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A Simple Synthesis of 2,4-Diaryl-1,3,5-triazines

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Summary. Arylamidines **2** react with 5-methoxymethylen-2,2-dimethyl-1,3-dioxan-4,6-dione **5** to give 2,4-diaryl-1,3,5-triazines in moderate to good yields. **5** can be comprehended as a formic acid derivative which transfers a C_1–building block. Other formic acid derivatives give only poor to moderate yields of triazines by treatment with amidines. The synthetic method is applicable to aromatic amidines.

Keywords. 5-Methoxymethylene *Meldrum*'s acid; 2,4-Disubstituted 1,3,5-triazines; C_1–building blocks.

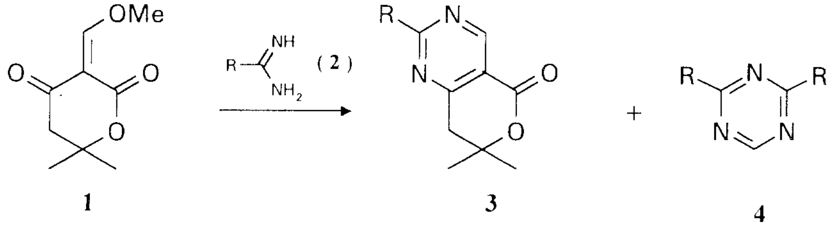
Eine einfache Synthese von 2,4-Diaryl-1,3,5-triazinen

Zusammenfassung. Die Arylamidine **2** reagieren mit 5-Methoxymethylen-2,2-dimethyl-1,3-dioxan-4,6-dion **5** in guten Ausbeuten zu 2,4-Diaryl-1,3,5-triazinen. Verbindung **5** kann als Derivat der Ameisensäure aufgefaßt werden, welches einen C_1–Baustein überträgt. Andere Derivate der Ameisensäure ergeben bei Umsetzung mit Amidinen nur schlechte Ausbeuten an Triazinen. Die beschriebene Methode ist auf aromatische Amidine anwendbar.

Introduction

Although 1,3,5-triazines are very interesting compounds with a lot of applications in synthesis, as pharmaca and herbicides [1], the preparation of 2,4-disubstituted 1,3,5-triazines is now as before a synthetic problem. *Bredereck et al.* describe the reaction of amidines with some derivatives of formic acid to give the appropriate amidines in only poor to moderate yields [2].

In connection with our investigations on the synthetic potential of 3,4-dihydropyrane-2,4-diones, we found that by treatment of 3-methoxymethylene-3,4-dihydropyrane-2,4-dione (**1**) with aromatic amidines 2,4-diaryl-1,3,5-triazines **4** are formed in 30–40% yield in addition to the desired pyrano[4,3-d]pyrimidines **3**, Scheme 1 [3].



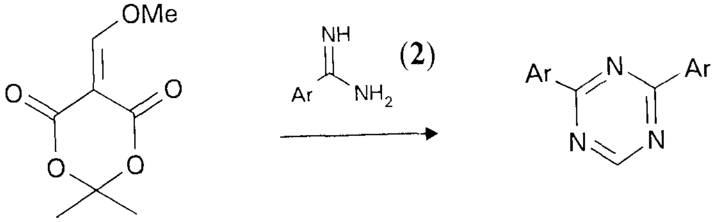
Scheme 1

Obviously, **1** transmits the methylene C-atom as a formal derivative of formic acid. However, the *β*-ketolactone **1** is a less suitable reagent for the preparation of triazines because of its expensive synthesis and the formation of pyrano[4,3-d]pyrimidines **3** as byproducts. Hence, it was necessary to substitute **1** by an easily accessible α-alkoxymethylene 1,3-dicarbonyl compound lacking the disadvantages of **1**.

Results and Discussion

We found that 5-methoxymethylene-2,2-dimethyl-1,3-dioxane-4,6-dione (α-methoxymethylene *Meldrum*'s acid, **5**), which can easily prepared from *Meldrum*'s acid and trimethyl orthoformate [4], is a very suitable reagent for the preparation of disubstituted 1,3,5-triazines. Investigations of facilities and limits of this method gave the following results.

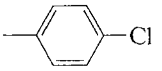
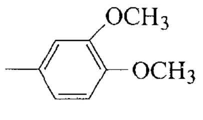
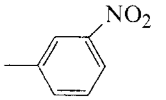
The method is restricted to aromatic amidines. By treatment of aliphatic amidines, guanidine, and S-ethyl isothiuronium bromide with **5** we could detect only traces of 1,3,5-triazines by TLC [5]. 5-Aminomethylene-2,2-dimethyl-1,3-dioxane-4,6-dione was isolated in this cases. **5** was treated with the hydrochlorides of aromatic amidines **2a–d** in the presence of equimolar amounts of potassium *tert.*-butylate in dry MeOH (Scheme 2, Table 1). By use of aprotic solvents (*e.g. DMF*), no triazines were formed.



5 **4a-d**

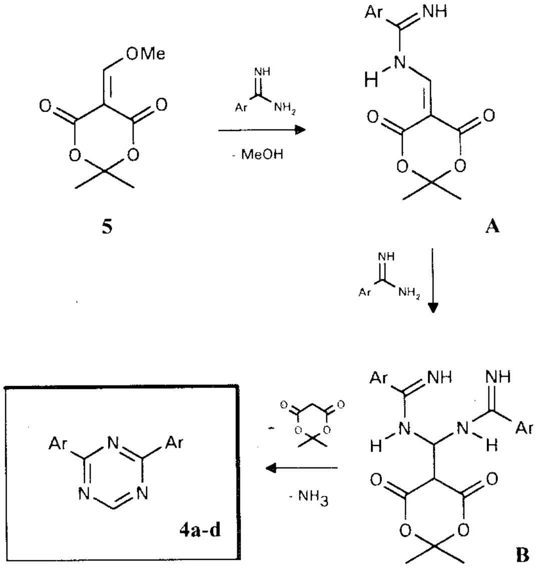
Scheme 2

Table 1. 1,3,5-Triazines from amidines

2	Ar	Yield of **4** (%)	mp. (°C)
a	-Ph	45	83–84 (76–78)
b		50	176–179 (187–188)
c		54	189–191
d		52	220–226

Triazines **4a**–**d** were characterized by IR, MS, and NMR spectroscopy. Analytical data of triazines **4a**–**b** were in agreement with the literature [6].

To understand the mechanism of this reaction, two facts are important. First, it is known that the vinylog ester **5** reacts with amines [4], urea, and thiourea [3], resp., to give the appropriate aminomethylene compounds [5]. On the other hand, treatment of amidines with other formylation reagents gives very poor yields of triazines [2]. Hence, we suppose the mechanism shown in Scheme 3. The intermediate amidinomethylene compound **A** adds a second molecule amidine to give aminal **B**, which fragments into triazine **4**, *Meldrum*'s acid, and ammonia (Scheme 3).



Scheme 3

In summary, we have developed a new method for the preparation of 2,4-diaryl-1,3,5-triazines. The described behaviour of methoxymethylene *Meldrum*'s acid differs from other formic acid derivatives such as alkyl formates and N,N-dimethylformamide dimethylacetal by the great mobility of *Meldrum*'s acid anion in the supposed intermediates.

Experimental

Melting Points: Boetius Heiztisch-Mikroskop (*Küster* Nachf., Dresden), uncorrected values; IR spectra: Perkin Elmer 881; NMR spectra: Bruker AM-300; MS: Hewlett-Packard GCMS-5995-A.

General Procedure for the Synthesis of Triazines **4a**–**d**

0.02 mol amidine·HCl in 80 ml dry MeOH were treated with 0.02 mol KO-*tert*.Bu at 0 °C. After stirring for 30 min, a solution of 0.01 mol 5-methoxymethylen-2,2-dimethyl-1,3-dioxane-4,6-dione (**5**) in 100 ml dry MeOH was added dropwise. After 30 min at 0 °C and *ca.* 2 h at r.t. (TLC-control), the solvent was removed at reduced pressure and the residue redissolved in CH_2Cl_2. The solution was washed with water, 10% NaOH, filtered over a plug of silica gel and dried. Evaporation of the solvent and recrystallization from ethanol gives the appropriate triazine **4**.

2,4-Diphenyl-1,3,5-triazine (**4a**)

Yield, 45%; m.p., 83–84 °C; IR (KBr), $\nu = 1583, 1547, 1535, 1514, 1417, 749, 687\,\mathrm{cm}^{-1}$; ^{1}H NMR (CDCl$_3$, 300 MHz), $\delta = 7.49$–7.61 (m, 6H), 8.60–8.64 (m, 4H), 9.22 (s, 1H) ppm; ^{13}C NMR (CDCl$_3$, 75.5 MHz), $\delta = 128.7, 128.8, 132.7, 135.5, 166.7, 171.2$ ppm; MS (70 eV), m/z (%) = 233 (46, M$^+$), 180 (12), 130 (28, M$^+$-PhCN), 103 (100,.PhCN$^+$), 76 (22).

2,4-bis-(4-Chlorphenyl)-1,3,5-triazine (**4b**)

Yield, 50%; m.p., 176–79 °C; IR (KBr), $\nu = 1579, 1540, 1511, 1416, 804\,\mathrm{cm}^{-1}$; ^{1}H NMR (CDCl$_3$, 300 MHz), $\delta = 7.52$ (d, 4H, $J = 8.8$ Hz), 8.56 (d, 4H, $J = 8.8$ Hz), 9.23 (s, 1H) ppm; ^{13}C NMR (CDCl$_3$. 75.5 MHz), $\delta = 129.1, 130.2, 133.9, 139.4, 166.8, 170.6$ ppm; MS (70 eV), m/z (%) = 301 (32, M$^+$, ^{35}Cl), 164 (4, M$^+$-ClPh), 137 (100, ClPhCN$^+$), 75 (14); $C_{15}H_9N_3Cl_2$ (302.16); calcd., C 59.63, H 3.00, N 13.91, Cl 23.47; found, C 59.56, H 3.02, N 13.48, Cl 23.17.

2,4-bis-(3,4-Dimethoxyphenyl)-1,3,5-triazine (**4c**)

Yield, 54%; m.p. 189–191 °C; IR (KBr), $\nu = 1579, 1540, 1511, 1416, 804\,\mathrm{cm}^{-1}$; ^{1}H NMR (CDCl$_3$, 300 MHz), $\delta = 7.52$ (d, 4H, $J = 8.8$ Hz), 8.56 (d, 4H, $J = 8.8$ Hz), 9.23 (s, 1H) ppm; ^{13}C NMR (CDCl$_3$, 75.5 MHz), $\delta = 129.1, 130.2, 133.9, 139.4, 166.8, 170.6$ ppm; MS (70 eV) m/z (%) = 353 (73, M$^+$), 338 (5, M$^+$-Me), 307 (7, M$^+$-Me, -OMe), 164 (100, (MeO)$_2$PhCN$^+$); $C_{19}H_{19}N_3O_4$ (353.37); calcd., C 64.58, H 5.42, N 11.89; found, C 64.48 H 5.39, N 11.70.

2,4-bis-(3-Nitrophenyl)-1,3,5-triazine (**4d**)

Yield, 52%; m.p. 220–226 °C; IR (KBr), $\nu = 1545, 1511, 1420, 803\,\mathrm{cm}^{-1}$; ^{1}H NMR (CDCl$_3$, 300 MHz), $\delta = 3.95$–4.04 (m, 12H), 6.99–7.03 (d, 2H), 8.14 (s, 2H), 8.27–8.31 (2d, 2H), 9.12 (s, 1H) ppm; ^{13}C NMR (CDCl$_3$, 75.5 MHz), $\delta = 110.8, 111.1, 122.3, 128.3, 149.1, 153.1, 166.3, 170.6$ ppm; MS (70 eV), m/z (%) = 323 (59, M$^+$), 277 (37, M$^+$-NO$_2$), 250 (14), 148 (15), 129 (83), 102 (100); $C_{15}H_9N_5O_4$ (323.26); calcd., C 55.73, H 2.81, N 21.66; found, C 53.95, H 2.73, N 21.25.

Acknowledgement

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[5] We have found that 3-methoxymethylen-furan-2,4-dione instead of **5** reacts with S-ethylisothiuronium-bromide to give 2,4-*bis*-(ethylthio)-1,3,5-triazine in 40% yield. We suppose that this tetronic acid derivative could be an alternative to **5** in several cases. We hope to confirm this in further investigations.

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