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A Convenient Method For The Synthesis of 2-Trichloromethyl-4-p-Substituted-Phenyl-3H-1,5-Benzodiazepines.

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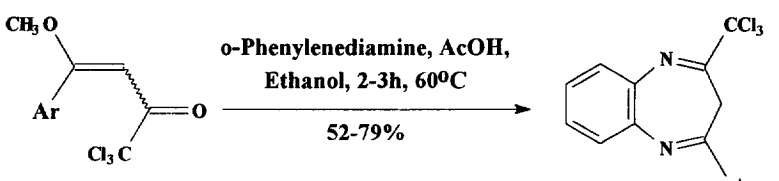
Abstract: A convenient method to obtain a new series of 2-trichloromethyl-4-aryl-3H-1,5-benzodiazepines from the reaction of β-methoxyvinyl trichloromethyl ketones derived from acetals and o-phenylenediamine is reported. Copyright © 1996 Elsevier Science Ltd

The condensation of o-phenylenediamine with β-dicarbonyl compounds has been the most widely used method for the synthesis of 3H-1,5-benzodiazepines.[1,2] Recently, considerable attention has been devoted to the synthesis of 1,5-Benzodiazepines containing ring fused heterocycles to different faces of the diazepine ring.[3,4] As part of our studies on the use of β-alkoxyvinyl trichloromethyl ketones[5,6] derived from acetals to synthesize heterocycle systems,[7,8] this work reports the synthesis of a new series of fused seven-membered 2-trichloromethyl-4-aryl-3H-1,5-Benzodiazepines **2a-e**. The compounds **2a-e** were obtained from the direct cyclo-condensation of o-phenylenediamine with β-methoxy-β-aryl-trichloromethyl vinyl ketones **1a-e**, which are readily available.

Scheme



1	Ar	Ph	p-MePh	p-BrPh	p-OMePh	p-NO_2Ph	2
	1,2	a	b	c	d	e	
	Yield (%)	67	79	66	52	55	

Although the obvious route to obtain 2-trichloromethyl-4-aryl-3H-1,5-benzodiazepines is the condensation of 1,3-dicarbonyl compounds with o-phenylenediamine, it is relatively difficult to obtain benzoyltrichloromethyl ketones. For example, a simple benzoyltrichloromethyl ketone[9] has been obtained in moderate yield using a laborious procedure which reacts trimethylsilyl alkenyl ethers with polychloroacetyl

chloride. The main difficulty in obtaining trichloromethyl substituted β-dicarbonyl compounds such as p-substituted-benzoyltrichloromethyl ketones was overcome in our laboratory, when in previous work we demonstrated the synthesis of β-methoxy-β-aryl-trichloromethyl vinyl ketones[5,6] from the acylation of acetophenone acetals with trichloroacetyl chloride in good yields (80-92%). In summary, we developed an efficent preparation of trichloromethyl-3H-1,5-Benzodiazepines from β-alkoxyvinyl trichlromethyl ketones under mild acid conditions in moderate to good yields (52-79 %).[10] Specific syntheses and proprieties of 2-trichloromethyl-4-aryl-3H-1,5-Benzodiazepines are not yet known.

Preparation of 2-Trichloromethyl-4-Aryl-3H-1,5-Benzodiazepines(**2a-e**).

General Procedure : To a stirred solution of o-phenylenediamine (6 mmoles) in 4.0 ml of dry ethanol and 1ml acetic acid, 4-methoxy-4-aryl-1,1,1-trichloro-3-buten-2-ones **1a-e** (6 mmoles) was added in small portions at 60°C. The mixture was stirred for 2-3 hours at 60°C. The solvent was removed and the crude solid product was recrystallized from methanol.

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References and Notes.

1. Katritzky, A.R., Rees, C.W. *Comprehensive Heterocyclic Chemistry*; Vol. *7*; Pergamon Press: Oxford, 1984; pp. 594-620.
2. Lloyd, D; Cleghorn, H.P. *Adv. Heterocyclic Chem.* **1974**, *17*, 27.
3. Martínez, R.; Hernández, P.E.; Angeles, E. *J. Heterocyclic Chem.* **1996**, *33*, 271.
4. Chimirri, A.; Gitto, R.; Grosso, S.; Monforte, A.; Romero, G.; Zappalá, M. *Heterocycles*, **1993**, *36*, 3.
5. Martins, M.A.P.; Siqueira, G.M.; Flores, A.F.C.; Clar, G.; Zanatta, N. *Química Nova*, **1994**, *17*, 24.
6. Martins, M.A.P.; Siqueira, G.M.; Flores, A.F.C.; Zanatta, N. *Química Nova*, **1994**, *17*, 298.
7. Martins, M.A.P.; Flores, A.C. ; Feitag, R.A.; Zanatta, N. *J. Heterocyclic Chem.* **1995**, *32*, 731.
8. Martins, M.A.P.; Freitag, R.A.; Flores, A.F.C.; Zanatta, N. *Synthesis*, **1995**, *12*, 1491.
9. Murai, S.; Kuroki, Y.; Hasegawa, K.; Tsutsumi, S. *J. Chem. Soc. Chem. Comm.* **1972**, 946.
10. All new compounds **2a-e** were fully characterized by spectroscopic methods.

Data for **2c**: yellow prisms (methanol) m.p. 154-155°C.^{1}H NMR (80 MHz, $CDCl_3$) δ 7.40-7.94 (m, 8H, aromatic C-H), 3.64 (s, 2H, aliphatic CH_2) ; ^{13}C NMR (20.15 MHz, $CDCl_3$) δ 154.83, 151.41, 140.59, 136.12, 135.04, 131.71, 131.50, 130.03, 129.01, 127.24, 125.95, 125.68, 96.34, 32.40. Analysis calcd. for $C_{16}H_{10}N_2Cl_3Br$ C 46.14, H 2.42, N 6.73. Found: C 45.99, H 2.58, N 6.56

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