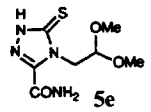
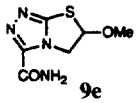
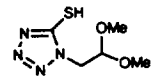
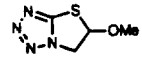
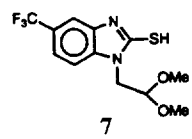
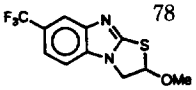
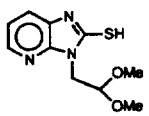
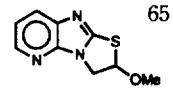
 5e	2.2	20	 9e	81	161-163 (THF/ EtOAc)	$C_6H_8N_4O_2S$ (200.2)	3.39 (s, 3H, OCH_3), 4.55 (d, 2H, J=2.8, H-5), 6.26 (t, 1H, J=2.7, H-6), 7.88, 8.24 (s, each 1H, NH_2)	200 (M^+, 18), 169 (100), 156 (21), 152 (21)
 6	3.3	60	 10	72	72-73 (EtOAc)	$C_4H_6N_4OS$ (158.2)	3.51 (s, 3H, OCH_3), 3.73 (d, 2H, J=3.0, H-6), 6.28 (t, 1H, J=3.0, H-5)	158 (M^+, 29), 97 (27), 76 (20), 72 (13), 58 (100)
 7	2.2	10	 11	78	162 (EtOAc)	$C_{11}H_{19}F_3N_2OS$ (274.3)	3.49 (s, 3H, OCH_3), 4.40 (dd, 1H, J=11.7, 4.9, H-3), 4.49 (dd, 1H, J=11.7, 1.1, H-3), 5.98 (dd, 1H, J=4.9, 1.1, H-2), 7.29, 7.46 (two d, J=8.3, each $1H_{aromatic}$), 7.90 (s, $1H_{aromatic}$)[d]	274 (M^+, 40), 243 (100), 231 (24), 229 (14), 187 (19)
 8	2.2	30	 12	65	210	$C_9H_9N_3OS$ (207.2)	3.49 (s, 3H, OCH_3), 4.44 (dd, 1H, J=12.1, 5.2, H-3), 4.67 (dd, 1H, J=12.1, 1.0, H-3), 5.99 (dd, 1H, J=5.2, 1.0, H-2), 7.15 (dd, J=8.0, 5.0, $1H_{aromatic}$), 7.86 (dd, J=8.0, 1.4, $1H_{aromatic}$), 8.21 (dd, J=5.0, 1.4, $1H_{aromatic}$)[d]	207 (M^+, 45), 176 (100), 164 (29), 135 (30), 108 (12)

[a] Yield of isolated product. [b] Recorded on a Bruker AM-200 spectrometer. [c] Recorded on a Hewlett Packard model 5985 B spectrometer. [d] Recorded on a Varian Gemini 300 spectrometer ($CDCl_3$).

and the yields of isolated product, together with spectral identification data.

Acknowledgment. The authors are indebted to the Minister of Science and Technology for financial support, project number N07532.

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6. The 2-mercaptobenzimidazole **7** and 3H-imidazo[4,5-b]pyridine **8** were prepared in 46, 60% overall yield from 4-chloro-3-nitrobenzotrifuoride and 2-chloro-3-nitropyridine, respectively.
7. Treatment of **5a-e** with 5 equiv. of $MeSO_3H$ (CH_2Cl_2, r.t., 2-5 h) and subsequent saturated aqueous $NaHCO_3$ work-up gave similar results.

Selectivity in the Lactone Formation *via* C-H Insertion Reaction of Diazoacetoacetates

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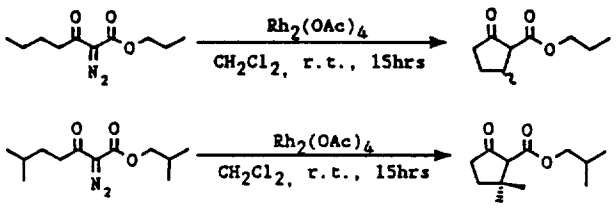
It is now well established that rhodium (II) catalyzed intramolecular C-H insertion reactions of α-diazo-β-ketocarboxylic acid methyl esters result in the formation of cyclopentanones.[1] Under similar conditions, α- diazoketones,[2,3] α-diazo-β-ketosulfones[4] and α-diazo-β-ketophosphonates[5] are also converted into five-membered carbocyclic systems. In these reactions, electron withdrawing substituents decrease the reactivity of the adjacent C-H bonds[1c,2] and the insertion reaction is promoted at the C-H bond adjacent to ether oxygens.[3] The propensity for the formation of five-membered carbocycles can sometimes be overcome: the dominating factor of ether activation may prevail and cyclohexanone derivatives may be formed[3], and subtler electronic factors may provide enough impetus for more favorable formation of cyclo-



Scheme 1

butanones.[6]

On the other hand, rhodium (II) catalyzed insertion reactions of diazoacetoacetamides are known to yield β-lactam products.[7] More recently, conformational and electronic preferences in the selective construction of β-lactams from N,N-disubstituted diazoacetoacetamides are described in detail.[8]

The scope and selectivity in the lactone formation *via* rhodium (II) catalyzed C-H insertion reaction are less well defined. Selective formation of a δ-lactone from a diazoacetate precursor is reported[9] on the way to the synthesis of pentalenolactone E. On the contrary, various diazoacetoacetates and sterically congested diazoacetates are now known to be selectively converted to γ-lactones in the presence of rhodium (II) carboxylate and carboxamide catalysts.[10]

In the study of rhodium (II) catalyzed insertion reactions of methyl diazomalonates,[11] we found that there was a delicate balance of factors in the formation of β- and γ-lactones and, in the absence of electronic bias and extraneous steric influence, β-lactones were favored products. We wish to communicate here results of our more recent experiments on insertion reactions of α-diazo-β-ketocarboxylates and diazoacetoacetates.

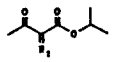
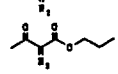
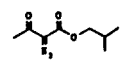
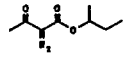
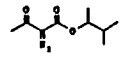
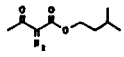
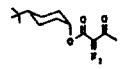
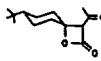
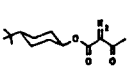
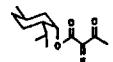
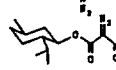
First, preferred mode of insertion (carbocycle *vs* oxacycle) was studied using substrates with near-perfect symmetry. For example, n-propyl 2-diazo-3-oxoheptanoate was converted under standard conditions to the cyclopentanone derivative in 72% yield and no trace of the alternative lactone product could be found. Reaction of isobutyl 6-methyl-2-diazo-3-oxoheptanoate also produced only the carbocyclic product in 87% yield (Scheme 1). It is obvious from these results that five-membered carbocycle construction *via* C-H insertion is the preferred process over oxacycle formation.

Next, rhodium (II) acetate catalyzed insertion reactions of various diazoacetoacetates were examined in detail. Isopropyl diazoacetoacetate (entry 1) produced a fair yield of the β-lactone product. However, γ-lactones were formed predominantly from n-propyl diazoacetoacetate (entry 2). Isobutyl diazoacetoacetate (entry 3) was converted to the γ-lactone product in good yield. 2-Butyl ester (entry 4) produced more β-lactones than γ-lactones whereas γ-lactones were favored products from 3-methyl-2-butyl ester (entry 5). The reaction of isoamyl diazoacetoacetate (entry 6) yielded only γ-lactone products in fair yield.

The following generalizations can be made from the results described above. β-Lactone formation is the preferred process when methine C-H bonds are available and the alternative is γ-lactone formation *via* either methyl or methylene C-H insertion (entry 1, 4). When methine C-H bonds are available for the five-membered ring formation, γ-lactones are favored products (entries 3, 5). γ-Lactone formation is the preferred process over β-lactone formation when only methylene C-H bonds are available in the substrate for insertion (entries 2, 6). δ-Lactone formation is not a favored process even when methine C-H bonds are available for insertion (entry 6). The reactions appear to be governed by two independent factors: the high reactivity of methine C-H bonds in insertion reactions and the conformational bias of metallocarbenoid species formed from diazoacetoacetate to favor five-membered ring formation. The preference for relatively electron-rich methine C-H bonds to participate in insertion reactions by electrophilic rhodium-carbene species was amply discussed by Taber in cyclopentanone formations[1c] and by us in diazomalonate insertion reactions.[11] The preferred γ-lactone formation shown above confirms the results reported by Doyle[10] and deviates radically from the conformational preference for β-lactone formation in diazomalonate C-H insertion reactions.[11] It is quite remarkable that species as closely related as diazomalonates and diazoacetoacetates show opposite selectivities in insertion reactions and more work is needed to clarify the subtle differences between them.

With cyclohexyl diazoacetoacetates, the same two factors appear to be operative. Both *cis*- and *trans*-4-*t*-butylcyclohexyl diazoacetoacetate yielded more β-lactones than corresponding γ-lactones reflecting the high reactivity of methine

Table 1. Insertion Reaction of Diazoacetoacetates Catalized by $Rh_2(OAc)_4$[a]

Entry	Starting material	Product (Yield, %)[b] β-lactones[c]	γ-lactones[d]	Diastereomeric ratios[e]
1		 (40)		
2		 (trace)	 (36)	γ-1 : 1
3			 (70)	
4		 (35)	 (9)	β-2 : 1 γ-2 : 1
5		 (13)	 (40)	β->20 : 1 γ-1 : 1
6			 (40)	γ-1.5 : 1
7[f]		 (50)	 (16)	γ-one isomer
8[g]		 (37)	 (25)	γ-1 : 1
9			 (59)	γ->20 : 1
10			 (64)	γ-5 : 1

[a] Reaction conditions: 0.01-0.03 M in dry CH_2Cl_2 under N_2 atmosphere at r. t., cat. $Rh_2(OAc)_4$, 15 hrs. [b] Isolated yield. [c] IR spectra exhibited the β-lactone carbonyl absorption at 1830 cm^{-1}, [d] IR spectra showed the γ-lactone carbonyl absorption at 1780 cm^{-1}. [e] Each ratio was determined by high resolution NMR analysis (80, 200 MHz). [f] 4-*t*-Butylcyclohexanone was also isolated in 34% yield. [g] Like entry 7, 4-*t*-butylcyclohexanone was obtained in 37% yield.

C-H bonds (entries 7, 8). Extraneous steric effects may substantially change the reaction course. Thus only γ-lactone products were obtained from both neomenthyl and menthyl diazoacetoacetates where insertion reaction occurred away from the neighboring isopropyl group (entries 9, 10). In two of the cases (entries 7, 9) five-membered ring formation is relatively more pronounced compared to the cases with corresponding methyl diazomalonates.

Use of insertion reactions of diazoacetoacetate and diazomalonate in organic synthesis will be the subject of future studies in these laboratories.

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Metallomicelle-Nucleic Acid Interaction: Copper(II) Dodecylsulfate-Catalyzed RNA Cleavage

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Numerous instances of catalytic hydrolysis of the sugar-phosphate backbone of RNA (especially $tRNA^{Phe}$) by several divalent metal ions such as Mg^{2+} [1], Zn^{2+} and Pb^{2+} [2], and also by Eu^{3+} [3] are known. The metal ion-catalyzed cleavage of $tRNA^{Phe}$ is thought to be an intramolecular version of a metallo-enzyme-catalyzed reaction[4]. Catalytic activities of most nucleases[5] and RNA catalysts[6] are also dependent on metal ions. On the other hand, studies as for the micellar models of hydrolytic metalloenzymes have been introduced very recently[7-11]. We can anticipate the alteration of the hydrolytic activity of the metal ions by being associated with the surfactant molecules in the micelle.

Metallomicelles formed from long-chained Cu^{2+} complexes had remarkable hydrolytic catalysis activity against phosphate triesters, diesters, and other phosphorus compounds[10]. The high hydrolytic catalysis activity of the metallomicelles may be due to enhanced electrophilicity of micellized metal and consequently the increased activity of the metal-bound water[10]. These previous reports prompted us to test any hydrolytic activity of some metallomicelles against nucleic acids. In this paper we show ribonuclease-like (RNase-like) activity of bivalent metal ion (Cu^{2+}, Mg^{2+}, and Pb^{2+}) complexes of sodium dodecyl sulfate (SDS, $CH_3(CH_2)_{11}SO_4^-Na^+$), which form metallomicelles $[CH_3(CH_2)_{11}SO_4^-]_2M^{2+}$, $M(DS)_2$.

Baker's yeast RNA type XI purchased from Sigma was used as substrate. Sodium dodecyl sulfate purchased from Wako Pure Chemical Industries, LTD was selected as surfactant for making micelle systems.

Buffer solution: Tris, despite its negligible interaction with the metal ions Mg^{2+} and Cu^{2+}, was abolished, since it interacts with the DS^-. Acetate buffer (pH 5.0), having no such interactions was used as buffer.

Assay of RNase-like activity: Among various assay methods, the method monitoring the activity producing the hydrolyzed soluble fraction by measuring the spectrophotometric absorbance at 260 nm of wavelength after precipitating unreacted substrate RNA was adopted. As the precipitation agent for unreacted RNA, perchloric acid containing lanthanum nitrate[12] was used. This technique gives reproducible results with low blanks and without overlapping light absorption in the region of 260 nm wavelength of RNA absorption peak, while inclusion of uranyl acetate instead of lanthanum nitrate affects the absorption peak of RNA at 260 nm. The biomimetic hydrolytic reaction was initiated by the addition of 1.5 m*l* of the RNA (substrate) solution to the equal volume of 8×10^{-5} M $Cu(DS)_2$ solution (the concentration far exceeding CMC, critical micelle concentration). The reaction mixture was well mixed and incubated at 25℃ or 60℃ for a difinite period of time (usually 7 hours). The reaction was terminated by the addition of 2 m*l* precipitant (perchloric acid/lanthanum nitrate) to 1 m*l* portion of the reaction mixture. The precipitant added reaction mixture was left alone for 40 min, and then centrifuged for 10 min, at 6000 rpm to remove the precipitates of unreacted RNA and $M(DS)_2$. The hydrolytic ribonuclease-like activity of the metallomicelles was determined by the measurement of the absorbance of the supernatant fraction at 260 nm by UVICON 860 Spectrophotometer after five-fold dilution with distilled water. In the absorbance measurement, the blank solution was that of the same composition as the reaction mixture except for the omission of the substrate RNA and treated in the same way along with the reaction mixture.

The buffer system for the RNA hydrolysis by Cu (II) dode-