A ONE-POT SYNTHESIS OF 1,3-DIOXAZINE-4-ONE DERIVATIVES

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Abstract: The cycloaddition of (chlorocarbonyl)Phenyl ketene (1) with C=N to form a six membered ring heterocycles is described. A mechanism involving a dipolar intermediate is provided. The reaction of (1) with dicyclohexylcarbodiimide, N-benzilideneaniline and phenylisocyanate gave 1,3-dioxazine-4-one or 1,3-dioxazine-2,4-dione derivatives in good to excellent yields.

Introduction:

There are numerous reports in the literature on the cycloaddition reactions of ketenes with carbodiimides compounds across the C=N linkage to yield imino β-lactams and evidence have been presented which indicates that the mechanistic pathway for such a reaction involves a dipolar intermediate (1, 2). The reaction of 2,2,6-trimethyl-1,3-dioxin-4-one, so called diketene acetone adducts (3, 4, 5) with several unsaturated compounds under mild experimental conditions to form six-membered ring adducts have also been reported (6). How ever the attempted [2+2] or [4+2] cycloaddition reactions of different kind of ketenes with a variety of trifluoroacetimidoyl chlorides (7) to prepare β-lactams or δ-lactams has been unsuccessful.

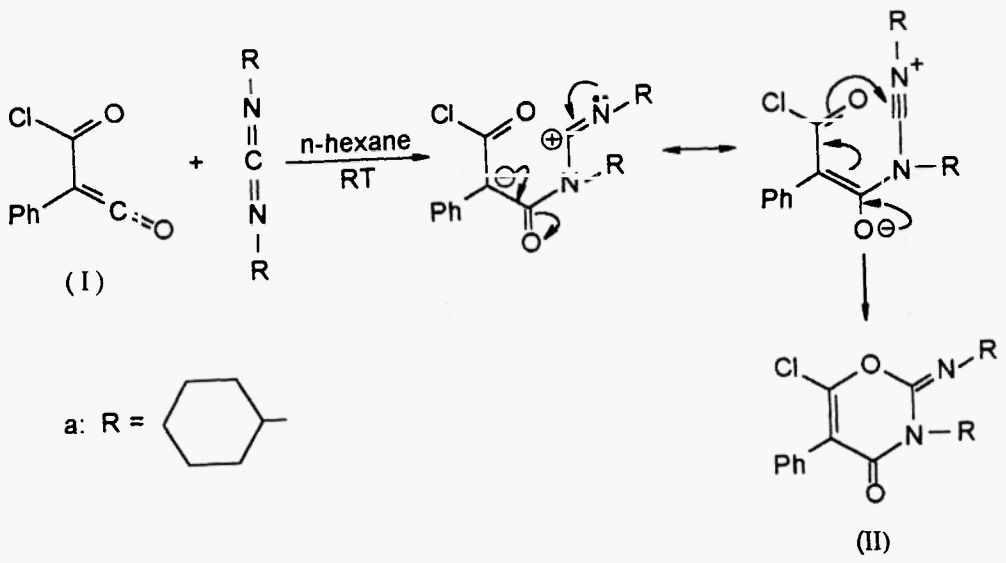
We now wish to describe the facile cycloaddition of (chlorocarbonyl)phenyl ketene (I) which is an isolable and stable ketene with some readily available unsaturated compounds such as dicyclohexylcarbodiimide, N-benzilideneaniline and phenylisocyanate in a [4+2] manner to give a six membered heterocycles.

Results and Discussion

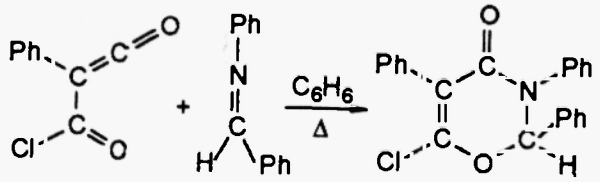
The title ketene (I) reacts smoothly with dicyclohexylcarbodiimide to give [4+2] cycloaddition products as shown in scheme 1. Thus the reaction of equimolar quantities of (1) with dicyclohexylcarbodiimide at ambient temperature in dry benzene or toluene or n-hexane (which were dried over sodium and distilled prior to use) resulted in a loss of all the ketene band at 2137 cm^{-1} and afforded a 72% yield of 6-chloro-3-cyclohexyl-2- cyclohexylimino- 5-phenyl-1,3-oxazine-4-one (II) after one hour. The solid product was easily isolated and purified by recrystallization.

The infrared spectrum of (II) revealed the carbonyl band at 1720 and 1685 cm^{-1} and the proton nmr spectrum revealed a singlet at δ 7.2 and two multiplets at δ 4.5 and 1-2.4 ppm.

Scheme I

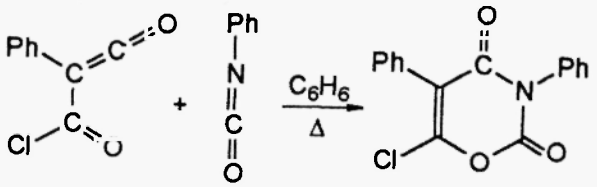


The reaction of (1) and N-benzilideneaniline resulted 6-chloro-2,3,5-triphenyl-1,3-oxazine-4-one in a 97% yield. The IR spectrum revealed a carbonyl band at 1740 cm^{-1} and ^1H NMR showed a multiplete at 7.5 and a singlet at 5.6 ppm corresponding to phenyl protons and CH proton respectively.



The cycloaddition reaction of (1) and phenylisocyanate afforded 6-chloro-3,5-diphenyl-1,3-oxazine -2,4-dione (IV). The cycloaddition was complete within 24 hours, and the solid product was isolated and purified by recrystalization to give (IV) in 84% yield.

The structure of compound (IV) was assigned an the basis of carbonyl band in the infrared, the proton NMR, ^{13}CNMR, mass spectrum and elemental analysis data.



In conclusion the (chlorocarbonyl)phenyl ketene is a useful compound because it's reaction with

double bonds seems to be a promising synthetic approach to 1,3-oxazine derivatives.

The cycloaddition of this ketene (1) with a variety of aldehyde[5] and ketones in the presence of a catalytic amount of $BF_3.Et_2O$ resulted in the formation of 5-phenyl-1,3-dioxane-4,6-dione derivatives (9).

Experimental

Infrared spectra were obtained on a Mattson 1000 series FT-IR instrument (Unicam Limited). The proton NMR and ^{13}CNMR spectra were recorded on JEOL, JNM-90 MHz FT nuclear magnetic resonance spectrometer employing $CDCl_3$ as the solvent and tetramethylsilane as the internal standard. Mass spectra were obtained on a shimodzu GC/MS QP 2000A spectrometer. Elemental analysis were performed by the NIOC research Lab. Tehran. Melting points were obtained with a Gallkamp apparatus (England) and uncorrected.

All reagents were obtained commercially. Thioyl chloride and phenylmalonic acid were used as purchased, benzene and ether were dried over sodium and distilled prior to use. Phenylisocyanate was distilled prior to use. N-benzylideneaniline was prepared by the condensation reaction of benzaldehyde and aniline. (chlorocarbonyl)phenyl ketene was prepared by a procedure similar to that of Nakanishi (8).

6-chloro-3-cyclohexyl-2-cyclohexylimino-5-phenyl-1,3-oxazine-4-one (II)

At ambient temperature, 17 mmol (3 g) of (1) in 50 ml of n-hexane was added dropwise to a stirred solution of 17 mmol (3.5 g) of dicyclohexylcarbodiimide in 50 ml of n-hexane. The addition was accompanied by a moderate exotherm and a solid precipitated.

After the addition was complete, the mixture was stirred for another 3 hours and it was subsequently filtered. The solid collected in the filter was washed throughly with ethanol and recrystalized yield 4.7 g (72%) Mp: 169-171°C, IR (KBr) 1720, 1685 cm^{-1}, ^{1}HNMR ($CDCl_3$, with TMS as reference) δ 7.2-7.3 (m, 5H), 4.4-4.5 (m, 2H), 1-2.2 (m, 20H), ^{13}CNMR 165.8, 149.8, 137.2, 130.7, 130.4, 129.6, 126.6, 105.2, 57.7, 30.0, 28.7, 26.7, 25.5, 25.1 ppm Anal. Calcd for $C_{22}H_{27}ClN_2O_2$ (386.5): C, 69.2; H, 7.5; N, 7.75. Found: C, 69.02; H, 7.06; N, 7.30.

6-chloro-2,3,5-triphenyl-1,3-oxazine-4-one (III).

A 15 mmol (2.71 g) of (1) in 20 ml benzene was added to 15 mmol (2.72 g) stirred solution of N-benzylideneaniline in 20 ml of benzene. The reaction mixture was refluxed under slow stream of nitrogen until the ketene band has been disappeared in the IR spectrum at 2137 cm^{-1}. The reaction mixture was filtered, the solid was washed several times with cold benzene to give 5.25 g (97%) of (III) Mp: 144°C. IR (KBr) 1740, 1725 cm^{-1}. ^{1}HNMR ($CDCl_3$ with TMS as reference) δ 7.5 (m, 15H), 5.6 (s, 1H) ppm ^{13}CNMR δ, 160.2, 137.5, 133.4, 130.7, 130.3, 130.2, 129.0, 128.4, 125.8, 116.6, 66.9 ppm

Anal. Calcd for $C_{22}H_{16}ClNO_2$ (361.5): C, 73.0; H, 4.4; Cl, 9.9; N, 3.9. Found: C, 72.6; H, 4.4; Cl, 10.4; N, 3.5

6-chloro-3,5-diphenyl-1,3-oxazine-2,4-dione (IV).

A 15 mmol (2.71 g) of (1) in 20 ml of benzene and 15 mmol (1.79 g) phenylisocyanate were reacted to give 3.76 g (84%) of (IV) Mp: 179°C: IR (KBr) 1760, 1687, 1640 cm^{-1} ^{1}HNMR ($CDCl_3$ with TMS as reference) δ 7.5 (m) ppm, ^{13}CNMR δ 160.1, 154.9, 134.5, 131.2, 130.5, 130.2, 129.7, 129.4, 128.8,115.1 ppm. mass spectrum parent peak m/z at 299 found 222 (5% M-Ph), 180 (92%), 145 (100% base peak), 119 (40%). Anal. Calcd for $C_{16}H_{10}ClNO_3$ (299.5): C, 64.1; H, 3.3; Cl, 11.9; N, 4.6. Found: C, 64.5; H, 3.3; Cl, 11.6; N, 4.3.

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References:

1. W. T. Brady and C. H. Shieh, J. Org. Chem., **48**, 2499 (1983).
2. W. T. Brady and E. D. Dorsey, J. Org. Chem., **34**(10), 2846 (1969).
3. M. Sato, H. Ogasawara, E. Yoshizumi and T. Kato, Chem. Pharm. Bull.,**31**(6), 1902 (1983).
4. M. Satao, H. Ogasawara and T. Kato, Chem. Pharm. Bull., **32**(7), 2602 (1984).
5. M. Sato, N. Yoneda and C. Kaneko, Chem. Pharm. Bull., **34**(2), 621 (1986).
6. W. Ried and H. Nenninger, Synthesis., 167, (1990).
7. K. Uneyama, K. Tamura, H. Mizukami, K. Maeda and H. Watanabe, J. Org. Chem., **58**, 32 (1993).
8. S. Nakanishi and K. Butler, Organic Preparations and Procedures. Int., **7**(4), 155 (1975).
9. K. Saidi, H. Shaterian and H. Sheibani. Synth. Comm., in press.

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