

## Photochemical Alkylation of Caffeine with Amino-acids

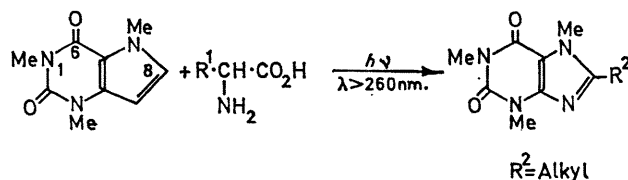
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*Summary* Photochemical reactions of caffeine with aliphatic  $\alpha$ -amino-acids lead to 8-alkylcaffeine derivatives.

PHOTOCHEMICAL reactions of purines with alcohols have been described recently.<sup>1,2</sup> These reactions result in addition of the alcohol across the 1,6-double bond<sup>1</sup> or substitution at the 8-position of the purine ring system.<sup>2</sup> We report photochemical reactions of caffeine with various aliphatic  $\alpha$ -amino-acids which lead to caffeine derivatives with different alkyl substituents in the 8-position of the

caffeine molecule. These reactions can be summarized as follows:



The reactions studied and the major products isolated are described in the Table.

TABLE  
*Photochemical alkylation of caffeine with amino-acids*

Amino acid	Product 8-substituted caffeine	Yield <sup>a</sup>
Alanine .. ..	Et	21%
2-Aminobutyric acid ..	{ Et Pr	{ 5 22
Serine .. ..	Et	21
Threonine .. ..	{ Et Pr	{ 12 10
Norvaline .. ..	Bu	22
Leucine .. ..	Me <sub>2</sub> CH[CH <sub>2</sub> ] <sub>2</sub>	19
Norleucine .. ..	Bu <sup>α</sup> CH <sub>2</sub>	22
Alanylglycine .. ..	Et	21

<sup>a</sup> Yields are based on caffeine used.

† Hanovia 450 w high pressure mercury vapour lamp with Corex filter.

<sup>1</sup> H. Linschitz and J. S. Connolly, *J. Amer. Chem. Soc.*, 1968, **90**, 2979; J. S. Connolly and H. Linschitz, *Photochem. and Photobiol.*, 1968, **7**, 791.

<sup>2</sup> D. Elad, I. Rosenthal, and H. Steinmaus, *Chem. Comm.*, 1969, 305.

<sup>3</sup> E. S. Golovchinskaya, *Sbornik Statei obshchei Khim., Akad. Nauk S.S.S.R.*, 1953, **1**, 692 (*Chem. Abs.*, 1955, **49**, 1070a).

<sup>4</sup> R. Santus, C. Helene, and M. Ptak, *Compt. rend.*, 1966, **262**, D, 2077.

<sup>5</sup> Cf. R. Noyori, M. Kato, M. Kawanishi, and H. Nozaki, *Tetrahedron*, 1969, **25**, 1125.

Typically, a solution of caffeine (500 mg.) and DL-alanine (500 mg.) in water (70 ml.) was irradiated† under nitrogen for 24 hr. The reaction mixture was concentrated to about half of its volume and extracted with chloroform. The organic solvent was evaporated and the residue was chromatographed on silica gel to isolate 8-ethylcaffeine (122 mg.). Products were isolated and identified by elemental analysis, n.m.r. and mass spectra, and in some cases by comparison with authentic samples.<sup>3</sup>

It has been reported that the interaction of photoactivated adenosine with glycine leads to the fragmentation of the latter and the formation of free radicals derived from the amino-acid.<sup>4</sup> A similar mechanism might be operating in the reported reactions, where caffeine serves as the light-absorbing system and the excited caffeine molecule induces fragmentation of the amino-acid to reactive species.<sup>5</sup>

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