Synthesis of 1,4-Diazabutadienes (= *N*,*N*′-Ethane-1,2-diylidenebis[amines]) by Grinding

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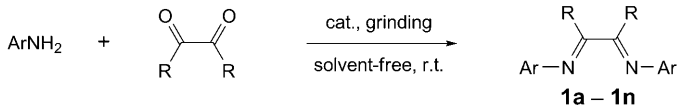
A simple and convenient method for the synthesis of 1,4-diazabutadienes (= *N*,*N*′-ethane-1,2-diylidenebis[amines]) by grinding glyoxal (= ethanedial) or an α-diketone and anilines (= benzenamines) in the presence of TsOH in a mortar with a pestle is described. By this way, 1,4-diazabutadienes were obtained in good to excellent yields.

Introduction. – The 1,4-diazabutadienes (= *N*,*N*′-ethane-1,2-diylidenebis[amines]) are versatile compounds in fine and pharmaceutical chemistry, especially in materials science as liquid crystalline and mesoporous materials [1][2]. The traditional method for the synthesis of 1,4-diazabutadienes is the condensation of α-diketones and anilines (= benzenamines) in organic solvents such as MeOH, i-PrOH, or CH_2Cl_2 [3–5]. However, harsh reaction conditions, long reaction times, and the use of organic solvents often present some disadvantages. Thus, the development of a simple and efficient method for the synthesis of 1,4-diazabutadienes is still a rewarding challenge.

According to the literature, a large number of organic reactions can be carried out in high yield under mild conditions simply by grinding [6]. We thought that this observation warranted further investigation to better understand the influence of grinding on the synthesis of 1,4-diazabutadienes **1** without solvent (*Scheme*).

Scheme



1a – 1n

Ar = 4-MeC_6H_4, 2-MeC_6H_4, 4-ClC_6H_4, 3,5-$(CF_3)_2C_6H_3$, 2,6-$(i\text{-}Pr)_2C_6H_3$, 2,6-$Me_2C_6H_3$, 4-$MeOC_6H_4$
R = H, Me

Results and Discussion. – A preliminary test was carried out to survey the requisite conditions and establish modifications required for this methodology. Glyoxal trimer dihydrate (instead of aqueous glyoxal solution) and anilines containing different substituents were ground at room temperature (glyoxal = ethanedial). The reaction time and yields of **1** are summarized in *Table 1* and compared with those of traditional

methods. The data in *Table 1* showed that, in all cases, the reactions exhibited high selectivity toward corresponding 1,4-diazabutadienes and short reaction times (30 to 90 min). The long reaction time (*e.g.*, 24 and 96 h for **1g** and **1h**), which is one of the main drawbacks of the traditional method, is substantially shortened by our method. Moreover, the isolation of the products was simplified since the 1,4-diazabutadienes were the main products which were purified by washing or recrystallization from minimum amounts of EtOH. The conventional method gave the 1,4-diazabutadienes with by-products such as 1,2-diamino-1,2-diols, or ethanetri- or ethanetetraamine derivatives, requiring purification by column chromatography [3].

Table 1. *Formation of 1,4-Diazabutadienes* **1** *by Different Methods*

	Ar	R	Grinding method[a])		Traditional method[b])	
			time [min]	yield [%][c])	time [h]	yield [%][d])
1a	4-MeC_6H_4	H	90	36	2	26 [3]
1b	4-MeC_6H_4	Me	40	69	2.5	50 [4]
1c	2-MeC_6H_4	H	60	68	2	58 [3]
1d	2-MeC_6H_4	Me	30	74	20	54 [5b]
1e	4-ClC_6H_4	H	50	56	10	37 [3]
1f	4-ClC_6H_4	Me	50	75	20	60 [5c]
1g	3,5-$(CF_3)_2C_6H_3$	H	50	73	24	73 [5a]
1h	3,5-$(CF_3)_2C_6H_3$	Me	40	71	96	26 [7a]

[a]) Glyoxal trimer dihydrate (1 mmol) or butane-2,3-dione (3 mmol), corresponding aniline (6 mmol), and grinding. [b]) Glyoxal (40% aq. soln.; 1 mmol) or butane-2,3-dione (1 mmol), corresponding aniline (2 mmol), organic solvent. [c]) Yield of isolated product. [d]) Yield after purification by column chromatography or recrystallization.

The catalytic activity of *Lewis* acid and TsOH was also studied. A blank reaction was conducted with *p*-toluidine (= 4-methylbenzenamine) and glyoxal in the absence of catalysts by grinding at room temperature, and 1,4-bis(4-methylphenyl)diazabutadiene (= *N*,*N*′-ethane-1,2-diylidenebis[4-methylbenzenamine]; **1a**) was obtained in 36% yield after 90 min. In the presence of a catalytic amount of TsOH (5 mol-%), **1a** was produced in 81% yield within 50 min. The effect of *Lewis* acids such as $ZnCl_2$, $AlCl_3$, $FeCl_3$, and $SnCl_4$ are summarized in *Table 2*. The results show that *Lewis* acids can also accelerate the formation of **1a**, but TsOH was superior as catalyst for this reaction.

Table 2. *Effects of Catalysts on the Synthesis of* **1a** *by Grinding*

Catalyst	Time [min]	Yield [%][a])	Catalyst	Time [min]	Yield [%][a])
no	90	36	$AlCl_3$	80	70
TsOH	50	81	$FeCl_3 \cdot 6\,H_2O$	70	75
$ZnCl_2$	80	74	$SnCl_4 \cdot 5\,H_2O$	70	76

[a]) Yield of isolated product.

The reaction outcome with increasing amounts of TsOH (1, 5, 10, 15, and 20 mol-%) resulted in an increase of yield (from 65 to 89%) and shortening of the reaction time

(from 60 to 30 min) as shown in *Table 3*. The use of 10 mol-% of TsOH was sufficient to push the reaction forward, while a larger amount of the catalyst did not improve the results greatly. Therefore, 10 mol-% of TsOH were chosen as the optimal catalyst amount for all other syntheses of **1**.

Table 3. *Effects of the Amount of TsOH on the Synthesis of* **1a** *by Grinding*

TsOH [mol-%]	Time [min]	Yield [%][a])	TsOH [mol-%]	Time [min]	Yield [%][a])
1	60	65	15	30	87
5	50	81	20	30	89
10	30	86			

[a]) Yield of isolated product.

The reactions generally gave high yields of products (*Table 4*). No obvious electronic effect of the substituents of the anilines was observed in the reactions since electron-donating as well as electron-withdrawing groups were well tolerated. Compound **1a** was previously prepared in 26% yield in i-PrOH as solvent, and **1c** and **1m** in 58% yield in MeOH [3], whereas our procedure gave these 1,4-diazabutadienes in 86, 88, and 93% yield, respectively. Compounds **1g** and **1h** were previously prepared in 73 and 26% yield, respectively, catalyzed by HCOOH in MeOH with reaction times of 24 and 96 h [5a][7a]. The present procedure gave **1g** and **1h** in 84 and 91% yield, respectively, within 30 min.

Table 4. *Synthesis of 1,4-Diazabutadienes* **1**[a]) *by the Grinding Method*

	Ar	R	Time [min]	Yield [%][b])		M.p. [°]	
				found[c])	reported	found[c])	reported
1a	4-MeC_6H_4	H	30	86	26 [3]	131.8–132.7	132–133 [3]
1b	4-MeC_6H_4	Me	30	82	50 [4]	110.2–111.6	112 [4]
1c	2-MeC_6H_4	H	30	88	58 [3]	123.2–125.0	123–124 [3]
1d	2-MeC_6H_4	Me	30	81	54 [5b]	70.8–71.6	73 [5b]
1e	4-ClC_6H_4	H	50	86	37 [3]	107.5–108.9	107–110 [3]
1f	4-ClC_6H_4	Me	45	85	60 [5c]	172.4–173.8	172 [9]
1g	3,5-$(CF_3)_2C_6H_3$	H	30	84	73 [5a]	223.4–224.6	–
1h	3,5-$(CF_3)_2C_6H_3$	Me	30	91	26 [7a]	198.2–199.6	–
1i	2,6-(i-Pr)$_2C_6H_3$	H	35	88	78 [7b]	102.2–103.5	104 [5b]
1j	2,6-(i-Pr)$_2C_6H_3$	Me	45	80	76 [5b]	95.5–97.3	99 [5b]
1k	2,6-$Me_2C_6H_3$	H	50	84	85 [5b]	151.4–152.6	151 [5b]
1l	2,6-$Me_2C_6H_3$	Me	30	76	83 [5b]	85.3–86.5	88 [5b]
1m	4-MeOC_6H_4	H	45	93	58 [3]	154.2–155.3	153–154 [3]
1n	4-MeOC_6H_4	Me	30	89	35 [8]	186.3–187.6	186–187 [9]

[a]) All the isolated products were characterized by their physical properties, by ^{1}H-NMR and IR spectra, and by direct comparison with literature data [3–5][7–9]. [b]) Yield of isolated product. [c]) This work.

Conclusions. – We developed an efficient method for the synthesis of 1,4-diazabutadienes *via* condensation of glyoxal or an α-diketone and anilines in the

presence of 10 mol-% of TsOH as catalyst by simple grinding at room temperature without a solvent.

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Experimental Part

General. All chemicals and reagents were purchased from commercial sources and used without further purification. Grinding was performed in a 100 ml mortar with a pestle. M.p.: *X-5* melting-point apparatus; uncorrected. IR Spectra: *Vertex-70-FT-IR* spectrophotometer; KBr pellets. ^{1}H-NMR Spectra: *Bruker-Avance-II-400* instrument (400 MHz); in $CDCl_3$.

General Procedure. Aniline (= benzenamine; 6 mmol), glyoxal trimer dihydrate (1 mmol, 210 mg) or butane-2,3-dione (3 mmol, 258 mg), and TsOH (10 mol-%) were placed in a mortar. Then, the mixture was ground with a pestle at r.t. The reactions were completed within 30–50 min. The product was washed with EtOH or recrystallized from a minimum amount of EtOH to afford the 1,4-diazabutadiene. All products were identified by their melting points, IR and ^{1}H-NMR spectra, and comparison with reported data [3–5][7–9] (see also *Table 4*).

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