Phytochemistry, 1972, Vol. 11, pp. 1623 to 1630. Pergamon Press. Printed in England.

CYTOKININ ACTIVITY OF AZAINDENE, AZANAPHTHALENE, NAPHTHALENE, AND INDOLE DERIVATIVES

YASUYOSHI TORIGOE, MINORU AKIYAMA, MASAAKI HIROBE and TOSHIHIKO OKAMOTO

Laboratory of Pharmaceutical Chemistry, Faculty of Pharmaceutical Sciences, University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113, Japan

and

YO ISOGAI

Biological Institute, College of General Education, University of Tokyo. Komaba, Meguro-ku, Tokyo 153, Japan

(*Received* 28 *September* 1971)

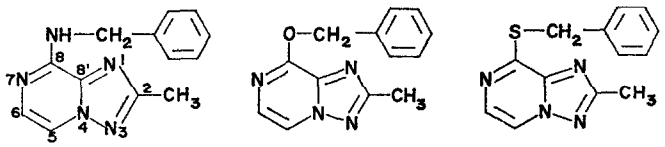
Abstract—Eight azaindenes, namely 8-benzylamino-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (I), 8-benzyloxy-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (II), 8-benzylthio-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (III), 6-benzylamino-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (IV), 6-benzyloxy-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (V), 6-benzylthio-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (VI), 8-benzylamino-2-methyl-*s*-triazolo[1,5-*a*]pyridine (VII), and 4(7)-benzylaminobenzimidazole (VIII), three azanaphthalenes, namely 5-benzylaminoquinoxaline (IX), 5-benzylaminoquinoline (X), and 8-benzylaminoquinoline (XI), a naphthalene α-benzylaminonaphthalene (XII), and four indoles 4-aminoindole (XIII), 4-benzylaminoindole (XIV), 7-aminoindole (XV), and 7-benzylaminoindole (XVI) were synthesized and tested for their cytokinin activity by the tobacco pith callus bioassay. Of these compounds, I, VII and VIII were active and at 20–40 μM gave a callus yield similar to that produced by an optimum concentration (10^{-1} μM) of kinetin; IV, VI, IX and X were slightly active, while II, III, V, XI, XIII, XIV, XV and XVI were almost or completely inactive.

INTRODUCTION

SINCE kinetin was first reported as an active agent for the growth of tobacco callus in the presence of auxin, various other biological activities have been studied[1] and used in the bioassay of kinetin.[2] Also, many homologues or analogues of kinetin have been synthesized and tested for kinetin activity by bioassay, and the structure–activity relationship has been discussed.[3]

At the same time, studies have been carried out on natural kinins and several active compounds have been isolated, zeatin,[4] 9-β-D-ribofranosylzeatin,[5] N^6-isopentenyladenine,[6,7] (—)-dihydrozeatin,[8] N^6-isopentenyladenosine,[9] 9-β-D-ribofuranosylzeatin-5′-phosphate,[10]

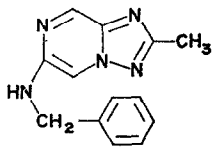
[1] C. O. MILLER, *Ann. Rev. Plant Physiol.* **12,** 395 (1961).
[2] D. S. LETHAM, *Ann. Rev. Plant Physiol.* **18,** 349 (1967).
[3] F. SKOOG, Q. HAMZI, A. M. SZEWEYKOWSDA, N. J. LEONARD, I. O. CARRAWAY, O. FUJII, J. P. HELGESON and R. N. LOEPPKY, *Phytochem.* **6,** 1169 (1967).
[4] D. S. LETHAM, *Life Sci.* **2,** 569 (1963).
[5] D. S. LETHAM, *Life Sci.* **5,** 551 (1966).
[6] H. G. ZACHAU, D. DÜTTING and H. FELDMANN, *Angew. Chem.* **78,** 392 (1966).
[7] R. H. HALL, *J. Am. Chem. Soc.* **88,** 2614 (1966).
[8] K. KOSHIMIZU, T. TUSAKI, T. MITSUI and S. MATSUBARA, *Tetrahedron Letters* **14,** 1317 (1967).
[9] R. H. HALL, *Biochem.* **6,** 1836 (1967).
[10] D. S. LETHAM, *Life Sci.* **5,** 1994 (1966).



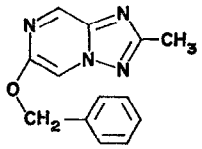
(I)

(II)

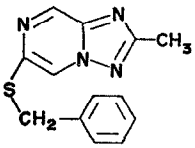
(III)



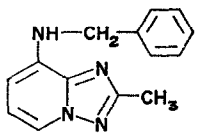
(IV)



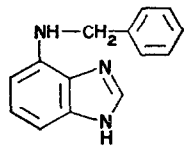
(V)



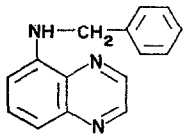
(VI)



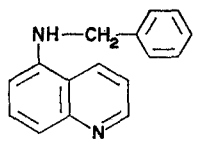
(VII)



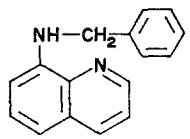
(VIII)



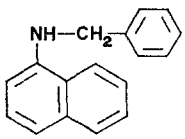
(IX)



(X)



(XI)



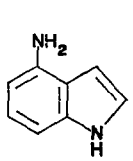
(XII)

6-(*cis*-4-hydroxy-3-methybut-2-enylamino)-9-β-D-ribofuranosylpurine,[11] *cis*-ribosylzeatin,[12] 6-(3-methylbut-2-enylamino)-2-methylthio-9-β-D-ribofuranosylpurine,[13] 1,3-diphenylurea,[14] and leucoanthocyanins.[15] Also, triacanthine, which is inactive itself, becomes active after autoclaving, possibly due to the formation of 6-(γ,γ-dimethyl-allylamino)-purine.[16] The generic term 'cytokinin' has been given to these compounds.[17]

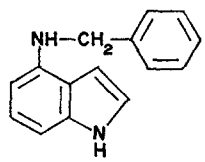
Most active compounds have a purine ring, but there are some exceptions. (1) 8-Azakinetin[18] and 6-benzylamino-8-azapurine[3] have activities similar to kinetin in various bioassay methods. (2) Kulayeva *et al.*[19] reported that some pyrimidines have cytokinin activity. (3) 4(7)-Benzylaminobenzimidazole (VIII), synthesized by Bräuniger and Koine[20] in 1966,

[11] R. H. HALL, L. CSONKA, H. DAVID and B. MCLENNAN, *Science* **156,** 69 (1967).
[12] D. S. LETHAM, *Life Sci.* **7,** 7 (1968).
[13] W. J. BURROWS, D. J. ARMSTRONG, F. SKOOG, S. M. HECHT, J. T. A. BAYLE, J. N. LEONARD and J. OCCOLOWITZ, *Science* **161,** 691 (1968).
[14] E. M. SHANTZ and F. C. STEWARD, *J. Am. Chem. Soc.* **77,** 6351 (1955).
[15] E. M. SHANTZ and F. C. STEWARD, *Plant Physiol.* **30** Suppl. XXXV (1963).
[16] J. H. ROGOZINSKA, J. P. HELGESON and F. SKOOG, *Physiol. Plantarum* **17,** 165 (1964).
[17] F. SKOOG, F. M. STRONG and C. O. MILLER, *Science* **148,** 534 (1965).
[18] F. C. STEWARD, E. M. SHANTZ, J. K. POLLARD, M. O. MAPES and J. MITRA, in *Synthesis of Molecular and Cellular Structure, 19th Growth Symposium* (edited by D. RUDNICK), pp. 193, Ronald Press, New York (1961).
[19] O. N. KULAYEVA, E. A. CHERNYSHEVA, L. A. KOLOTENKO, N. E. DOLGOVA, I. P. VOROBYOVA, E. A. POPOVA and M. E. KLYACHKO, *U.S.S.R. Acad. Sci. Mos.* **12,** 902 (1965).
[20] H. BRÄUNIGER and A. KOINE, *Arch. Pharmazie* **299,** 193 (1966).

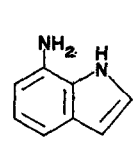
retention test under certain conditions, but to have no activity in the tobacco seed germination test and in the carrot callus assay. To explain these inconsistent results, Kuraishi and Yamaki suggested that VIII might be labile in dilute solution and concluded that a long-term test such as cultured callus assay was not suitable for the assay of its activity.[21] In this connection, benzimidazole itself was reported to be active in the chlorophyll retention assay.[22,23] (4) 1,3-Diphenylurea (DPU), isolated from coconut milk by Shantz and Steward,[14] promoted the growth of carrot root explant in the presence of casein hydrolysate and the absence of auxin,[24] and also induced growth in potato tuber explants and artichoke explants in the presence of 2,4-dichlorophenoxyacetic acid (2,4-D) or similar compounds.[25] Strong reported that DPU had activity in the tobacco pith callus bioassay at a rather higher concentration than kinetin but the effect seemed delayed and somewhat sporadic.[26] Miller reported that DPU was slightly active in his soybean callus bioassay.[27] Using the induction of cell division in tobacco pith tissue, senescence retardation of radish leaves, pea lateral bud development, and lettuce seed germination, Bruce *et al.* tested cytokinin activities of about 500 derivatives of urea and thiourea and concluded that many of them had consistent cytokinin activity.[28] By contrast, Kuraishi reported that DPU was quite inactive in his radish leaf disk test.[29] (5) Steward *et al.* reported that 2-benzothiazolyloxyacetic acid was



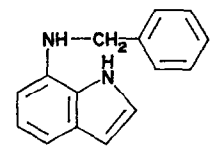
(XIII)



(XIV)



(XV)



(XVI)

TABLE 1. LIST OF COMPOUNDS TESTED FOR CYTOKININ ACTIVITY

I	8-Benzylamino-2-methyl-*s*-triazolo[1,5-*a*]pyrazine
II	8-Benzyloxy-2-methyl-*s*-triazolo[1,5-*a*]pyrazine
III	8-Benzylthio-2-methyl-*s*-triazolo[1,5-*a*]pyrazine
IV	6-Benzylamino-2-methyl-*s*-triazolo[1,5-*a*]pyrazine
V	6-Benzyloxy-2-methyl-*s*-triazolo[1,5-*a*]pyrazine
VI	6-Benzylthio-2-methyl-*s*-triazolo[1,5-*a*]pyrazine
VII	8-Benzylamino-2-methyl-*s*-triazolo[1,5-*a*]pyridine
VIII	4(7)-Benzylaminobenzimidazole
IX	5-Benzylaminoquinoxaline
X	5-Benzylaminoquinoline
XI	8-Benzylaminoquinoline
XII	α-Benzylaminonaphthalene
XIII	4-Aminoindole
XIV	4-Benzylaminoindole
XV	7-Aminoindole
XVI	7-Benzylaminoindole

[21] S. KURAISHI and T. YAMAKI, *Physiol. Plantarum* **20**, 208 (1967).
[22] D. J. OSBORNE and D. R. MCCALLA, *Plant Physiol.* **36**, 219 (1961).
[23] L. ENGELBRECHT, H. BRÄUNIGER and A. KOINE, *Flora* **158**, 109 (1967).
[24] F. C. STEWARD and S. M. CAPLIN, *Science* **113**, 518 (1951).
[25] E. M. SHANTZ, F. C. STEWARD, M. S. SMITH and R. L. WAIN, *Ann. Bot.* N.S. **19**, 49 (1955).
[26] F. M. STRONG, *Topics in Microbial Chemistry*, pp. 97, Wiley, New York (1958).
[27] C. O. MILLER, *Plant Physiol.* **35**, Suppl. XXVI (1960).
[28] M. I. BRUCE, J. A. ZWAR and N. P. KEFFORD, *Life Sci.* **4**, 461 (1965).
[29] S. KURAISHI, *Sci. Pap. Coll. Gen. Educ. Univ. Tokyo* **9**, 67 (1959).

active in the carrot tissue assay but was quite inactive in the tobacco callus assay and in the was reported by Kuraishi and Yamaki to be active in the radish leaf disk test and chlorophyll radish leaf disk assay.[18] (6) Leucoanthocyanins also seem to belong to this category of compounds.[15]

To further define structure-activity relationships, we synthesized seven new azaindenes I–VII, 4(7)-benzylaminobenzimidazole (VIII), three azanaphthalenes IX–XI, the former two having not yet been reported in the literature, a naphthalene (XII), and four indoles (XIII–XVI) and tested their cytokinin activity in the tobacco pith callus bioassay in the presence of 10 μM of β-indoleacetic acid (IAA). The results are reported here.

RESULTS AND DISCUSSION

Azaindene Compounds

2-Methyl-s-triazolo[1,5-a]*pyrazine derivatives.* First, 2-methyl-*s*-triazolo[1,5-*a*]pyrazine was synthesized and from it six kinetin analogues, I–VI, were synthesized. As shown in Fig. 1, I had a strong cytokinin activity at the concentration of 40 μM and always gave a better callus yield than that of the optimum concentration (10^{-1} μM) of kinetin. IV and VI were slightly active, while II, III and V were inactive.

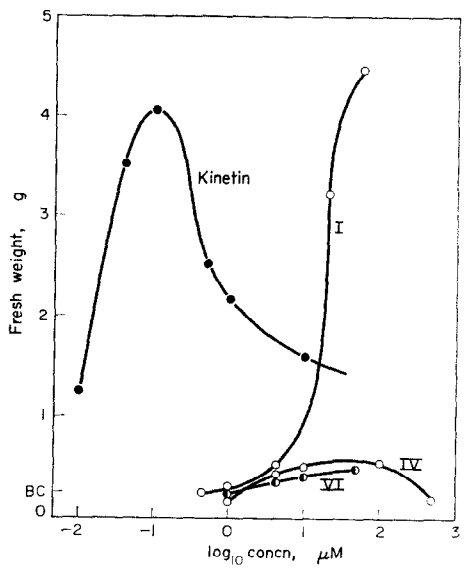


FIG. 1. EFFECT OF I, IV, VI AND KINETIN ON FRESH WEIGHT YIELDS OF TOBACCO CALLUS. Ordinate: Mean value of twelve calluses; BC: Basal medium control; Low solubility of compounds I and VI prevented their being tested in a concentration higher than 40 μM.

2-Methyl-s-triazolo[1,5-a]*pyridine derivatives.* Subsequently, 2-methyl-*s*-triazolo[1,5-*a*]-pyridine was synthesized, from which the kinetin analogue, VII, was prepared. As shown in Fig. 2, it has almost the same degree of cytokinin activity as I; thus, the nitrogen atom at position 7 in I–VI has nothing to do with cytokinin activity.

4(7)-Benzylaminobenzimidazole. In order to clarify whether the nitrogen atom at the 4-position in 2-methyl-*s*-triazolo[1,5-*a*]pyridine is necessary for cytokinin activity or not, 4(7)-benzylaminobenzimidazole (VIII) was synthesized by the method of Bräuniger and Koine,[21] and tested for its activity by the tobacco pith callus bioassay. As shown in Fig. 2,

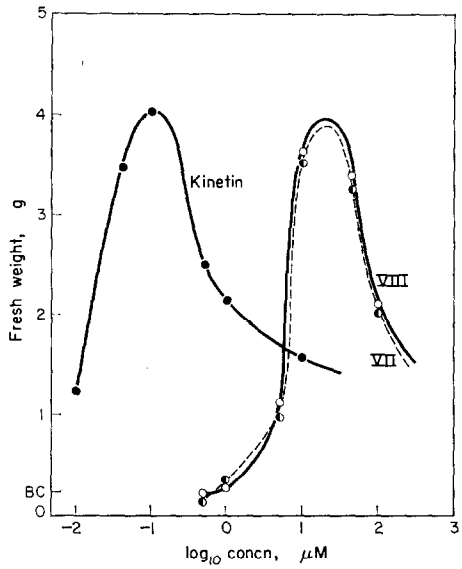


FIG. 2. EFFECT OF VII, VIII AND KINETIN ON FRESH WEIGHT YIELDS OF TOBACCO CALLUS. Ordinate: Mean Value of twelve calluses; BC: Basal medium control.

it had an activity similar to that of I and VII. This means that 4(7)-benzylaminobenzimidazole is not labile as has been suggested by Kuraishi and Yamaki[22] but has a definite activity in the tobacco pith callus bioassay.

Azanaphthalene Compounds

Three kinetin analogues (IX, X, XI) having an azanaphthalene ring instead of an indene ring were synthesized and tested by the same bioassay. Among them, 5-benzylaminoquinoxaline (IX) has a cytokinin activity at a concentration of 40 μM and gave a callus yield nearly 50 % of that produced by an optimum concentration of kinetin. 5-Benzylaminoquinoline (X) was also slightly active at a concentration of 40 μM and gave a callus yield about 25 % of that induced by the optimum concentration of kinetin, while XI was quite inactive. These results are shown in Fig. 3.

A Naphthalene

α-Benzylaminonaphthalene, a kinetin analogue having a naphthalene ring, was also synthesized and tested but it was inactive.

Indoles

Four indoles 4-aminoindole (XIII), 4-benzylaminoindole (XIV), 7-aminoindole (XV), and 7-benzylaminoindole (XVI) were synthesized and tested for their activity in the same bioassay. Among them, XIII and XIV were active but the activity was very weak and sporadic, while XV and XVI were quite inactive.

1,3-*Diphenylurea*

In view of the varying reports of the activity of 1,3-diphenylurea, we also tested it by the same bioassay. As shown in Fig. 3 it has a definite cytokinin activity at a concentration of

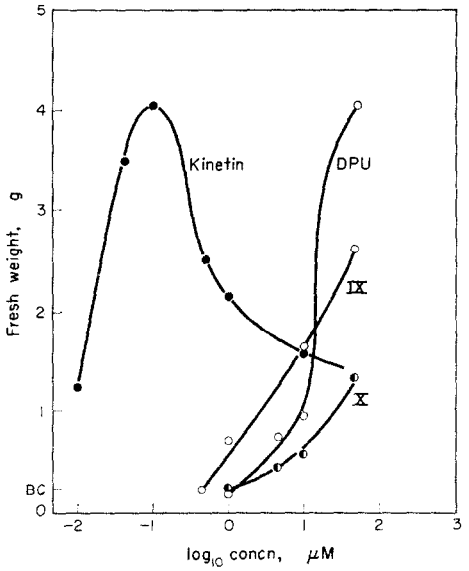


FIG. 3. EFFECT OF IX, X, DPU AND KINETIN ON FRESH WEIGHT YIELD OF TOBACCO CALLUS. Ordinate: Mean value of twelve calluses; BC: Basal medium control; Low solubility of compounds IX, X and DPU prevented their being tested in a concentration higher than 40 μM.

40 μM and gives a callus yield similar to that caused by the optimum concentration of kinetin, I, VII and VIII.

In discussing the activity of various cytokinins, two criteria have been considered, callus yield (or weight of callus) and the optimum concentration. The optimum concentration of kinetin (0·1 μM) is very low when compared with that of auxin and other plant growth regulators (4–40 μM). Hence, although optimum concentrations of I, VII, VIII and kinetin all produced similar callus yields, the optimum concentrations of the three kinetin analogues were 100–300 times the kinetin optimum. These analogues therefore possess only weak cytokinin activity. This finding extends the range of compounds without a purine ring now known to possess cytokinin activity.

EXPERIMENTAL

Bioassay procedures. Cytokinin activities were assayed by the method of Murashige and Skoog,[30] with the following modifications. Tobacco plants (*Nicotiana tabacum* cv. Bright Yellow*) were cultivated in a growth chamber (26° with nearly 6000 lx of fluorescent light mixed with incandescent light). Tests were carried out in test tubes containing 20 ml of culture medium and various concentrations of test compounds. Each tube was inoculated with 50–60 mg of the second generation of pith callus and the tubes were kept at 26° under weak diffuse light for 30 days. Fresh weight of the callus was measured and the mean value of fresh weight of twelve calluses was compared with that of basal and kinetin controls. Each sample was tested at least three times.

Synthesis of test substances. All UV spectra were determined in 95% EtOH Pyrazines (I–VI). *N*-2-Pyrazylacetamidine†, m.p. 127°,† UV λ_{max} 258 (14 000), 322 nm (ϵ 8300); NMR ($CDCl_3$) τ:1·27 (1 H, d, J = 1·5 cps, C_3-proton), 1·56 (1 H, q, J = 3 cps, J = 1·5 cps, C_5 or C_6-proton), 1·66 (1 H, d, J =3 cps,

* In the case of I, the test was also carried out with the pith callus of *Nicotiana tabacum* cv. Wisconsin No. 38 and the same result was obtained.

† Satisfactory elemental analyses were obtained for all the new compounds reported here. All m.ps. were measured on a micromelting point measuring apparatus and are uncorrected.

[30] T. MURASHIGE and F. SKOOG, *Physiol. Plantarum* **15**, 473 (1962).

C_5 or C_6-proton), 7·72 (3 H, s, C—H_3) was obtained by the reaction of 2-aminopyrazine with acetonitrile in the presence of $AlCl_3$. This amidine was readily cyclised by $Pb(OAc)_4$ in boiling HOAc to 2-methyl-*s*-triazolo[1,5-*a*]pyrazine, m.p. 132°; UV λ_{max} EtOH 283 nm (ϵ 4100); NMR ($CDCl_3$) τ:0·63 (1 H, d, J = 2 cps, C_8-proton), 1·34 (1 H, q, J = 5 cps, J = 2 cps, C_5 or C_6-proton), 1·71 (1 H, d, J = 5 cps, C_5 or C_6-proton), 7·27 (3 H, s, —CH_3). N-Oxidation with H_2O_2 in HOAc gave 2-methyl-*s*-triazolo[1,5-*a*]pyrazine 7-oxide, m.p. 228° (decomp.), UV λ_{max} 247 (13 500), 299 nm (ϵ 9100), NMR (CH_3COOH) τ:0·89 (1 H, d, J = 2 cps, C_8-proton), 1·16 (1 H, d, J = 6 cps, C_5 or C_6-proton), 1·80 (1 H, d, J = 6 cps, J = 2 cps, C_5 or C_6-proton), which afforded the original pyrazine by catalytic reduction over Raney nickel.

The reaction of the N-oxide with $POCl_3$ in boiling $CHCl_3$ gave two isomeric chloro derivatives, 8-chloro-2-methyl-*s*-triazolo[1,5-*a*]pyrazine, m.p. 111·5–112°, UV λ_{max} 292 nm (ϵ 5000), NMR ($CDCl_3$) τ:1·57 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 2·08 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 7·30 (3 H, s, —CH_3), and 6-chloro-2-methyl-*s*-triazolo[1,5-*a*]pyrazine, m.p. 112°, UV λ_{max} 294 nm (ϵ 5200), NMR ($CDCl_3$) τ:0·84 (1 H, s, C_5 or C_8-proton), 1·76 (1 H, s, C_5 or C_8-proton), 7·22 (3 H, s, —CH_3).

Condensation of the 8-chloro isomer with benzylamine in butanol, benzyl alcohol, or benzylthiol in MeOH provided I to III respectively. 8-Benzylamino-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (I), m.p. 136–137°, UV λ_{max} 260 (11 200), 266 (10 700), 303 nm (ϵ 7500), NMR ($CDCl_3$) τ:2·24 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 2·50 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 2·68 (5 H, s, benzene ring protons), 3·70 (1 H, broad, —NH—), 5·23 (2 H, d, J = 6 cps, —CH_2—), 7·43 (3 H, s, —CH_3); 8-benzyloxy-2-methyl-*s*-triazolo[1,5-*a*]-pyrazine (II), m.p. 93–94°, UV λ_{max} 243 (4600), 283 nm (ϵ 5700), NMR ($CDCl_3$) τ:1·99 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 2·50 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 2·66 (5 H, m, benzene ring protons), 4·42 (2 H, s, —CH_2—), 7·41 (3 H, s, —CH_3); 8-benzylthio-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (III), m.p. 76–77°, UV λ_{max} 250 (8800), 310 nm (ϵ 10 900), NMR ($CDCl_3$) τ:1·88 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 2·12 (1 H, d, J = 4·5 cps, C_5 or C_6-proton), 2·70 (5 H, m, benzene ring protons), 5·44 (2 H, s, —CH_2—), 7·38 (3 H, s, —CH_3).

In a similar manner the 6-chloro isomer yielded IV to VI. 6-Benzylamino-2-methyl-*s*-triazolo[1,5-*a*]-pyrazine (IV), m.p. 131°, UV λ_{max} 268 (5600), 329 nm (ϵ 14 400), NMR ($CDCl_3$) τ:1·48 (1 H, s, C_5 or C_8-proton), 2·59 (1 H, s, C_5 or C_8-proton), 2·66 (5 H, s, benzene ring protons) 4·00 (1 H, broad, —NH—), 5·40 (2 H, d, J = 6 cps, —CH_2—), 7·38 (3 H, s, —CH_3); 6-benzyloxy-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (V), m.p. 182°, UV λ_{max} 257 (3200), 300 nm (ϵ 9200), NMR ($CDCl_3$) τ:1·23 (1 H, s, C_5 or C_8-proton), 2·35 (1 H, s, C_5 or C_8-proton), 2·58 (5 H, s, benzene ring protons), 4·50 (2 H, s, —CH_2—), 7·31 (3 H, s, —CH_3); 6-benzylthio-2-methyl-*s*-triazolo[1,5-*a*]pyrazine (VI), m.p. 97–89°, UV λ_{max} 250 (16 800), 335 nm (ϵ 2100), NMR ($CDCl_3$) τ:0·91 (1 H, d, J = 1·5 cps, C_5 or C_8-proton), 1·69 (1 H, d, J = 1·5 cps, C_5 or C_8-proton), 2·74 (5 H, s, benzene ring protons), 5·63 (2 H, s, —CH_2—), 7·38 (3 H, s, —CH_3).

8-Benzylamino-2-methyl-s-triazolo[1,5-a]*pyridine* (VII). A mixture of 8-amino-2-methyl-*s*-triazolo[1,5-*a*]-pyridine[31] (50 mg) and $NaHCO_3$ (28 mg), dissolved in aq. MeOH, was heated and stirred at 85–105°. Then benzyl chloride (42 mg) was added dropwise and the mixture was heated for 2 hr. After cooling, the mixture was made alkaline with Na_2CO_3 and extracted with CH_2Cl_2. The extract was dried over anhyd. Na_2SO_4 and evaporated. The residue was purified by chromatography on Al_2O_3 and gave pale yellow scales (from ether–hexane), m.p. 84·5–86·0°. (Found: C, 70·57; H, 5·94: N, 23·14. $C_{14}H_{14}N_4$ required: C, 70·56; H, 5·92; N 23·51%.)

4(7)-Benzylaminobenzimidazole[20] (VIII). To a mixture of 4(7)-aminobenzimidazole[32] (588 mg), $NaHCO_3$ (302 mg), and MeOH (10 ml), benzaldehyde (302 mg) was added dropwise and the mixture was stirred for 1 hr at room temp. After cooling, $NaBH_4$ (310 mg) was added in small portions with stirring. The mixture was evaporated to dryness, the residue was dissolved in H_2O (10 ml), and extracted with ether. The extract was dried, and the solvent was evaporated to leave 540 mg of viscous oil, which was chromatographed over Al_2O_3. 4(7)-Benzylaminobenzimidazole (310 mg) was obtained by recrystallization from ether as colorless scales, m.p. 145–146·5° (reported,[20] m.p. 144–145°). (Found: C, 74·79; H, 5·88; N, 18·72. Calc. for $C_{14}H_{13}N_3$: C, 75·31; H, 5·87; N, 18·82%.)

5-Benzylaminoquinoxaline (IX). To a solution of 5-aminoquinoxaline (145 mg) in MeOH (3 ml), $NaHCO_3$ (84 mg), H_2O (40 drops), and benzyl chloride (125 mg) were added and the mixture was refluxed for 5·5 hr. After evaporation of MeOH, the reaction mixture was made alkaline with Na_2CO_3 and extracted with CH_2Cl_2. The CH_2Cl_2 layer was dried and the solvent was evaporated to leave a brown viscous oil, which was chromatographed over Al_2O_3 and 59 mg of 5-benzylaminoquinoxaline was obtained as yellow viscous oil. This oil gave one spot on TLC and homogeneity of the sample was also shown by its NMR spectrum.

5-Benzylaminoquinoline (X). A mixture of 5-aminoquinoline (144 mg) in MeOH (10 ml), $NaHCO_3$ (84 mg), and H_2O (20 drops) was stirred, and then benzyl chloride (135 mg) was added and the reaction mixture was refluxed for 6 hr. After evaporation of MeOH, the reaction mixture was made alkaline with Na_2CO_3 and extracted with CH_2Cl_2. The extract was dried and evaporated. The residue was chromatographed over

[31] T. Okamoto, M. Hirobe and E. Yabe, *Chem. Pharm. Bull., Tokyo* **14**, 523 (1966).
[32] G. M. Van Der Want, *Rec. Trav. Chim.* **67**, 45 (1948).

Al_2O_3 and 5-benzylaminoquinoline (55 mg) was obtained by recrystallization from ether–hexane as yellow needles, m.p. 167–169°. (Found: C, 82·28; H, 5·97; N, 12·17. $C_{16}H_{14}N_2$ required: C, 82·02; H, 6·02; N, 11·96%.)

8-*Benzylaminoquinoline* (XI) was obtained from 8-aminoquinoline in the same way as described for 5-benzylaminoquinoline. Column chromatography afforded 8-benzylaminoquinoline as viscous oil (44 mg). Picrate: Orange plates (from MeOH), m.p. 190°. (Found: C, 56·96; H, 3·61; N, 15·33. Calc. for $C_{22}H_{17}N_5O_7$: C, 57·02; H, 3·70; N, 15·11%.) Mass: M^+ 222.

α-*Benzylaminonaphthalene* (XII). A solution of α-aminonaphthalene (143 mg) in MeOH (10 ml), $NaHCO_3$ (84 mg), and H_2O (8 ml) was heated, benzyl chloride (126 mg) was added and refluxed for 5 hr. After evaporation of MeOH, the residue was dissolved in water, made alkaline with Na_2CO_3, and extracted with CH_2Cl_2. The extract was dried, the solvent was evaporated, and the resulting crude product was purified on Al_2O_3. After recrystallization from ether–hexane, α-benzylaminonaphthalene was obtained as colorless needles, m.p. 70–71°. (Found: C, 87·64; H, 6·42; N, 5·93. Calc. for $C_{17}H_{15}N$: C, 87·51; H, 6·48; N, 6·00%.)

4-*Benzylaminoindole* (XIV). To a solution of 4-aminoindole (132 mg) obtained by the Pd/C–H_2 reduction of 4-nitroindole,[33] and $NaHCO_3$ (84 mg) in aq. MeOH, benzyl chloride (130 mg) was added dropwise, and heated at 70–80° with stirring for 1 hr. The tarry substance obtained from the reaction mixture was made alkaline with Na_2CO_3 solution and extracted with CH_2Cl_2. The dried extract was evaporated and the residue (204 mg) was chromatographed over Al_2O_3. The first fraction gave di(4-benzyl)aminoindole, which was confirmed by IR and NMR. The second fraction afforded 4-benzylaminoindole as colorless prisms, m.p. 119–120°. (Found: C, 80·26; H, 6·41; N, 12·10. Calc. for $C_{15}H_{14}N_2$: C, 81·05; H, 6·35; N, 12·60%.) NMR ($CDCl_3$) τ: 6·02 (1 H, broad singlet, 4-NH), 5·54 (2 H, s, —CH_2—), 3·65 (2 H, m, indole ring protons), 3·05 (3 H, m, indole ring protons), 2·70 (5 H, s, benzene ring protons). Mass: M^+ 222.

7-*Benzylaminoindole* (XVI) was obtained from 7-aminoindole in the same way as in the case of 4-benzylaminoindole. Recrystallization from ether–hexane yielded scales, m.p. 133–134°. NMR ($CDCl_3$) τ: 7·02 (1 H, broad singlet, 7-NH), 5·71 (2 H, s, —CH_2—), 3·57 (2 H, m, indole ring protons), 3·00 (3 H, m, indole ring protons), 2·74 (5 H, s, benzene ring protons). Mass: M^+ 222.

[33] S. M. PARMERTER, *J. Am. Chem. Soc.* **80**, 4621 (1958).

Key Word Index—*Nicotiana tabacum*; Solanaceae; azaindenes; azanaphthalenes; indoles; cytokinin activities.