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## Phosphorus, Sulfur, and Silicon and the Related Elements

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### <sup>31</sup>P NMR Kinetic Studies of Alkylation Chemistry of N,N'-Bis(2-Chloroethyl)Phosphordiamidic Acid and Its Congeners

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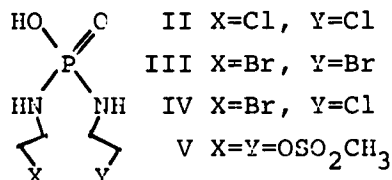
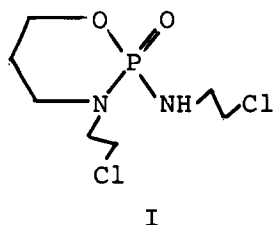
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# <sup>31</sup>P NMR KINETIC STUDIES OF ALKYLATION CHEMISTRY OF N,N'-BIS(2-CHLOROETHYL)PHOSPHORDIAMIDIC ACID AND ITS CONGENERS

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Ifosfamide (I), like isomeric cyclophosphamide, belongs to the most effective anticancer drugs currently in clinically therapeutic use. It has been demonstrated that I require metabolic activation to exert its cytotoxic activity.



New congeners III, IV and V of a key metabolite of I, N,N'-bis(2-chloroethyl)phosphorodiamidic acid II, have been synthesized and <sup>31</sup>P NMR spectroscopy was used to study their alkylating abilities. The half-lives of III, IV and V under the standard set of reaction conditions (1M Tris-HCl buffer, pH 7.4, 37°C) were considerably shorter than that of II.