Predicting the Mutagenic Potential of Chemicals in Tobacco Products Using *In Silico* Toxicology Tools

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Supplementary Data

Figure S1: Distribution plots of selected physicochemical properties in the validation dataset. Mutagens are shown in red and non-mutagens in green. MW: molecular weight, logP: estimation of octanol/water partition coefficient, PSA: polar surface area, Rotatable Bonds: number of rotatable bonds.

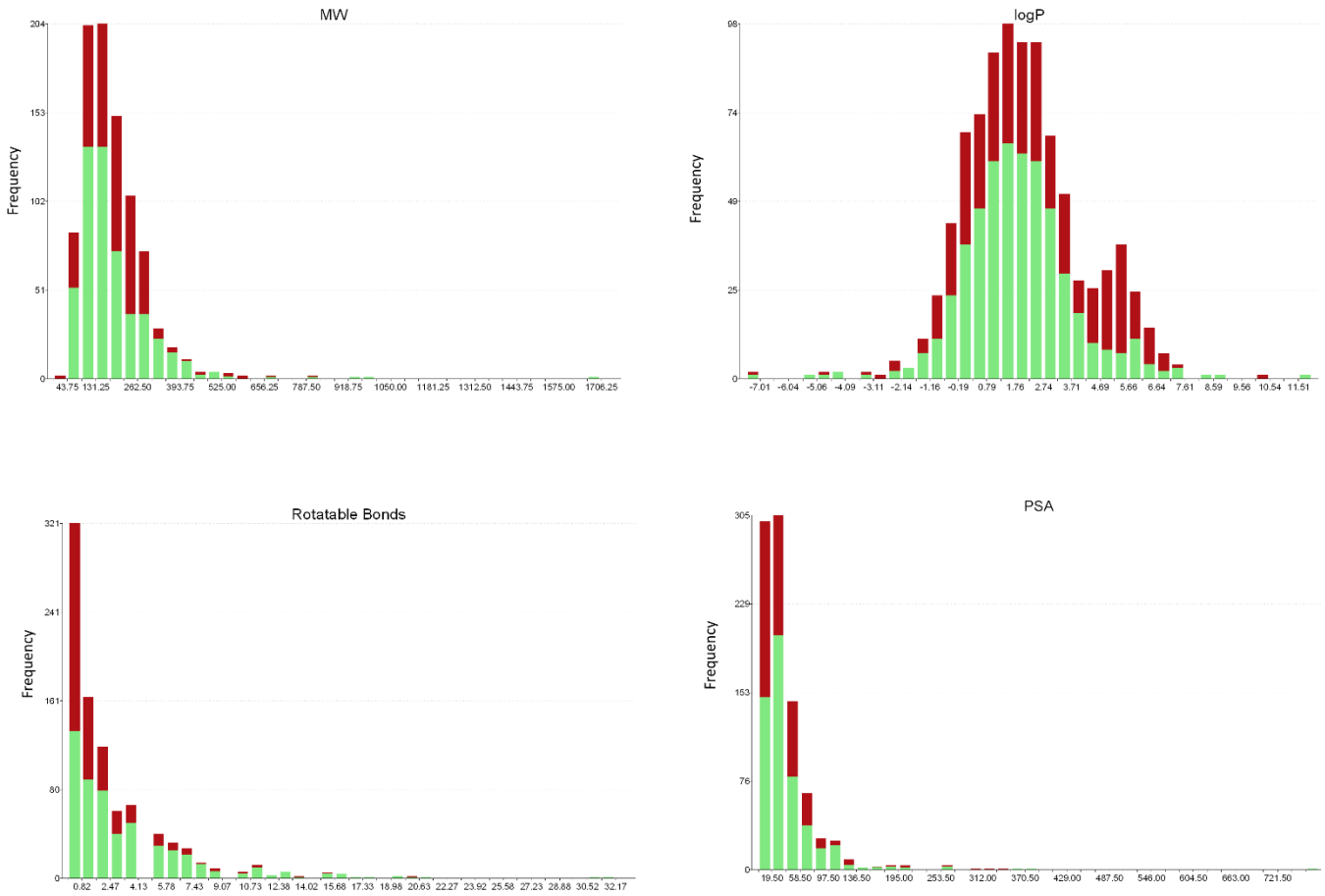


Figure S2: Distribution plots of selected physicochemical properties in the test dataset. Mutagens are shown in red and non-mutagens in green. MW: molecular weight, logP: estimation of octanol/water partition coefficient, PSA: polar surface area, Rotatable Bonds: number of rotatable bonds.

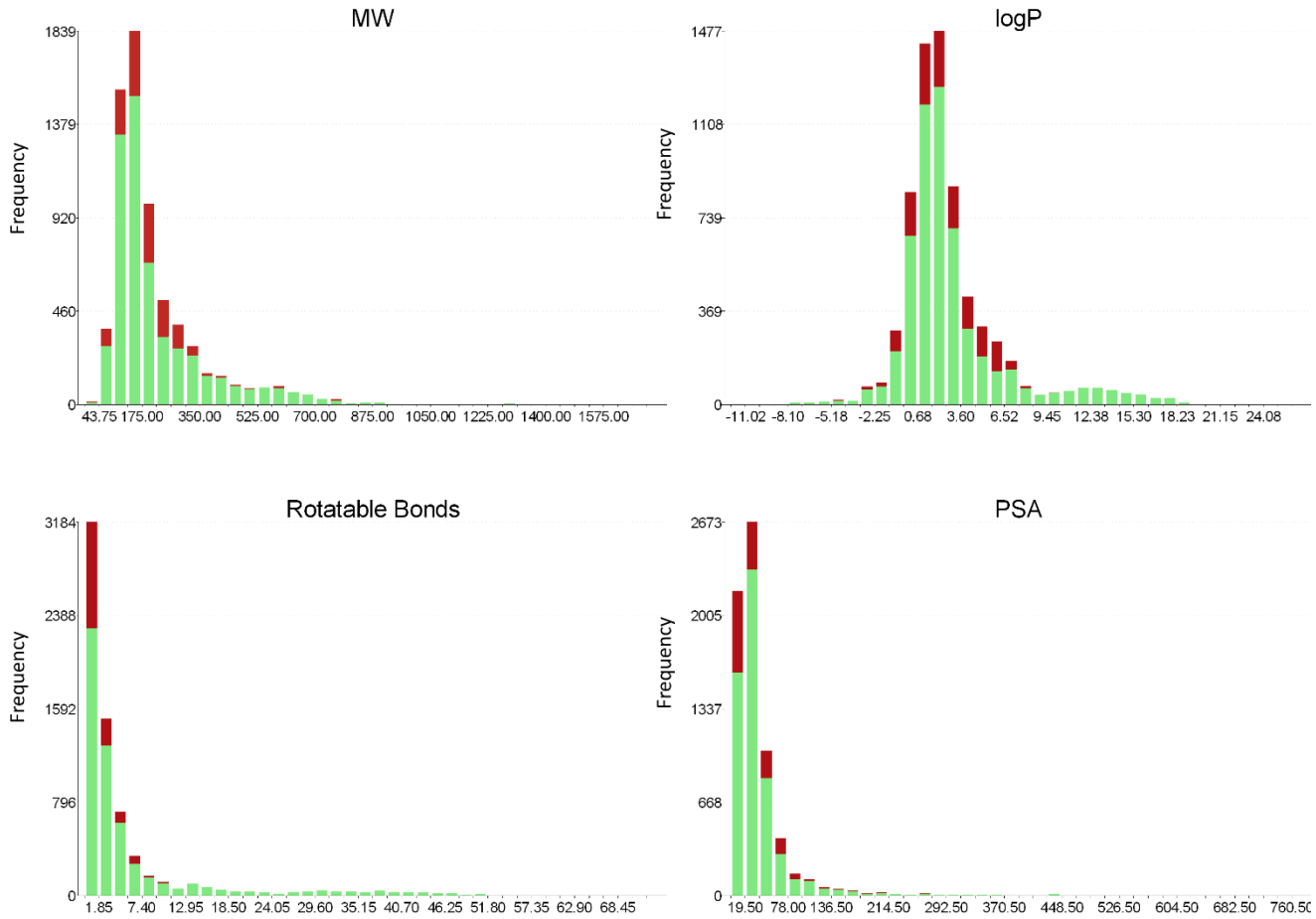
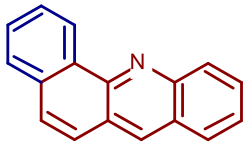
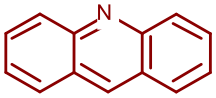
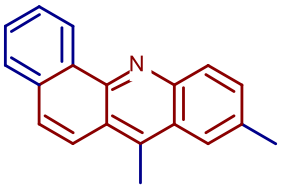
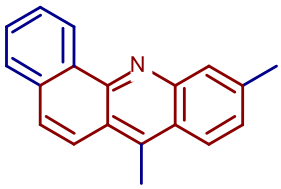
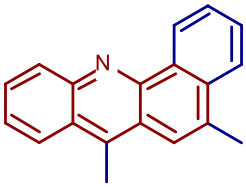
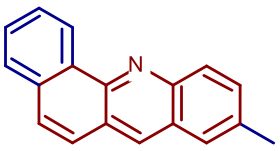
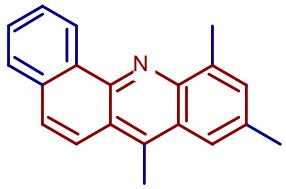
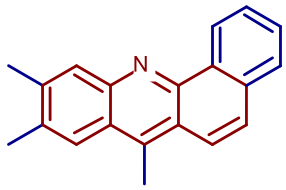
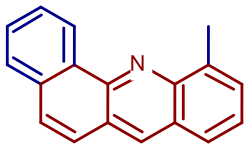
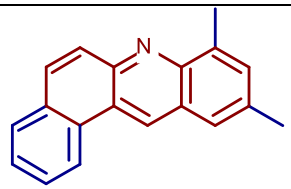
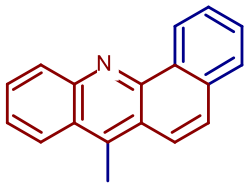
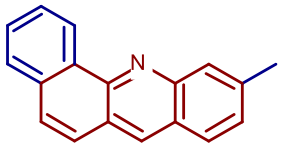
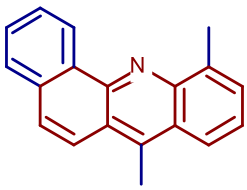
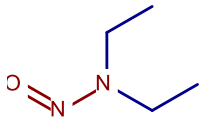
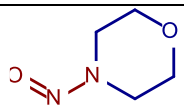
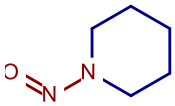
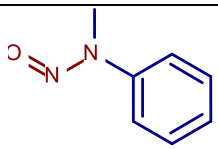
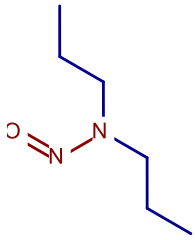
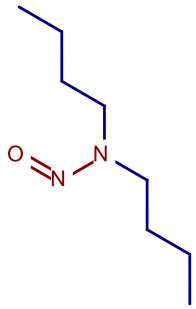
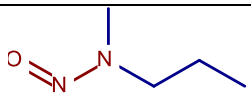
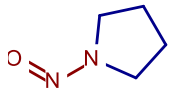
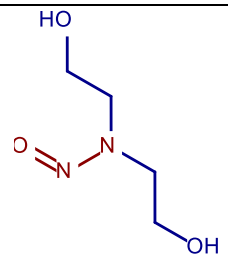
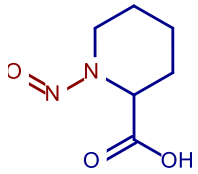
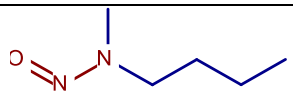
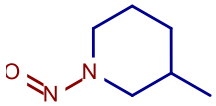
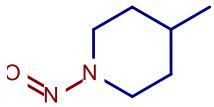
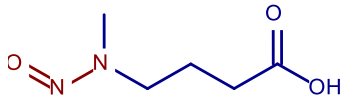
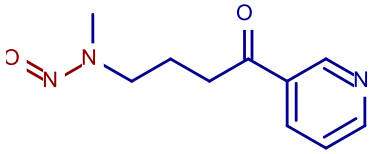
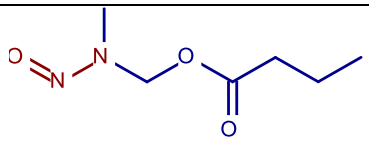
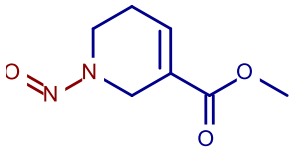
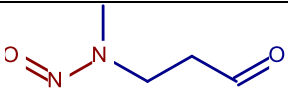


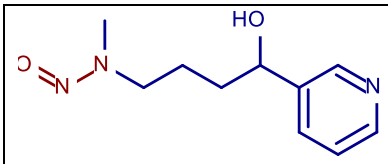
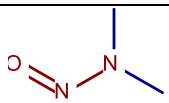
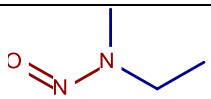
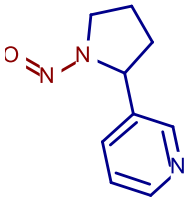
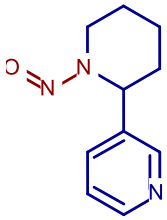
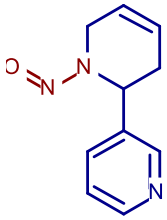
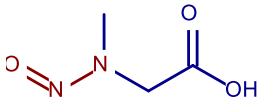
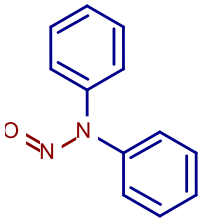
Table S1: Scaffolds strongly associated with mutagenic activity demonstrate: A) benzoquinoline, B) nitrosamino, and C) 4-pyranone scaffold present in compounds.

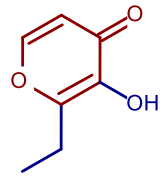
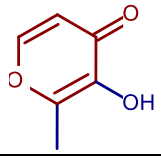
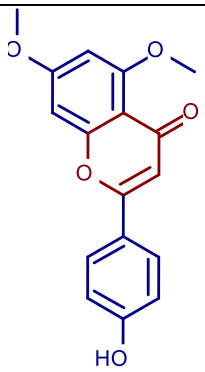
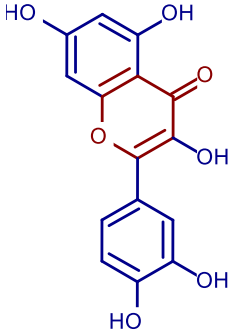
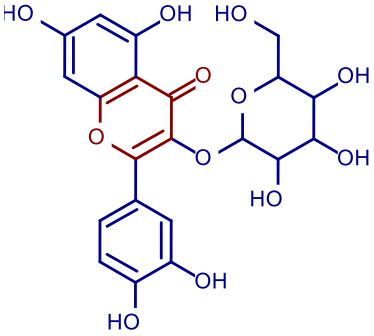
A**:** Benzoquinoline Scaffolds			
Structure	**Registry Number**	**Name**	**Ames Activity**
	225-51-4	Benz[C]Acridine	Positive
	260-94-6	Acridine	Positive
	963-89-3	7,9-Dimethylbenz[C]Acridine	Positive
	2381-40-0	7,10-Dimethylbenz[C]Acridine	Positive
	10567-95-0	5,7-Dimethylbenz(C)Acridine	Positive
	33942-93-7	9-Methylbenz(C)Acridine	Positive

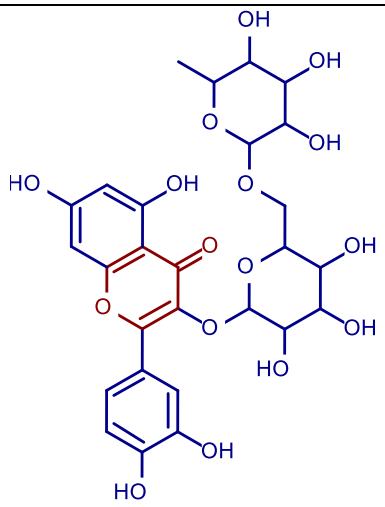
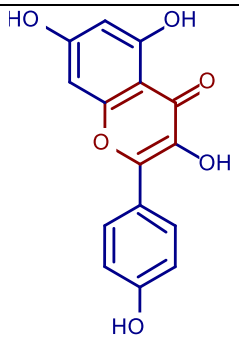
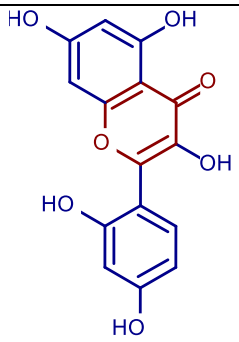
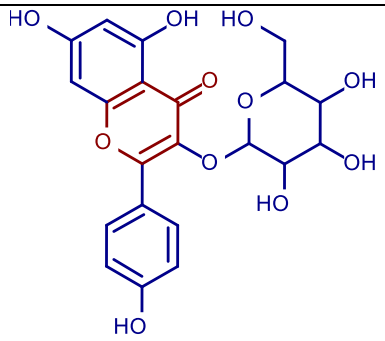
	51787-42-9	7,9,11-Trimethylbenz[C]Acridine	Positive
	58430-01-6	7,9,10-Trimethylbenz[C]Acridine	Positive
	67028-20-0	11-Methylbenz(C)Acridine	Positive
	53-69-0	8,10-Dimethylbenz(A)Acridine	Positive
	3340-94-1	7-Methylbenz(C)Acridine	Positive
	7230-71-9	10-Methylbenz(C)Acridine	Positive
	32740-01-5	7,11-Dimethylbenz(C)Acridine	Positive

B: Nitrosamino Scaffolds			
Structure	**Registry Number**	**Name**	**Ames Activity**
	55-18-5	N-Nitrosodiethylamine	Positive
	59-89-2	N-Nitrosomorpholine	Positive
	100-75-4	1-Nitrosopiperidine	Positive
	614-00-6	N-Nitroso-N-Methylaniline	Positive
	621-64-7	N-Nitrosodipropylamine	Positive
	924-16-3	N-Nitrosodibutylamine	Positive
	924-46-9	Methylpropylnitrosamine	Positive
	930-55-2	1-Nitrosopyrrolidine	Positive

	1116-54-7	N-Nitrosodiethanolamine	Positive
	4515-18-8	1-Nitrosopiperidine-2-Carboxylic acid	Positive
	7068-83-9	Methylbutylnitrosamine	Positive
	13603-07-1	1-Nitroso-3-Pipecoline	Positive
	15104-03-7	1-Nitroso-4-Pipecoline	Positive
	61445-55-4	N-Nitroso-N-methyl-4-aminobutyric acid	Positive
	64091-91-4	4-(Methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK)	Positive
	67557-56-6	Butyric Acid	Positive
	55557-02-3	N-Nitrosoguvacoline	Positive
	85502-23-4	3-(N-Nitrosomethylamino) Propionaldehyde	Positive

	76014-81-8	4-(Methylnitrosamino)-1-(3-Pyridyl)-1-Butanol (Nnal)	Positive
	62-75-9	N-Nitrosodimethylamine	Positive
	10595-95-6	N-Nitrosomethylethylamine	Positive
	80508-23-2	N'-Nitrosonornicotine (NNN)	Positive
	37620-20-5	N'-Nitrosoanabasine	Positive
	887407-16-1	N-Nitrosoanatabine	Positive
	13256-22-9	N-Nitrososarcosine (NSAR)	Negative
	86-30-6	N-Nitrosodiphenylamine	Negative

C: 4-pyranone Scaffolds			
Structure	**Registry Number**	**Name**	**Ames Activity**
	4940-11-8	Ethylmaltol	Positive
	118-71-8	Maltol	Positive
	16290-50-9	5,7-Dimethoxy-4-Hydroxyflavone	Positive
	117-39-5	Quercetin	Positive
	482-35-9	Isoquercitrin	Positive

	153-18-4	Rutin	Positive
	520-18-3	Kaempferol	Positive
	480-16-0	Morin	Positive
	480-10-4	Astragalin	Positive

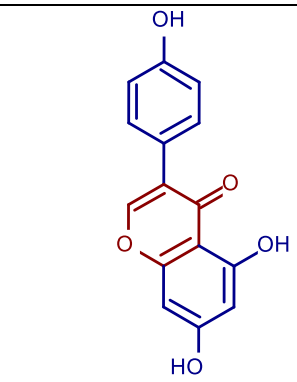
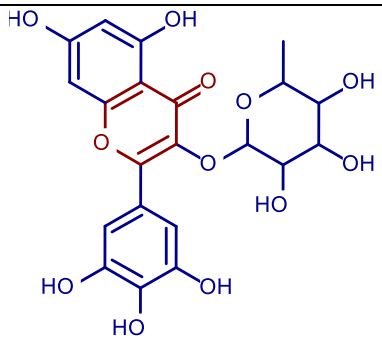
	446-72-0	Genistein	Positive
	17912-87-7	Myricitrin	Negative

Table S2: Representation of some of the basic functional groups in the test dataset of 6820 tobacco chemicals.

Functional Group	**% Dataset**
Carbonyls	48
Alcohols	47
Aromatic rings	44
Aliphatic rings	32
Ethers	27
Carboxylic acids	24
Heteroaromatic rings	21
Esters	12
Ketones	12
Phenols	10
Pyridines	8
Aldehydes	5
Amides	5
Lactones	3
Nitriles	2
Thiols	2
1,2-Dicarbonyls	1
Epoxides	1
Nitrosamines	1
Alkynes	0.5
Imines	0.4
Sulfoxides	0.2