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The direct arylation of 1,3,5-triazin-2,4(1*H*,3*H*)-dione

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ABSTRACT

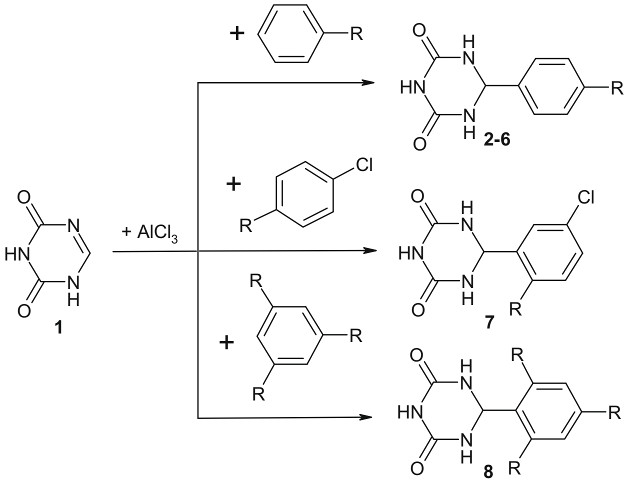
Direct introduction of non-activated arenes to 1,3,5-triazin-2,4(1*H*,3*H*)-dione in the presence of $AlCl_3$ is described.

New synthetic approaches to derivatives of 1,3,5-triazines are of significant interest because these compounds display various biological activities. Almitrine is a well-known remedy for respiratory insufficiency and triazine herbicides are the most commonly used to control weeds during the production of corn, sorghum and sugarcane in the USA.[1]

1,3,5-Triazines are π-deficient heteroaromatic compounds and display activity in reactions with a variety of nucleophiles.[1] Along with aromatic nucleophilic *ipso*-substitution reactions (S_NAr^{ipso}),[1,2] there are examples of nucleophilic addition to the C=N bond of 1,3,5-triazine-2,4(1*H*,3*H*)-dione.[3] This offers the possibility to insert a vast number of nucleophiles on the triazine substrate which does not possess good leaving groups. Arene nucleophiles are of interest because the formation of new C–C bonds between arenes and hetarenes is an important tool in modern organic synthesis.[4,5] Besides well-known reactions between π-deficient hetarenes and arenes with strong electron-donating substituents (OR, NR^1R^2),[4] there are a few examples of reactions with unactivated arene nucleophiles. Girke earlier described reactions of pyrimidine[6a] with perylene, and quinazoline[6b] with naphthalene, anthracene and mesitylene in the presence of trifluoroacetic acid. There is only one example of the reaction of benzene in the capacity of a nucleophile with 5,6-diphenyl-3-hydroxy- and 5,6-diphenyl-3-mercapto-1,2,4-triazines in the presence of $AlCl_3$.[7]

Here, we report a one-step method for the direct introduction of arenes on 1,3,5-triazine-2,4(1*H*,3*H*)-dione (**1**) by means of C–C bond formation in the presence of aluminium chloride. The reactions were carried out in the presence of various arenes without any solvent, (Scheme 1).

The structures of products **2–8** (Table 1) were confirmed by analytical methods including X-ray analysis of compound **8** (Fig. 1). In addition, 6-phenyl[1,3,5]triazinan-2,4-dione (**3**) was



Scheme 1.

Table 1

Entry	Product	R	Equiv of $AlCl_3$	*T* (°C)	Time (h)	Yield (%)
1	**2**	CH_3	3.0	25	18	45 (67)[a]
2	**2**	CH_3	3.0	110	3	61
3	**2**	CH_3	1.2	110	3	27
4	**3**	H	3.0	25	18	34
5	**3**	H	3.0	80	3	59
6	**4**	Br	3.0	25	18	21
7	**4**	Br	3.0	156	3	45
8	**5**	Cl	3.0	25	18	30
9	**5**	Cl	3.0	132	3	40
10	**6**	NMe_2	3.0	25	18	22
11	**7**	CH_3	3.0	25	18	44 (63)[a]
12	**7**	CH_3	3.0	162	3	52
13	**8**	CH_3	3.0	25	18	37 (65)[a]

[a] Yield of crude product.

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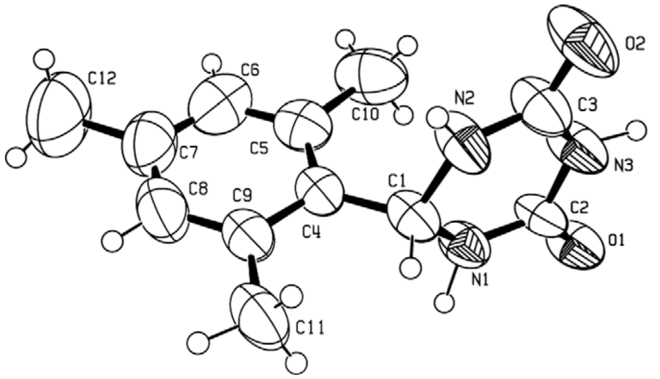
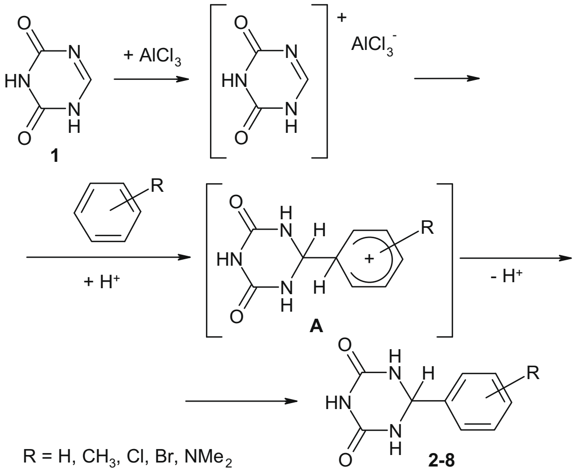


Figure 1. ORTEP diagram of compound **8**.[9]



Scheme 2.

prepared using a known method.[8] The ^{1}H NMR spectra of compound **3** synthesized by the two different methods were the same.

Investigation of the reaction conditions indicated that increasing the temperature led to higher yields in each case. The yields of products are not optimized at present. Reported methods give product **3** in similar yields, 60%,[8] 58%[10] and 54%.[11]

The proposed reaction mechanism includes initial formation of a complex between 1,3,5-triazine-2,4(1*H*,3*H*)-dione and AlCl$_3$. Next, the activated triazine attacks the arene resulting in the formation of a σ-complex of possible structure **A**; loss of a proton results in the formation of the aromatic system (Scheme 2).

In conclusion, a simple and convenient method for the addition of non-activated arenes to π-deficient heterocyclic compounds is described. This method may serve as an alternative to using activated (het)arenes as coupling agents in the presence of transition metal catalysts (including Suzuki, Kumada, Ullmann reactions) for C–C bond formation between arenes and hetarenes.[5]

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.01.086.

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