
Purine				c		H ·		N		
				Calcd	Found	Calcd	Found	Calcd	Found	
6-(2-Thenyl)-amino <sup>a)</sup>	120-30 <sup>e)</sup> , 12 hr. 120-5 <sup>c)</sup> , 10.	$\begin{array}{c} 19.3\\ 39.9 \end{array}$	247-7.50	52.17	51.94	3.48	3.70	30.43	30.18	
6-Benzylamino-b)	120-5 <sup>f</sup> ), 10.	44.3	229-30i)	64.29	64.01	4.46	4.76	31.25	31.00	
6-( <i>a</i> -Phenylethyl)- amino- <sup>c)</sup>	120-30°), 8.	54.2	240-1 <sup>i</sup> )	65.55	65.29	5.04	5.27	29.41	29.19	
6-(n-Amyl)-amino-	90-100°, 15.	36.7	164-5j)	58.82	58.50	6.86	7.03	34.31	34.15	
6-(n-Hexyl)-Amino-	130-5, 9.	31.0	177-8 <sup>k</sup> )	60.23	60.13	7.82	7.70			
6-(p-Methoxybenzyl)- amino-	120-30 <sup>e)</sup> , 8.	48.2	233-4 <sup>i</sup> )	61.42	61.15	4.72	5.00	27.56	27.28	
6-(3, 4-Dimethoxy- benzyl)-amino	120-5 <sup>(r)</sup> , 10.	48.1	240.5-1 <sup>i</sup> )	59.16	59.41	4.93	5.10	24.65	24.58	
6-(3, 4-Methylenedioxy- benzyl)-amino-	120-30 <sup>g</sup> ), 12.	40.3	259-60 <sup>i</sup> )	58.21	57.95	3.73	4.02	26.12	25.90	
6-Furfurylthio-d)	h)	26.2	$174-5^{k}$	51.72	52.56	3.47	3.70			

. 1 .

	TABLE I	I
SYNTHESES OF	6-SUBSTITUTED	3-METHYLPYRIDAZINES

	Temp. (°C) and time (hr.) of run	Yield (%)	M. p. (°Ĉ)	Analysis					
3-Methylpyridazine				c		H		N	
	(			Calcd	Found	Calcd	Found	Calcd	Found
6-(2-Furfuryl)-amino-	125 <sup>f)</sup> , 24 hr.	66.0	161-2 <sup>j</sup> )	63.49	63.68	5.82	6.06	22.22	22.05
6-Benzylamino-	100-30 <sup>c</sup> ), 18.	59.0	138.5-9 <sup>j</sup> )	72.36	72.10	6.53	6.68	21.11	21.01
6-Anilino-	100 <sup>r</sup> ), 1.	56.0	167.5-81)	71.35	71.51	5.95	6.14	22.70	22.82
6-(2-Thenyl)-amino-	130 <sup>f</sup> ), 20.	81.0	178-9 <sup>m</sup> )					20.49	20.21
6-(p-Methoxybenzyl)- amino-	1250, 18.	79.5	142-3 <sup>j</sup> )					18.34	18.25
6-(3, 4-Dimethoxy- benzyl)-amino-	135-40 <sup>f</sup> ), 16.	49.6	127-81)					16.22	16.01

a) M. p., 241.5-2°C<sup>3</sup>), M. p., 250°C<sup>4</sup>). b) M. p. 231°C<sup>3</sup>), M. p. 229°C<sup>4</sup>), M. p. 216-8°C<sup>2</sup>).

c) M. p., 199-202°C<sup>3</sup>). d) M. p., 178-8.5°C<sup>3</sup>). e) In H<sub>2</sub>-Stream. f) In sealed tube.

g) In air without  $CO_2$ . h) Prepared with 6-mercaptopurine and furfurylchloride in air.

i) Absolute alcohol j) Benzene (Solvents of recrystallization)

k) 60% alcohol 1) Water m) Alcohol

sperm deoxyribonucleic acid as a cell division factor for tobacco callus tissue), has stimulated an interest in preparing various 6-substituted purines through the use of 6-chloropurine<sup>2,3</sup>) or 6-methylmercaptopurine<sup>4)</sup> as possible cytokinetic agents.

Recently Kuraishi and Okumura<sup>5)</sup> found that kinetin is the leaf-growth factor for Raphanus sativus L.

In Tokushima we have synthesized various kinetin-analogs such as 6-substituted purines and 6-substituted 3-methylpyridazines by condensing 6-methylmercaptopurine<sup>6)</sup> and 6-chloro-3-methylpyridazine<sup>7</sup>) respectively with various amines. The results are shown in Tables I and II.

The biological test on 6-(2-thenyl)-amino-, 6-benzylamino- and 6-n-hexylamino-purines prove to have the same effect on the growth of Raphanus leaf as kinetin. It is very interesting that 6-benzylaminopurine shows leaf-growth activity but 6-phenylethylaminopurine does not.

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- 2) J. W. Daly and B. E. Christensen, J. Org. Chem., 21, 177 (1956).
- 3) M. W. Bullock, J. J. Hand and E. L. R. Stokstad, J. Am. Chem. Soc., 78, 3693 (1956).
  4) C. G. Skinner and W. Shive, ibid., 77, 6692 (1955).
  5) S. Kuraishi and F. S. Okumura, Bot. Mag. (1954).
- (Tokyo), 69, 300 (1956).
- 6) G. B. Elion, E. Burgi and G. H. Hitchings, J. Am. Chem. Soc., 74, 411 (1952).
- 7) W. G. Overend and L. F. Wiggins, J. Chem. Soc., 1947, 239.

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