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The synthesis and isolation of the intermediates *N*-[1-aryl(alkyl)-3-oxo-4,4,4-trichloro-1-buten-1-yl]-*o*-phenylenediamines **2a-f** and the corresponding 2-trichloromethyl-4-aryl-3*H*-1,5-benzodiazepines **3c-g** or benzimidazoles **4a-b** derivatives obtained from the intramolecular cyclization of **2a-f** or from direct cyclocondensation reaction of β -alkoxyvinyl trichloromethyl ketones **1a-g** with *o*-phenylenediamine, is reported. Depending of the structure of the β -alkoxyvinyl trichloromethyl ketones or the *N*-[1-aryl(alkyl)-3-oxo-4,4,4-trichloro-buten-1-yl]-*o*-phenylenediamines and the reactions conditions, benzimidazoles or 3*H*-1,5-benzodiazepines were obtained.

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In 1965, Effenberger [1] observed that 1,6-diethoxy-1,5-hexadiene-3,4-dione reacted with several primary and secondary amines (alkyl- and arylamines) in molar ratio 1:2 leading to the 1,6-diamino-1,5-hexadiene-3,4-dione in high yields. In recent years, Gerus and co-workers [2] reported the reaction of the β -alkoxyvinyl trifluoromethyl ketones with ammonia and primary amines to afford β -aminovinyltrifluoromethyl ketones. The reactions of the diamino compounds, ethylenediamine or *o*-phenylenediamine, with two equivalents of the enone gave the respective *N,N*-diaminotrifluoromethyl derivatives. In 1991, protected amino acids were prepared by the reaction of β -ethoxyvinyl trifluoromethyl ketone with L-amino acids in aqueous sodium hydroxide solution and the products were isolated in high yield after acidification of the reaction mixture [3]. We have previously found that the *EE*-conformer of 1,6-diethoxy-1,5-hexadiene-3,4-dione reacts with primary amines in molar ratio 1:1 to give mainly 1-aminoalkyl-6-ethoxy-1,5-hexadiene-3,4-diones exclusively as *Z,E* isomers. These 1-aminoalkyl-6-ethoxy-1,5-hexadiene-3,4-diones cyclize, under reflux in 1,2-dichlorobenzene, to yield 1-alkyl-1*H*-azepine-4,5-diones by an intramolecular cyclocondensation reaction [4].

On the other hand, it is well known that the intermolecular condensation of *o*-phenylenediamine with β -dicarbonyl compounds, as a one-pot procedure, has been the most widely used method for the synthesis of 3*H*-1,5-benzodiazepines [5,6]. Considering this information, we have investigated the reactions of some β -alkoxyvinyl trichloromethyl ketones with *o*-phenylenediamine, under various conditions. We have found that the synthesis of trichloroacetylated enaminones from β -alkoxyvinyl trichloromethyl ketones, as precursor from trichloromethylated heterocycles has not been reported yet.

As a part of our research program we have developed a general one-step procedure for preparing analytical, pure

β -alkoxyvinyl trihalomethyl ketones from the acylation of several enol ethers [7] or acetophenone dimethyl acetals [8,9], and trichloroacetyl chloride or trifluoroacetic anhydride, in molar quantities. These compounds have been used as precursors of a variety of substituted five- and six-membered heterocyclic halomethyl substituted compounds, *e.g.* isoxazoles [7,10-13], pyrazoles [14,15] and pyrimidines [16-18]. Recently, we have communicated the synthesis of substituted seven-membered 2-trichloromethylated-3*H*-1,5-benzodiazepines from the reaction of β -alkoxyvinyl trichloromethyl ketones with *o*-phenylenediamine [19].

The purpose of this work is to report the results of the synthesis of a series of fused seven-membered 2-trichloromethyl-4-aryl-3*H*-1,5-benzodiazepines **3c-g** and the isolation of the intermediates *N*-[1-aryl(alkyl)-3-oxo-4,4,4-trichloro-1-buten-1-yl]-*o*-phenylenediamines **2a-f** from the reactions of the 4-alkoxy-4-aryl(alkyl)-1,1,1-trichloro-3-buten-2-ones **1a-f** and *o*-phenylenediamine (Scheme 1).

The reactions of compounds **1a-g** with *o*-phenylenediamine, in dichloromethane at room temperature, led to the *N*-[1-aryl(alkyl)-3-oxo-4,4,4-trichloro-1-buten-1-yl]-*o*-phenylenediamines **2a-f**. The enaminone **2g** was not isolated as a pure compound. The same reaction carried out for compounds **1c-g** (R = aryl) in ethanol/acetic acid 4:1 for 2 or 3 hours at 60°, produced only the compounds **3c-g** in 52-79% yields. This reaction was carried out for compounds **1a-b** (R = alkyl) in the same solvent but for 3 or 4 hours at 80°, afforded benzimidazole **4a,b** in 70% and 75% yield, respectively.

Depending on the structure of the precursor, the intramolecular cyclocondensation of compounds **2a-f**, in ethanol/acetic acid 4:1 for 2 or 3 hours at 60° or for 3 or 4 hours at 80°, furnished the 3*H*-1,5-benzodiazepines **3c-f** or the benzimidazole **4a-b** in good yields.

Scheme 1

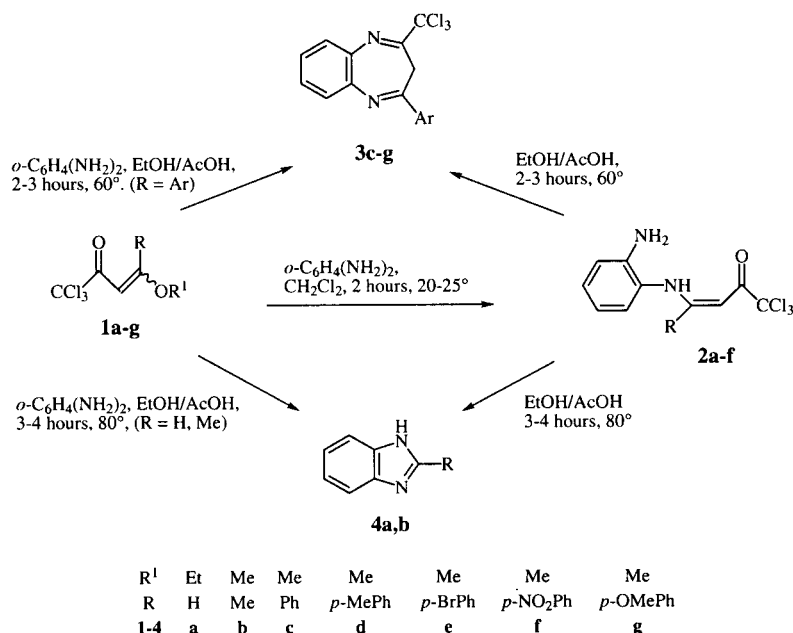


Table 1

Selected Physical Data for *N*-[1-Aryl(alkyl)-3-oxo-4,4,4-trichloro-1-buten-1-yl]-*o*-phenylenediamines **2a-f**

Compound	Yield (%) [a]	Mp (°) [b]	Molecular Formula	Analysis (%) [c]		
				C	Calcd./Found H	N
2a	90	107-108	C ₁₀ H ₉ N ₂ OCl ₃ 279.50	42.96 42.90	3.24 3.24	10.02 9.98
2b	92	109-110	C ₁₁ H ₁₁ N ₂ OCl ₃ 295.50	45.00 44.97	3.78 3.77	9.54 9.45
2c	68	131-133	C ₁₆ H ₁₃ N ₂ OCl ₃ 355.50	54.01 53.96	3.65 3.81	7.88 7.81
2d	76	138-139	C ₁₇ H ₁₅ N ₂ OCl ₃ 369.50	55.12 55.24	4.06 4.23	7.58 7.57
2e	94	159-161	C ₁₆ H ₁₂ N ₂ OBrCl ₃ 434.50	44.20 44.21	2.76 2.87	6.44 6.30
2f	71	169-170	C ₁₆ H ₁₂ N ₃ O ₃ Cl ₃ 400.50	47.94 47.83	3.00 3.12	10.49 10.40

[a] Yields of isolated compounds. [b] The melting points are uncorrected. [c] Elemental analysis were performed on a Vario EL Elementar Analysensysteme.

Table 2

Selected ¹H and ¹³C NMR Spectral Data [a] of Compounds **2a-f**

Compound	¹ H NMR, δ (ppm)
	¹³ C NMR, δ (ppm)
2a	11.2 (bs, 1H, N-H), 7.5-7.6 (dd, 1H, H1), 6.8-7.5 (m, 4H, aromatic-H), 6.0 (d, 1H, H2), 3.0 (bs, 2H, NH ₂).
	182.8 (C=O), 151.3 (C1), 137.6-117.7 (6C, aromatic-C), 96.4 (CCl ₃), 88.2 (C2).
2b	11.5 (bs, 1H, N-H), 6.6-7.2 (m, 4H, aromatic-H), 5.9 (s, 1H, H2), 3.8 (bs, 2H, NH ₂), 2.0 (s, 3H, -CH ₃).
	180.3 (C=O), 168.7 (C1), 141.7-115.4 (6C, aromatic-C), 96.2 (CCl ₃), 87.1 (C2).
2c	11.6 (bs, 1H, N-H), 6.4-6.9 and 7.2 (m, 9H, aromatic-H), 6.0 (s, 1H, H2), 3.6 (bs, 2H, NH ₂).
	181.8 (C=O), 168.1 (C1), 141.3-116.0 (12C, aromatic-C), 96.9 (CCl ₃), 90.3 (C2).
2d	11.7 (bs, 1H, N-H), 6.5-7.0 and 7.1-7.2 (m, 8H, aromatic-H), 6.1 (s, 1H, H2), 3.6 (bs, 2H, NH ₂), 2.3 (s, 3H, -CH ₃).
	181.6 (C=O), 168.2 (C1), 141.4-116.0 (12C, aromatic-C), 97.0 (CCl ₃), 90.1 (C2), 19.4 (<i>p</i> -CH ₃).
2e	11.4 (bs, 1H, N-H), 6.4-6.9 and 7.1-7.5 (m, 8H, aromatic-H), 6.0 (s, 1H, H2), 3.5 (bs, 2H, NH ₂).
	181.9 (C=O), 166.8 (C1), 141.3-115.9 (12C, aromatic-C), 96.8 (CCl ₃), 90.3 (C2).

Table 2 (continued)
Selected ^1H and ^{13}C NMR Spectral Data [a] of Compounds **2a-f**

Compound	^1H NMR, δ (ppm) ^{13}C NMR, δ (ppm)
2f	1.3 (bs, 1H, N-H), 6.4-7.6 and 8.0-8.2 (m, 8H, aromatic-H), 6.0 (s, 1H, H2), 3.8 (bs, 2H, NH_2), 182.2 (C=O), 165.8 (C1), 148.6-116.2 (12C, aromatic-C), 96.6 (CCl_3), 90.8 (C2).

[a] The nmr spectra were recorded on a Bruker DPX-200 (^1H at 200.13 MHz and ^{13}C at 50.32 MHz) in deuteriochloroform/tetramethylsilane.

Table 3
Selected Physical Data for 2-Trichloromethyl-4-aryl-3*H*-1,5-benzodiazepines **3c-g**

Compound	Yield (%) [a]	Mp ($^\circ$) [b]	Molecular Formula	Analysis (%) [c] Calcd./Found		
				C	H	N
3c	67	110-112	$\text{C}_{16}\text{H}_{11}\text{N}_2\text{Cl}_3$ 337.50	56.88 56.83	3.26 3.34	8.30 8.09
3d	79	129-130	$\text{C}_{17}\text{H}_{13}\text{N}_2\text{Cl}_3$ 351.50	58.04 57.79	3.70 3.74	7.96 7.82
3e	66	153-154	$\text{C}_{16}\text{H}_{10}\text{N}_2\text{Cl}_3\text{Br}$ 416.50	46.10 45.99	2.76 2.58	6.44 6.56
3f	55	148-149	$\text{C}_{16}\text{H}_{10}\text{N}_3\text{O}_2\text{Cl}_3$ 382.50	50.20 50.25	2.61 2.62	10.98 10.65
3g	52	125-127	$\text{C}_{17}\text{H}_{13}\text{N}_2\text{OCl}_3$ 367.50	55.21 55.00	3.54 3.62	7.62 7.59

[a] Yields of isolated compounds. [b] The melting points are uncorrected. [c] Elemental analysis were performed on a Vario EL Elementar Analysensysteme.

Table 4
Selected ^1H and ^{13}C nmr Spectral Data [a] for Compounds **3c-g**

Compound	^1H -NMR, δ (ppm) ^{13}C NMR, δ (ppm)
3c	8.0-7.9 and 7.6-7.2 (m, 9H, aromatic-H), 3.6 (s, 2H, $-\text{CH}_2-$). 156.3 (C2/C4), 151.7 (C4/C2), 140.0-125.5 (12C, aromatic-C), 96.5 (CCl_3), 32.8 (C3)
3d	7.9-7.8 and 7.6-7.0 (m, 8H, aromatic-H), 3.7 (bs, 2H, $-\text{CH}_2-$), 2.3 (s, 3H, $-\text{CH}_3$). 156.9 (C2/C4), 152.4 (C4/C2), 142.0 (CCl_3), 33.4 (C3), 22.0 (<i>p</i> - CH_3).
3e	7.9-7.8 and 7.6-7.4 (m, 8H, aromatic-H), 3.6 (bs, 2H, $-\text{CH}_2-$). 154.8 (C2/C4), 151.4 (C4/C2), 140.4-125.7 (12C, aromatic-C), 96.3 (CCl_3), 32.4 (C3).
3f	8.3-8.2 and 7.6-7.3 (m, 8H, aromatic-H), 3.7 (bs, 2H, $-\text{CH}_2-$). 154.0 (C2/C4), 151.6 (C4/C2), 149.0-124.0 (12C, aromatic-C), 96.3 (CCl_3), 33.0 (C3).
3g	7.9-7.8 and 7.5-6.0 (m, 8H, aromatic-H), 3.6 (bs, 2H, $-\text{CH}_2-$), 3.4 (s, 3H, <i>p</i> - OCH_3). 162.1 (C2/C4), 150.0 (C4/C2), 141.0-125.9 aromatic-C), 96.7 (CCl_3), 32.7 (C3), 55.2 (<i>p</i> - OCH_3).

[a] The nmr spectra were recorded on a Bruker DPX-200 (^1H at 200.13 MHz and ^{13}C at 50.32 MHz) in deuteriochloroform/tetramethylsilane.

The results of this work suggest that the synthesis of 1,5-3*H*-benzodiazepines **3c-g** or the benzimidazoles **4a-b** does not depend on the first step of the reaction, the synthesis of the β -enaminones **2a-f**. It was observed that the bulky groups at the 4-position of **1a-g** or at **2a-f** favours the formation of the benzodiazepines **3c-g** and that compounds **1a-b** or **2a-b** with small groups at this position, are readily converted into benzimidazole **4a-b**.

All reactions are presented in Scheme 1 and the best results of these reactions are shown in Tables 1 and 3.

Selected physical and spectral data are presented in Tables 2 and 4.

EXPERIMENTAL

The β -alkoxyvinyl trichloromethyl ketones **1a-b** were prepared according to reference [7] and the β -aryl- β -methoxyvinyl trichloromethyl ketones **2c-f** were synthesized from the reaction of the respective acetophenone dimethyl acetals with trichloroacetyl chloride [8,9]. The ^1H - and ^{13}C -nmr spectra, at

200.13 and 50.32 MHz respectively, were recorded on a Bruker DPX-200 in a 5 mm probe in chloroform- d_1 and tetramethylsilane was used as internal reference. The melting points were taken on a melting point microscope Reichert-Thermovar and are uncorrected. The elemental analysis were performed on an Elementar Analysensysteme Vario EL equipment.

N-[1-Aryl(alkyl)-3-oxo-4,4,4-trichloro-1-buten-1-yl]-*o*-phenylenediamines **2a-f**.

General Procedure.

To a stirred solution of *o*-phenylenediamine (20 mmoles) in 80 ml of dry dichloromethane, a solution of the 4-alkoxy-4-aryl(alkyl)-1,1,1-trichloro-3-buten-2-one **1a-f** (20 mmoles) in dry dichloromethane was added for 1 hour at 20-25°. The mixture was stirred for 1 hour at 20-25°. The solvent was evaporated and the solid or crude oily products **2a-b** were recrystallized from methanol or dichloromethane/diethyl ether (3:1) (yields, 68-94%, Table 1). Compound **2g** could not be isolated as a pure compound.

2-Trichloromethyl-4-aryl-3*H*-1,5-benzodiazepines **3c-g** and Benzimidazoles **4a-b** from 4-Alkoxy-4-aryl(alkyl)-1,1,1-trichloro-3-buten-2-ones **1a-g**.

General Procedure.

To a stirred solution *o*-phenylenediamine (6 mmoles) in 4 ml of dry ethanol and 1 ml acetic acid, 4-alkoxy-4-aryl(alkyl)-1,1,1-trichloro-3-buten-2-ones **1a-g** (6 mmoles) were added in small portions at 60°. The mixture was stirred for 2-3 hours at 60° for **1c-g** or for 3-4 hours at 80° for **1a-b**. The solvent was removed and the crude solid products were recrystallized from methanol for **3c-g** or from water for **4a-b** (yields 52-79%, Table 3, **4a** 70%, **4b** 75%).

2-Trichloromethyl-4-aryl-3*H*-1,5-benzodiazepines **3c-g** and Benzimidazoles **4a-b** from *N*-[1-Aryl(alkyl)-3-oxo-4,4,4-trichloro-1-buten-1-yl]-*o*-phenylenediamines.

General Procedure.

A solution *N*-[1-aryl(alkyl)-3-oxo-4,4,4-trichloro-1-buten-1-yl]-*o*-phenylenediamines **2a-f** (6 mmoles) in 4 ml of dry ethanol and 1 ml of acetic acid was stirred for 2-3 hours at 60° for **2c-f** or for 3-4 hours at 80° for **2a-b**. The solvent was removed and the crude solid products were recrystallized from methanol **3c-g** or from water for **4a-b** (yields **3c-g** 50-72%, **4a** 73%, **4b** 75%).

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