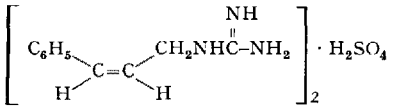
Hypotensive Activity of *cis*-Cinnamyl Guanidine Sulfate

The *cis* and *trans* isomers of cinnamyl guanidine sulfate were found to possess hypotensive activity in animals, the *cis* form (Su-13,686) being more active than the *trans*:



Su-13,686

Su-13,686 was orally active with a rapid onset of action in normotensive anesthetized and unanesthetized dogs and in unanesthetized renal hypertensive dogs; in anesthetized cats it also produced a hypotensive response. In the anesthetized dogs doses of 2.5 and 7.9 mg/kg, injected into a loop of the small intestine produced a 31 and 50 mm decrease in mean arterial blood pressure. The pressor responses produced by injected l-epinephrine and l-norepinephrine were augmented, while the pressor response produced by injected amphetamine was inhibited or greatly decreased.

The oral administration of 7.9 mg/kg to unanesthetized normotensive dogs for two weeks produced a 20 to 40 mm decrease in mean arterial pressure, while the oral administration of 2.0 mg/kg of Su-13,686 to unanesthetized renal hypertensive dogs produced a 31 mm decrease in mean arterial pressure. The drug appeared to be more effective in the renal hypertensive dog than in the normotensive dog.

In normotensive dogs anesthetized with barbital sodium, Su-13,686 produced a significant increase in coronary and renal blood flow. Cardiac output was not altered.

This compound differs from guanethidine[1] in that it is more potent, manifests a more rapid onset and shorter duration of action and produces less cumulation.

The available pharmacological evidence indicates that Su-13,686 produces its hypotensive effect by some degree of blockade of the post-ganglionic sympathetic fibers.

The *trans*-cinnamylamine was prepared by Gabriel synthesis from the commercially available *trans*-cinnamyl chloride according to the method of GENSLER and ROCKETT[2], b.p. 71–74°/mm; hydrochloride, m.p. 246 to 250°; calculated for $C_9H_{11}N \cdot HCl$: C 63.70, H 7.12, N 8.24; found: C 63.51, H 7.11, N 8.21. Reaction of the free amine with 2-methylthiopseudourea sulfate gave *trans*-cinnamyl guanidine sulfate, which was recrystallized from aqueous ethanol and melted with decomposition at 248 to 251°; calculated for $(C_{10}H_{13}N_3)_2 \cdot H_2SO_4$: C 53.62, H 6.30, N 18.76; found: C 53.62, H 6.36, N 18.52.

To prepare the corresponding *cis*-compound, 1-chloro-3-phenyl-2-propyne[3] which was obtained from 3-phenyl-2-propyn-1-ol[4], was allowed to react with potassium phthalimide to give the N-(3-phenyl-2-propynyl)-phthalimide, m.p. 158–160°; calculated for $C_{17}H_{11}NO_2$: C 78.23, H 4.25, N 5.37; found: C 78.22, H 4.14, N 5.32. LINDLAR[5] palladium-lead catalyst reduction of the phthalimide gave the N-*cis*-cinnamyl phthalimide which was recrystallized from aqueous ethanol, m.p. 110–111°; calculated for $C_{17}H_{13}NO_2$: C 77.63, H 4.98, N 5.33; found: C 77.46, H 4.84, N 5.23. Hydrazinolysis of this material gave *cis*-cinnamylamine, b.p. 104–105°/12 mm; hydrochloride m.p. 177–178°; calculated for $C_9H_{11}N \cdot HCl$: C 63.70, H 7.12, N 8.24; found: C 64.12, H 7.11, N 8.51. Reaction of the free *cis*-cinnamylamine with 2-methylthiopseudourea sulfate gave *cis*-cinnamyl guanidine sulfate which was recrystallized from butanol and water and melted with decomposition at 149–151°; calculated for $(C_{10}H_{13}N_3)_2 \cdot H_2SO_4$: C 53.62, H 6.30, N 18.76; found: C 53.86, H 6.36, N 18.87. IR-spectra served to confirm the *cis* and *trans* isomerism of the aforedescribed compounds.

Zusammenfassung. Es wird die Synthese und Pharmakologie eines neuen blutdrucksenkenden Mittels, *cis*-Cinnamyl-guanidinsulfat, beschrieben.

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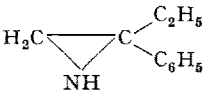
[1] R. A. MAXWELL, R. P. MULL, and A. J. PLUMMER, Exper. *15*, 267 (1959).
[2] W. J. GENSLER and J. C. ROCKETT, J. Am. chem. Soc. *77*, 3262 (1955).
[3] M. J. MURRAY, J. Am. chem. Soc. *60*, 2662 (1938).
[4] L. F. HATCH and H. E. ALEXANDER, J. Am. chem. Soc. *72*, 5643 (1950).
[5] H. LINDLAR, Helv. chim. Acta *35*, 446 (1952).

Mutagenic Action of 2-Ethyl-2-phenyl-ethyleneimine

Since the discovery of the mutagenic effect of mustard gas[1] and allied compounds, a large number of chemical compounds have been systematically tested for their mutagenic properties in different laboratories of the world[2–4].

In this laboratory, a derivative of ethyleneimine, 2-ethyl-2-phenylethyleneimine (Figure), was recently tried on barley (*Hordeum vulgare*), and some of the results obtained are presented below. 2-Ethyl-2-phenylethyleneimine is a liquid at room temperature and is practically insoluble in water, but a temporary emulsion is obtained when shaken vigorously.



[1] C. AUERBACH and I. M. ROBSON, Nature *154*, 81 (1944).
[2] M. WESTERGAARD, Exper. *13*, 224 (1957).
[3] H. HESLOT, R. FERRARY, R. LEVI, and C. MONARD, Proc. Symp. on the Effects of Ionizing Radiations on Seeds, Karlsruhe (1960). International Atomic Energy, Vienna (Austria, 1961).
[4] L. EHRENBERG, Å. GUSTAFSSON, and U. LUNDQVIST, Hereditas *47*, 243 (1961).