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Reaction of N,N-Dimethylacrylamide/Trifluoromethanesulfonic Anhydride Complex with Electron-Rich Aromatic Compounds

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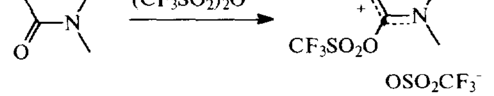
Abstract: The reaction of N,N-dimethylacrylamide/trifluoromethanesulfonic anhydride complex with electron-rich aromatic compounds affords after hydrolysis the corresponding indanones and 1,3-diarylpropanones. Copyright © 1996 Elsevier Science Ltd

The reaction of aromatic compounds with dimethylformamide/phosphorus oxychloride complex (Vilsmeier-Haack reaction) is a convenient method for formylation. However, only the formylation has a synthetic significance, because amides other than dimethylformamide are inactive or react only with the most active aromatics, such as pyrrole and indole (vinylogous Vilsmeier-Haack reaction).[1,2] α,β-Unsaturated N-acylureas was found to react with aryl alkyl ethers in the presence of polyphosphoric acid to give β-substituted arylvinylketones and 3-substituted indanones.[3]

Earlier it was found[4] that the use of trifluoromethanesulfonic anhydride, instead of phosphorus oxychloride, leads to a more reactive iminium salt, which reacts with less activated aromatic compounds under mild conditions. This reagent allows to formylate compounds which do not react under conditions of Vilsmeier-Haack reaction.

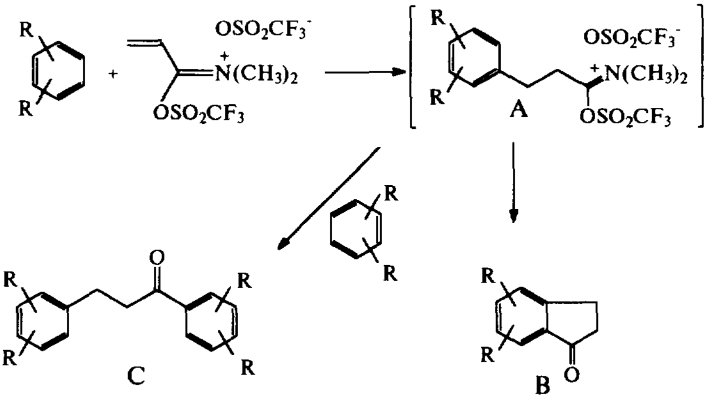
In this paper we report the reaction of some electron-rich aromatic compounds with N,N-dimethylacrylamide/trifluoromethanesulfonic anhydride complex. This complex is obtained by treatment of the corresponding amide with triflic anhydride at 0^0 C (Scheme 1). The application of dimethylacrylamide in Vilsmeier-Haack reaction was not described earlier.



Scheme 1

This complex has two electrophilic reaction centers and reacts with alkoxy benzenes and thiophene to give two types of compounds after hydrolysis. The products of type B result from the intramolecular cyclisation of intermediate A while the products of type C are formed from the intermolecular reaction of intermediate A with another molecule of the aromatic compound

(Scheme 2). Less active aromatic compounds like benzene, toluene and naphthalene do not enter into the reaction.



Scheme 2

The reactions with 1,2-dimethoxybenzene and 1,4-dimethoxybenzene give only the product of type B. In the case of 1,3-dimethoxybenzene, anisole and ethoxybenzene only the products of type C were obtained (Table 1).

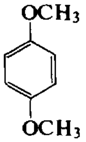
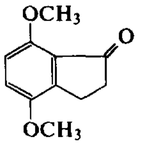
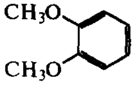
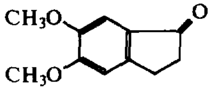
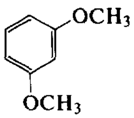
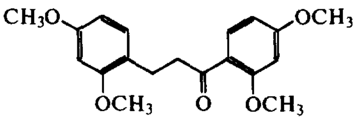
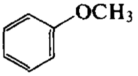
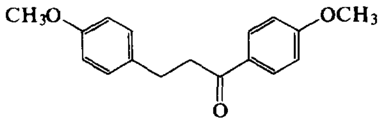
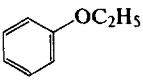
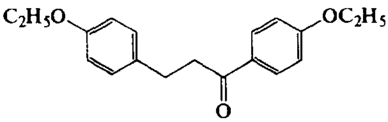
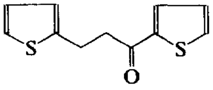
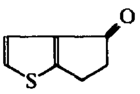
The reaction mode in the case of thiophene depends upon the reaction conditions. In the case of considerable dilution of reaction mixture the products B/C ratio > 4 was obtained. The using of the small amount of solvent and excess of thiophene (over 100%) leads to the B/C ratio 1:6 (Table 1).

We suppose that the first step of the reaction is the reaction of the double bond and the aromatic nucleus to form intermediate A. The second step is the cyclization of the corresponding iminium triflate or the reaction of the iminium salt with another molecule of the aromatic compound. This mechanism is supported by formation of the corresponding indanone from thiophene[5].

We explain the formation of two types of products by differences in reactivity of adjacent positions of aromatic substrate. In the case of 1,2-dimethoxybenzene and 1,4-dimethoxybenzene the adjacent positions are still activated, resulting in the formation of the corresponding indanones. In the cases of anisole, ethoxybenzene and 1,3-dimethoxybenzene the difference in reactivity of para- and meta- positions of aromatic ring is significant and the intermolecular reaction is preferable. The α/β position reactivity ratio for thiophene is lower than that for alkoxybenzenes and both types of the products are obtained. We succeed in finding reaction conditions for the preparative synthesis of both indanone and 1,3-dithienylpropanone.

Thus, the reaction of N,N-dimethylacrylamide with triflic anhydride leads to the formation of the iminium salt which reacts with electron-rich aromatic compounds. This reaction is a simple one-step method for the conversion of the aromatic compounds into the corresponding indanones or 1,3-diarylpropanones depending on the properties of substrate, in moderate yields.

Table 1. Reaction of aromatic compounds with N,N-dimethylacrylamide/ trifluoromethanesulfonic anhydride complex

Entry	Substrate	Reaction time, h	Product	Mp, °C	Yield, %
1		8		125-126	60 (75)[a]
2		6		118	42 (67)[a]
3		3		81-83	46
4		3		37-39	56
5		3		79-80	40
6		3		29-30	48[b]
7		8		114	40[c]

[a] - yield based on conversion of substrate

[b] - the reaction carried out with small amount of solvent and two equivalents of substrate (10-15 ml $C_2H_4Cl_2$ per gram of thiophene); yield of indanone less then 8%

[c] - the reaction proceeded with over 200 ml of solvent per gram of thiophene; yield of 1,3-dithienylpropanone 10%

General procedure

A solution of 0.86 g (8.5 mmol) of N,N-dimethylacrylamide in 15 ml anhydrous dichloroethane was cooled to 0° C. Over a period of 10 min, 2.4 g (8.5 mmol) of triflic anhydride in 10 ml of dichloroethane was added dropwise. Then 8.5 mmol of the aromatic substrate[6] in 10 ml dichloroethane was added. The reaction mixture was refluxed 3-8 h and then was added to a mixture of diethyl ether and aqueous K_2CO_3 and stirred for an additional 1 h. The organic layer was separated, the aqueous layer was extracted with ether (2×50 ml). The organic solvents were removed *in vacuo*. The products were purified by column chromatography (silica gel, benzene).

All compounds obtained were reliably characterised by their NMR (^{1}H, ^{13}C) and IR spectra and satisfactory elemental analyses (δ(C, H) 0.5%).[7]

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References and Notes

1. Simchen, G. In *Houben-Weyl*. Thieme: Stuttgart. 1983. vol. E3. p. 36.
2. *Iminium Salts in Organic Chemistry*. Bohme, H.; Viehe, H.G.; John Wiley and Sons, Inc.: New York, 1976. pp 196-274.
3. Ramana, M.M.V., Kudav, N.A. *Ind. J. Chem., Sect. B.* **1988**, 27, 339-341.
4. Martinez, A.G.; Alvarez, R.M.; Barcina, J.O.; Cerero, S.M.; Vilar, E.T.; Fraile, A.G.; Hanack, M.; Subramanian, L.R. *J. Chem. Soc., Chem. Commun.* **1990**, 1571-1572.
5. Sam, J. U.S. patent. **1967**. N° 3301874 670131. *Chem. Abst.*; **1967**, 67, 90661.
6. In the case of 1,3-dimethoxybenzene two equivalents of substrate were used and the reaction mixture maintained at room temperature for 3h.
7. Selected physical data: **1,3-Di(2,4-dimethoxyphenyl)propan-1-one,** mp 81-83 °C. IR (ν,cm^{-1}): 1690 (CO). ^{1}H NMR (400MHz, $CDCl_3$, δ ppm): 7.75 d (1H, H-2, ^{3}J 8.67 Hz), 7.00 d (1H, H-1', ^{3}J 8.50 Hz), 6.45-6.30 m (4H, 4CH), 3.72 s, 3.68 s (12H, $4CH_3O$), 3.20-3.10 m (2H, CH_2-α), 3.95-2.85 m (2H, CH_2-β). ^{13}C NMR (100MHz, $CDCl_3$, δ ppm): 199.50 (CO), 163.65, 160.33, 158.62, 157.95 (C-2, C-2', C-4, C-4'), 132.14, 127.89 (C-6, C-6'), 121.95, 120.61 (C-1, C-1'), 104.65, 103.34 (C-5, C-5'), 97.87, 97.70 (C-3, C-3'), 54.91 (2C), 54.72, 54.68 ($4CH_3O$), 43.53 (C-α), 24.52 (C-β). Elemental analysis: found (%): C, 69.01; H, 6.79; Calc. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71.

   5,6-Dihydro-[6H]-cyclopenta-[b]-thiophene-4-one, mp 114 °C (lit.[5] 115 °C). IR (ν,cm^{-1}): 1700 (CO). ^{1}H NMR (400MHz, $CDCl_3$, δ ppm): 7.25 d (1H, H-3, ^{3}J 5.10 Hz), 7.08 d (1H, H-2, ^{3}J 5.10 Hz), 3.15-3.11 m (2H, CH_2-6), 2.95-2.91 m (2H, CH_2-5). ^{13}C NMR (100MHz, $CDCl_3$, δ ppm): 198.15 (CO), 170.50 (C-6a), 145.55 (C-2a), 130.87 (C-2), 119.05 (C-3), 41.61 (C-6), 24.30 (C-5). Mass (m/z, (I,%)): 138 (96)-M$^+$, 110 (100), 64 (59), 84 (35), 69 (20).

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