N-[[(Chlorosulfinyl)oxy]methylene]-*N*-methylmethanaminium Chloride as A Dehydrating Agent. A Direct and Efficient One-Pot Synthesis of Various Pyrimidinones, Azetidinones and Pyridones via Cycloaddition Reactions

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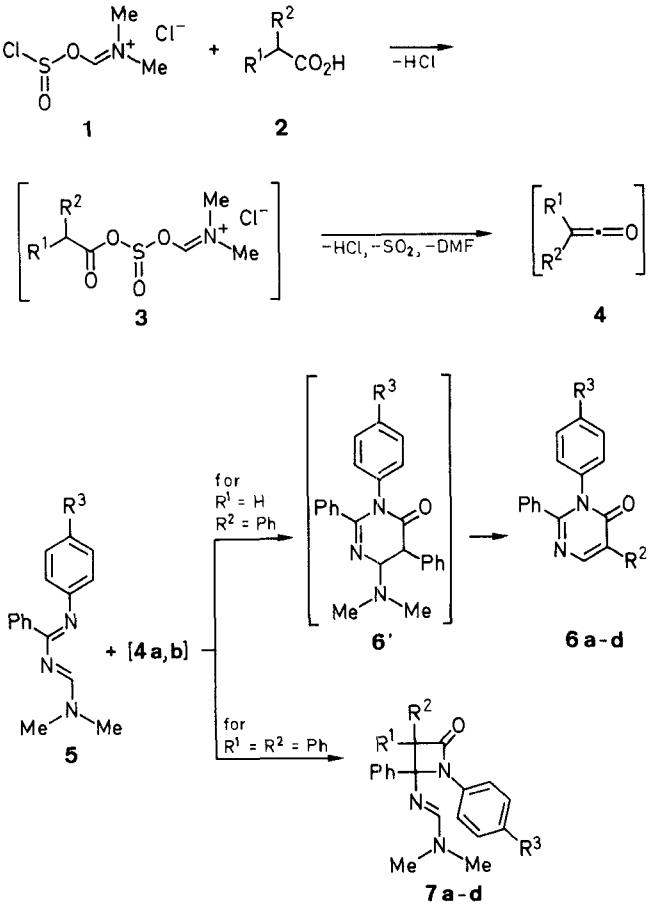
N-[[(Chlorosulfinyl)oxy]methylene]-*N*-methylmethanaminium chloride (**1**) is found to be an efficient and mild dehydrating agent for the in situ generation of monophenyl- (**4a**) diphenyl- (**4b**) and monochloroketenes (**4c**) directly from the corresponding carboxylic acids **2**. These ketenes undergo cycloaddition reactions with 1,3-diaza-1,3-butadienes **5** to afford 4(3*H*)-pyrimidinones **6** and azetidones **7**, and with 3-(aryliminomethyl)chromones **8** to give [1]benzopyrano[3,2-*c*]pyridine-3,10[2*H*]diones **9**.

Cycloaddition reactions of heterodienes with ketenes have been shown to be very useful in the synthesis of natural products and molecules of biological significance.[1] The conventional methods for the ketene generation include the dehydrohalogenation of an appropriately substituted acid halide and the zinc dehalogenation of an α-halo acid halide.[2] Both methods require the preparation, isolation and purification of the acid halide. We now report a direct and efficient one-pot procedure for the preparation of ketenes from carboxylic acids using the relatively less explored *N*-[[(chlorosulfinyl)-oxy]methylene]-*N*-methylmethanaminium chloride (**1**)[3] as the dehydrating agent, and their utility in [4 + 2] and [2 + 2] cycloaddition reactions. This reagent has been used for the activation of carboxylic acid groups,[3,4] for the preparation of acid chlorides,[5] alkyl chlorides[6] and *gem*-dichlorides.[7] The method appears to be quite convenient and in most of the instances the present procedure is a substantial improvement over the existing methods.

Preparation of the ketenes and its cycloaddition reactions were carried out by the dropwise addition of a dichloromethane solution of the dehydrating agent **1** to a dichloromethane solution of phenylacetic acid followed by 4-dimethylamino-1,2-diphenyl-1,3-diaza-1,3-butadiene (**5a**)[8] and anhydrous triethylamine (Scheme **1**). The product could be purified by preparative TLC to give **6a** in 35% yield. Similarly the reaction of the 1,3-diaza-1,3-butadiene **5a** with one equivalent of diphenylketene



2–4	R^1	R^2
a	H	Ph
b	Ph	Ph
c	H	Cl

Scheme 1

proceeded smoothly at room temperature to give the azetidinone **7a** quantitatively instead of the expected 5,5-diphenyl-4(3*H*)-pyrimidinones corresponding to **6'**. The IR spectrum of **7a** showed the presence of a β-lactam ring at $\nu = 1726\,cm^{-1}$ and a C=N double bond at $\nu = 1645\,cm^{-1}$. The structure of the azetidinone **7a** was confirmed by comparing the physical and spectroscopical data with an authentic sample.[10] However, the reaction of **5** with diphenylketene was reported[9] to give 5,5-diphenyl-4(3*H*)pyrimidinones, but this has been recently disputed[10] and the formation of azetidinone **7** is confirmed. Other azetidinones **7b–d** were prepared similarly and their characteristics are recorded in the Table.

Table. Compounds **6**, **7** and **9** Prepared

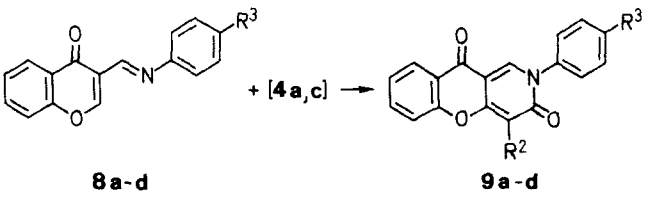
Product	R^1	R^2	R^3	Yield (%)	mp (°C)	Molecular Formula[b] or Lit. mp (°C)
6a	H	Ph	H	85	165	166–167[9]
6b	H	Ph	Me	83	195–196	196–197[9]
6c	H	Ph	Cl	80	161–163	163–164[9]
6d	H	Ph	Br	79	222–223	222–223[9]
7a	Ph	Ph	H	87	162	164–165[10]
7b	Ph	Ph	Me	80	146	148[9]
7c	Ph	Ph	Cl	82	180	180[9]
7d	Ph	Ph	Br	86	173–175	174–176[9]
9a	H	Ph	OMe	65	175–176	$C_{25}H_{17}NO_4$ (395.4)
9b	H	Ph	Me	60	243–245	250–252[11]
9c	H	Ph	Br	70	300	$C_{24}H_{14}BrNO_3$ (444.4)
9d	H	Cl	OMe	63	310	310[11]

[a] All products were identified by TLC, mp, IR and/or ^{1}H-NMR data.

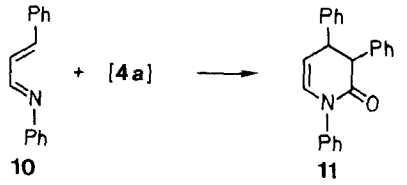
[b] Satisfactory microanalyses obtained: C ±0.14, H ±0.15, N ±0.12.

Preparation of 3-formylchromones have been the focus of much interest since these compounds undergo both nucleophilic attack at the carbonyl function, as well as conjugate additions.[11–13] The imines **8a–d** were readily obtained by reacting 3-formylchromone with an appropriate aromatic amine in refluxing benzene with azeotropic removal of water. Reaction of 3-(arylimino-methyl)chromones **8** with various ketenes were carried out in anhydrous dichloromethane at room temperature in the presence of **1** to furnish the heterocycles **9** in 60–70% yield. The structure assignments for **9** are fully established on the basis of spectral data and comparison with authentic samples[11] (Scheme **2**). From *N*-(3-phenyl-2-propenylidene)aniline (**10**) and phenylacetic acid, the pyridone **11** is obtained in 50% yield. There is no evidence for the formation of a product arising from the addition accross the azomethine function (Scheme **3**).

In conclusion, the procedure constitutes a convenient method for the preparation of pyrimidinones, azetidinones and pyridones from 1,3-diaza-1,3-butadienes and 3-(aryliminomethyl) chromones, respectively.



Scheme **2**



Scheme **3**

Melting points were determined by using a Büchi melting point apparatus and are uncorrected. The IR spectra were obtained on a Perkin-Elmer 237B IR spectrophotometer in KBr discs. The imines described in this report were prepared from freshly crystallised primary amines and aldehydes. All reagents were of commercial quality from freshly opened containers and were purchased from Aldrich Chemical Co. and used without further purification. Solvents were dried according to standard procedures. 3-(Arylimino-methyl)chromones **8a–d** were prepared by refluxing a solution of equimolar amounts of 3-formylchromones with the appropriate aromatic amines in anhydrous benzene in the presence of a catalytic amount of TsOH using a Dean-Stark apparatus for 30 min. The solvent was evaporated under reduced pressure and the products were recrystallized from benzene/light petroleum (1:1).[11]

2,3,5-Triphenyl-5,6-dihydro-4(3*H*)-pyrimidinone (6a); Typical Procedure:

To a solution of phenylacetic acid (**2a**; 1.36 g, 10 mmol) in anhydrous CH_2Cl_2 (20 mL) is added freshly prepared **1**[3] (2.88 g, 15 mmol) at 0–5°C. After stirring at this temperature for 10 min, freshly recrystallised **5a** (2.51 g, 10 mmol) is added followed by dropwise addition of anhydrous Et_3N (2.02 g, 20 mmol) in CH_2Cl_2 (10 mL). The resulting mixture is then stirred at r.t for 4 h (monitored by TLC). On completion of the reaction, the mixture is quenched with cold water and extracted with CH_2Cl_2 (2 × 40 mL). The combined organic extracts are washed with cold water (50 mL), dried (Na_2SO_4) and evaporated under reduced pressure to furnish a residue which is purified by TLC using silica gel as adsorbant and $CHCl_3$/MeOH (9:1) as the eluent; yield: 3.10 g (85%); yellow crystalline solid; mp 165°C (Lit.[9] 166–167°C) (Table).

***N,N*-Dimethyl-*N'*-(4-oxo-1,2,3,3-tetraphenyl-2-azetidinyl)methanimidamide (7a); Typical Procedure:**

To a solution of diphenylacetic acid (**2b**; 2.12 g, 10 mmol) in anhydrous CH_2Cl_2 (20 mL) is added at 0–5°C, freshly prepared **1** (2.88 g, 15 mmol) at 0–5°C. After stirring at this temperature for 10 min, freshly prepared **5a** (2.51 g, 10 mmol) in CH_2Cl_2 (5 mL) is added followed by anhydrous Et_3N (2.02 g, 20 mmol) in CH_2Cl_2 (10 mL). The resulting mixture is stirred at r.t. for 4 h and worked up as above to afford **7a** (Table).

2-Methoxyphenyl-10H-[1]benzopyrano[3,2-*c*]pyridine-3,10(2*H*)-dione (9a); Typical Procedure:

A solution of phenylacetic acid (**2a**; 1.36 g, 10 mmol) in anhydrous CH_2Cl_2 (25 mL) is added dropwise freshly prepared **1** (2.88 g, 15 mmol) at 0–5°C. After stirring at this temperature for 10 min, freshly prepared **8a** (2.79 g, 10 mmol) is added followed by dropwise addition of anhydrous pyridine (1.58 g, 20 mmol) in CH_2Cl_2 (10 mL). The resulting mixture is then stirred at r.t. for 3 h (monitered by TLC). On completion of the reaction, the mixture is quenched with cold water and extracted with CH_2Cl_2 (2 × 40 mL).

The combined organic extracts are washed with cold water (50 mL), dried (Na_2SO_4) and evaporated under reduced pressure to furnish a residue which is purified by TLC using silica gel as adsorbant and $CHCl_3$ as the eluent; yield: 2.6 g (65%); yellow solid; mp 175–176°C (Table).

^{1}H-NMR ($CDCl_3$/TMS): δ = 4.04 (s, 3H), 7.18–8.10 (m, 13H), 9.03 (s, 1H).

1,3,4-Triphenyl-3,4-dihydro-2(1*H*)pyridone (11):

To a solution of phenylacetic acid (**2a**; 1.36 g, 10 mmol) in anhydrous CH_2Cl_2 (25 mL) is added freshly prepared **1**(2.88 g, 15 mmol) at 0–5°C. After stirring at this temperature for 10 min, freshly prepared *N*-(3-phenyl-2-propenylidene)aniline (**10**; 2.07 g, 10 mmol) in CH_2Cl_2 (10 mL) is added followed by dropwise addition of anhydrous Et_3N (3.03 g, 30 mmol) in CH_2Cl_2 (15 mL). The resulting mixture is stirred at r.t. for 5 h. Workup as above gives **11**; yield: 1.60 g, (50%); mp 106°C (Lit.[14] mp 107°C).

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