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A FACILE SYNTHESIS OF N-(p-TOLUENESULFONYL)-2-OXOALKANECARBOXAMIDES BY THE REACTION OF SILYL ENOL ETHERS WITH p-TOLUENESULFONYL ISOCYANATE

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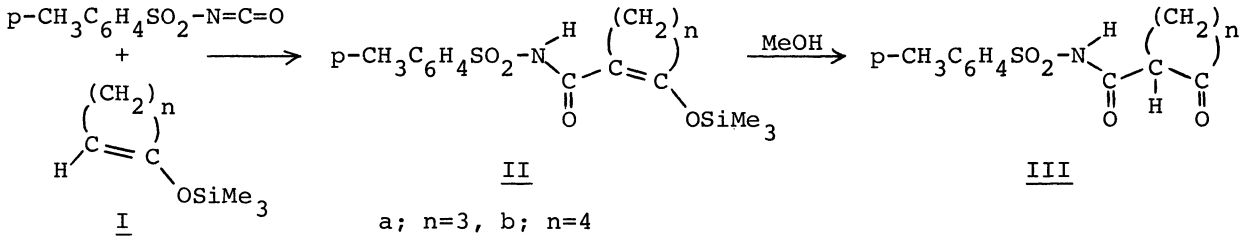
It was found that silyl enol ethers reacted with p-toluenesulfonyl isocyanate to afford either N-sulfonyl-2-silyloxycycloalkanecarboxamides or N-sulfonyl-4-silyloxy-2-azetidinones. Both adducts were easily hydrolyzed to the corresponding N-sulfonyl-2-oxoalkanecarboxamides.

It has been shown that an enamine which has a β-hydrogen reacts with isocyanates through the nucleophilic addition to afford N-substituted-2-oxocarboxamides after hydrolysis[1]. It is also known that enamines such as morpholinocyclopentene tend to undergo dicarbamoylation with aryl isocyanates[2]. The reaction was applied to the syntheses of polyamides using diisocyanates such as diphenylmethane diisocyanate[3]. In the case of β,β-disubstituted enamines[4], however, 1,2-cycloaddition reaction took place to give β-lactams. Vinyl ethers are also known to react with sulfonyl isocyanates to produce N-sulfonyl-2-azetidinones as a major product irrespective of the presence of β-hydrogen[5].

On the other hand, silyl enol ethers are currently much interested in respect to the reaction of enolate anion, and many reports have been made on the formation and reaction of these compounds[6]. However, little has been known about the reactivity of these compounds toward heterocumulenes[7].

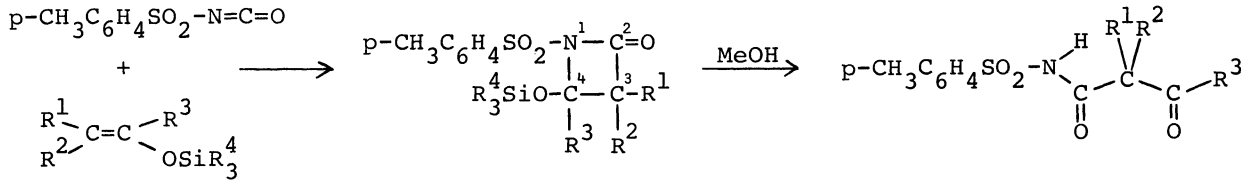
In the present communication, we describe either nucleophilic addition or 1,2-cycloaddition of a silyl enol ether with p-toluenesulfonyl isocyanate, which proceeds under much milder conditions compared with those employed in the case of aryl isocyanate[7]. We found that silyl enol ethers of cycloalkanones[6d] gave N-sulfonyl-2-silyloxycycloalkenecarboxamides(II) through nucleophilic addition[8], while open chain ones afforded N-sulfonyl-4-silyloxy-2-azetidinones(V) through 1,2-cycloaddition, and that both the alkenecarboxamides(II) and the azetidinones(V) were easily hydrolyzed to N-sulfonyl-2-oxoalkanecarboxamides(III and VI).



I II III

a; n=3, b; n=4

In a typical procedure, 1-trimethylsilyloxycyclopentene(Ia, 1.56g, 10mmol) was slowly added to p-toluenesulfonyl isocyanate(1.97g, 10mmol) without solvent at ambient temperature. After an exothermic reaction subsided, the stirring was continued for additional 10 min. Then, 10 ml of n-hexane was added to the reaction mixture for crystallization. The resulting crystals of N-(p-toluenesulfonyl)-2-trimethylsilyloxycyclopent-1-enecarboxamide(IIa)(3.45g, 97% yield) were pure enough to satisfy the elemental analysis. [IIa: IR(KBr disk): 3250(ν_{NH}), 1670(ν_{CO}), 1340 and 1155 cm^{-1}(ν_{SO_2}), NMR(CCl_4): δ 0.33(s, 9H, $SiCH_3$), 9.57(s, 1H, NH), Mass: m/e=353 (M^+)] Treatment of IIa with ten hold excess of methanol at ambient temperature for 30 min, gave N-(p-toluenesulfonyl)-2-oxocyclopentanecarboxamide(IIIa) in nearly quantitative yield. The nucleophilic addition was also observed in the reaction of the silyl enol ether of cyclohexanone with the sulfonyl isocyanate. Accordingly, the β-carbon of the silyl enol ether of cycloalkanones undergo the nucleophilic attack to the sulfonyl isocyanate like corresponding enamines such as morpholinocyclohexene[8].



IV V VI

a; $R^1=R^2=H$, $R^3=C(CH_3)_3$, $R^4_3=(C_2H_5)_3$

b; $R^1=R^2=H$, $R^3=C_6H_5$, $R^4_3=(CH_3)_3$

c; $R^1=H$, $R^2=R^3=CH_3$, $R^4_3=(CH_3)_2(C_2H_5)$

d; $R^1=(CH_3)_2HC$, $R^2=H$, $R^3=CH_3$, $R^4_3=(C_2H_5)_3$

e; $R^1=H$, $R^2=C_6H_5$, $R^3=CH_3$, $R^4_3=(C_2H_5)_3$

On the other hand, open chain silyl enol ethers[6d,6h,6i] were found to afford 1-(p-toluenesulfonyl)-4-silyloxy-2-azetidinones(V) through 1,2-cycloaddition to the sulfonyl isocyanate. 4-Silyloxy-2-azetidinones(V) were easily converted to N-(p-toluenesulfonyl)-2-oxoalkanecarboxamides(VI) by the action of methanol.

Results are summarized in Table 1. The azetidinone structure of the adducts was confirmed on the basis of IR and NMR spectra, e.g., Va[IR(neat): 1710(ν_{CO}), 1350 and 1160 cm^{-1}(ν_{SO_2}) there were no absorption in the region 3100-3500 cm^{-1} due to NH stretching, NMR(CCl_4): δ 4.10(s, 2H, $^3CH_2$)], Vc[IR(neat): 1730(ν_{CO}), 1350 and 1160 cm^{-1}(ν_{SO_2}) there were no absorption in the region 3100-3500 cm^{-1} due to NH stretching, NMR(CCl_4): δ 1.33(d, J=7Hz, 3H, ^3C-CH_3), 2.20(S, 3H, ^4C-CH_3) and 4.52 (q, 1H, ^3C-H)].

Table-1. N-Sulfonyl-2-oxoalkanecarboxamides(III and VI) Obtained from the Addition of Silyl Enol Ethers to p-Toluenesulfonyl Isocyanate followed by Methanolysis

Product	m.p. (°C)	Yield (%)	IR (cm^{-1})[a]		NMR ($CDCl_3$, δ)		keto/enol[b]
			ν N-H	ν C=O	N-H	O-H	
IIIa	93-94	95	3230	1735, 1710	9.47		100/0
IIIb	143-145	90	3260	1660	9.47	13.63	0/100
VIa	122-123	98	3220	1720, 1690	9.27, 10.22	13.38	75/25
VIb	116-117	98	3210	1645, 1625	9.12, 10.30	13.32	65/35
VIc	93-94	80	3220	1735, 1705	9.55		100/0
VId	106-107	88	3230	1730, 1700	9.56		100/0
VIe	127-128	92	3170	1710, 1690,	9.55		100/0

a measured as a KBr disk b determined on the basis of nmr spectra which were measured in $CDCl_3$

A keto-enol tautomerism of 2-oxoalkanecarboxamides(III and VI) could be observed by means of nmr spectroscopy. For example, an enol proton of N-(p-toluenesulfonyl)-2-oxocyclohexanecarboxamide(IIIb) appeared at δ 13.63 ppm(s, 1H) and IR spectrum displayed only one absorption band due to the carbonyl stretching at 1660 cm^{-1}. Thus, IIIb may be present only in the enol form, while the keto form was found to be rather stable in the case of VIa and VIb on the basis of nmr spectra. In other cases, the keto form seems to be far more stable than the enol form, so that any evidence for the presence of the enol form could not be obtained. A further investigation on the stereochemistry and application of the reaction are now in progress.

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8. A possibility that the alkenecarboxamides (II) were formed through the azetidinones (V) followed by proton migration i.e., ring cleavage, cannot be ruled out, however.

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