thiazolidineacetic acid, formed by quantitative paper chromatography using ninhydrin as the color reagent. From a suitable batch of reaction mixture 6-aminopenicillanic acid (II) has been isolated by absorption on IR-120 (H^+), elution with NH_4OH at *p*H 7.0, concentration *in vacuo*, and adjusting the *p*H to 4.4. The recrystallized product had m.p. 207–208° (dec.) and $[\alpha]D^{25}$ +277 (*C* 1.0 in 0.1 *N* hydrochloric acid).[5] It assayed approximately 2750 u./mg. based on sodium benzylpenicillin by the hydroxylamine colorimetric procedure[6] and by microbiological determination after phenylacetylation[1] (theor., 2752 u./mg.). Acylation of (II) with the appropriate acid chlorides in aqueous acetone buffered at *p*H 7.0 to 7.5 has given good yields of crystalline potassium salts of benzylpenicillin and phenoxymethylpenicillin, which are identical in all respects to the product prepared by fermentation.

Both phenoxymethylpenicillin (V) and allylmercaptomethylpenicillin (O) are hydrolyzed by this microbial acylase system. Details on the distribution of this acylase in microörganisms, and its activity on a series of penicillins, including a large number of new semi-synthetic penicillins will be reported elsewhere.

(5) J. C. Sheehan and K. R. Henery-Logan, THIS JOURNAL, **81**, 5835 (1959), report $[\alpha]^{21}D$ +273 (*C* 1.2 in 0.1 *N* hydrochloric acid).

(6) G. Boxer and P. M. Everett, *Anal. Chem.*, **21**, 670 (1949).

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SEPARATION OF ALKALOIDS BY GAS CHROMATOGRAPHY

Sir:

In the past, the separation of alkaloids from crude alkaloid mixtures has depended upon fractional crystallization, precipitation, countercurrent extraction and either adsorption or liquid phase partition chromatography. Several recent communications have reported the use of gas phase chromatographic techniques for the separation and identification of steroids[1,2] and high molecular weight fatty primary amines.[3] This communication demonstrates the feasibility of this method for the isolation, separation and identification of alkaloids. Our attention has been focused on alkaloids with molecular weights above 250, since suitable modifications of the conditions should permit separations of lower molecular weight substances without difficulty.[4]

Alkaloids listed in the table gave single component sharp peaks, consistent with the absence of decomposition. A typical sample was 1–3 μl. of a 0.5–1.0% solution of the alkaloid in methanol, acetone or chloroform. In several cases (N-methylcytisine, crinine, ibogaine and solanidine) macro samples were chromatographed and the product was identified as unchanged starting material by standard methods. The power of this analytical tool is illustrated in a separation of *Papaveraceae* alkaloids (Fig. 1).

TABLE I
ALKALOID RETENTION TIMES

Compound	Time, min.[a,b]
1. Lupin alkaloids	
Cytisine	5.1
Methylcytisine	4.3
Methylcytisine N-oxide	5.8
Lupanine	5.5
13-Hydroxylupanine	11.6
Matrine	8.5
Lupinine	1.5[d]
Sparteine	5.9[d]
α-Isosparteine	5.2[d]
13-Hydroxysparteine	14.3[d]
2. Amaryllidaceae	
Galanthine	19.0
Acetylcaranine	10.5
Lycorenine	10.6
Galanthamine	7.8
Crinine	9.5
Powelline	15.8
Tazettine	15.2
Belladine	8.7
3. *Papaveraceae*	
Codeine	8.2
Gnoscopine	90.6
Laudanosine	21.0
Morphine	11.0
Neopine	9.1
Papaverine	35.3
Thebaine	13.2
4. Indole Alkaloids	
Brucine	80.0[c]
Coronaridine	8.2[c]
Ibogamine	15.4
Ibogaine	35.1
Serpentine	16.8[c]
Strychnine	25.9[c]
Voacangine	40.3
5. Steroidal alkaloids	
Solanidine	40.6[c,e]
Solasodine	74.3[c,e]
Tomatidine	77.3[c,e]
6. Miscellaneous	
Atopine	5.0
Caffeine	1.6
Cinchonine	6.7[c]
Cocaine	4.8[c]
Corydaline	16.2[c]
Cryptopine	50.8
Himbacine	12.7[c]
Piperine	33.0
Protopine	44.7
Quinine	11.8[c]

[a] Argon ionization detector, 6 ft. × 4 mm. i.d. columns. [b] Pressure 15 psi., 2–3/100 SE-30 on Chromosorb W, 80–100 mesh, temperature 204° unless otherwise noted. [c] Temperature 222°. [d] Temperature 160°. [e] Pressure 10 psi.

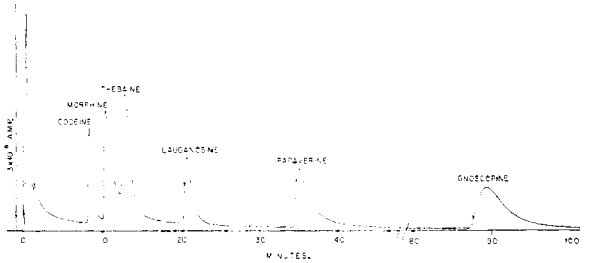

Fig. 1.

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THE ENTROPY OF ACTIVATION OF ADDITION OF METHYL RADICALS TO UNSATURATED COMPOUNDS POSSESSING THE SAME REACTION CENTER[1]

Sir:

Addition of methyl radicals to ethylene,[2] propylene,[2] isobutene,[2] styrene,[3] α-methylstyrene,[3] butadiene[4] and isoprene[4] was studied in this

(1) W. J. A. VandenHeuvel, C. C. Sweeley and E. C. Horning, THIS JOURNAL, **82**, 3481 (1960).

(2) R. K. Beerthuis and J. H. Recourt, *Nature*, **186**, 372 (1960).

(3) J. Nelson and A. Milun, *Chemistry & Industry*, 663 (1960).

(4) *Cf.* L. D. Quin, *J. Org. Chem.*, **24**, 911 (1959).

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(2) R. P. Buckley and M. Szwarc, *Proc. Roy. Soc.*, **A240**, 396 (1957).

(3) F. Leavitt, M. Levy and M. Szwarc, THIS JOURNAL, **77**, 5493 (1955).

(4) A. Rajbenbach and M. Szwarc, *Proc. Roy. Soc.*, **A251**, 1266 (1959).