S-N POLYHETERO-CLAISEN REARRANGEMENTS PROMOTED BY CARBOXYL GROUP

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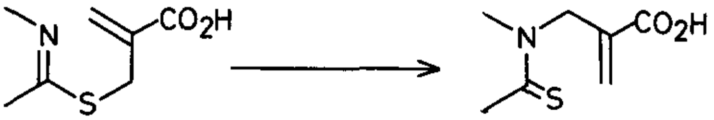
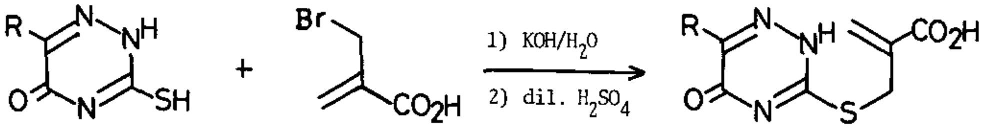
Abstract - S-N Polyhetero-Claisen rearrangements promoted by carboxyl group were studied. 2-Carboxyallyl groups in triazines (3a and b) migrated to nitrogen at 4-position of those rings and gave 4-(2-carboxyallyl)triazines (7a and b) by refluxing in ethanol. 2-(2-Carboxyallylthio)benzimidazole (10) and -thiazoline (12) were also converted to N-(2-carboxyallyl)heterocycles in the same fashion, respectively.

We describe here some examples of S-N polyhetero-Claisen rearrangements in comparatively milder conditions, which seems to be caused by carboxyl group attached to the 2-position of allyl group.



The reaction of α-(bromomethyl)acrylic acid (2) with 3-mercapto-2,5-dihydro-1,2,4-triazin-5-ones (1) in aqueaus potassium hydroxide gave 3-(2-carboxyallylthio)-1,2,4-triazin-5(2H)-ones (3) in good yields : ^{1}H nmr (DMSO-d_6) δ ; 3a 4.05(s, 2H), 5.99(d, 1H, J=1.5 Hz), 6.23(d, 1H, J=1.5 Hz), 7.66(s, 1H), 3b 2.14(s, 3H), 4.03(s, 2H), 5.96(d, 1H, J=1.5 Hz), 6.19(d, 1H, J=1.5 Hz) : mp °C ; 3a 127-129, 3b 137-139.



1a : R=H
1b : R=CH_3

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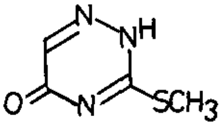
3a : R=H (74.4%)
3b : R=CH_3 (81.9%)

Selective S-alkylation was confirmed by the comparison of the uv data of 3a with that of the analogous methylthiotriazine (4) : λ_{max}^{EtOH} nm(log ε) of 3a are 231(4.21) and 299 sh(3.09) and λ_{max}^{EtOH} nm(log ε) of 3-methylthiotriazine (4) are 234(4.27) and 300 sh(3.00), while λ_{max}^{EtOH} nm(log ε) of

2-methyl- (5) and 4-methyltriazine (6) are 220(4.27), 267(4.40), 312 sh(3.56) and 218(4.40), 270(4.27), 310(3.55), respectively.[1]



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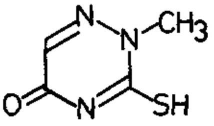

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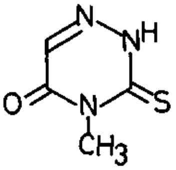

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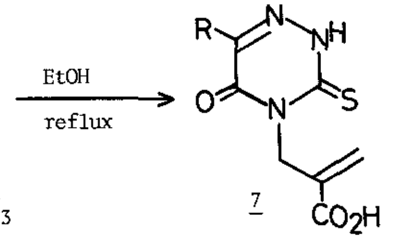
An ethanolic solution of 3a and b was refluxed and evaporated to give the compounds 7a and b in quantitative yields. The structures of 7a and b were confirmed from the uv and ^{1}H nmr spectra data : ^{1}H nmr (DMSO-d_6) δ ; 7a 4.95(m, 2H), 5.47(m, 1H), 6.05(m, 1H), 7.81(s, 1H), 7b 2.15(s, 3H), 4.97(m, 2H), 5.43(m, 1H), 6.04(m, 1H) : λ_{max}^{EtOH} nm(log ε) ; 7a 215(4.04), 269(4.07), 315 sh(3.36), $\lambda_{max}^{ph\ 11}$ nm(log ε) ; 7b 261(4.07), 330(3.70). And $\lambda_{max}^{ph\ 11}$nm(log ε) of 4,6-dimethyltriazine (8) are 264(4.05) and 326(3.74), while those of 2,6-dimethyltriazine (9) are 237(4.15) and 262(4.42).[2]



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a : R=H

b : $R=CH_3$

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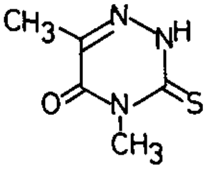
a : R=H, mp 154-156°C

b : $R=CH_3$, mp 157-159°C



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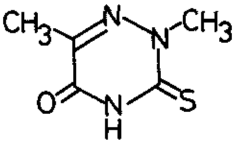

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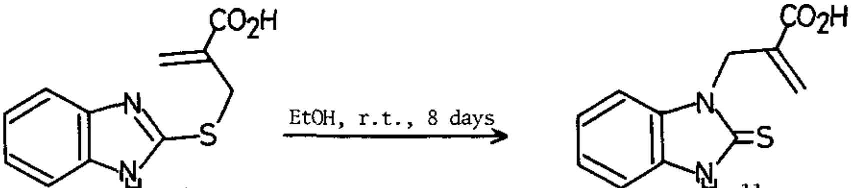
From these data it became clear that the allyl migration occurred from sulfur to nitrogen at 4-position (4-N) of the rings. Recently Yoshida and co-workers[3] reported an excellent palladium catalyzed allyl migration of allylthiotriazine in which the transformation proceeded predominantly from sulfur to 4-N and small amounts of 2-N substituted products were also obtained. In this point the non-catalyzed process is regiospecific one.

As expected, 2-(2-carboxyallylthio)benzimidazole (10)[4] also underwent this type of the rearrangement in ethanol at room temperature for 8 days and gave 11[5]. However, higher reaction temperature with shortened reaction time gave an intractable mixture of the products. Even at room temperature yield did not satisfy (20.9%). Exceptionally 2-(2-carboxyallylthio)thiazoline (12)[6], prepared (61.0%) from 2-mercaptothiazoline and 2 in the same way for 50 min, was also converted to 3-(2-carboxyallyl)-2-thioxothiazolidine (13)[7] in a methanolic solution of sodium hydroxide (1 equiv.)



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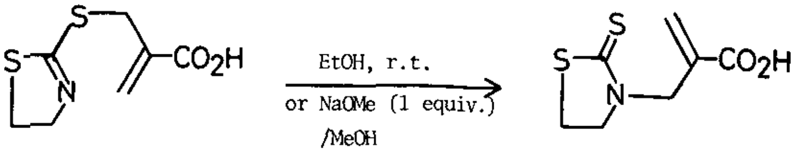

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at room temperature in quantitative yield like in ethanol. But in the presence of the excess of sodium methoxide (100 equiv.) this conversion did not take place.

To other heterocycles[8a-c], containing 2-carboxyallylthio group, prepared from thiouracil, 2-mercaptopyrimidine, and 2-amino-5-mercapto-1,3,4-thiadiazole this type of the rearrangement was applied but any rearranged products could not be obtained.

In comparison with the previous reports about S-N polyhetero-Claisen rearrangement which proceeded at high temperatures, these facile rearrangements might be attributed to the presence of electron withdrawing group and proceed via dipolar intermediate as proposed by Gompper and his co-workers.[9]

REFERENCES AND NOTES

1. J. Jonaš and J. Gut, Collect. Czech. Chem. Commun., 1962, 27, 1886.
2. K. Y. Zee-Cheng and C. C. Cheng, J. Org. Chem., 1962, 27, 976.
3. M. Mizutani, Y. Sanemitsu, Y. Tamaru, and Z. Yoshida, J. Org. Chem., 1983, 48, 4585.
4. ^{1}H nmr (DMSO-d_6) δ 4.29(s, 2H), 5.99(d, 1H, J=1.5 Hz), 6.18(d, 1H, J=1.5 Hz), 7.15-7.85(m, 4H) : mp 150°C
5. ^{1}H nmr (DMSO-d_6) δ 5.03(m, 1H), 5.09(m, 2H), 6.12(m, 1H), 7.23(m, 4H) : mp 148-150°C
6. ^{1}H nmr (DMSO-d_6) δ 3.20-3.70(m, 2H), 3.90-4.40(m, 2H), 3.96(s, 2H), 5.86(d, 1H, J=1.5 Hz), 6.14 (d, 1H, J=1.5 Hz) : mp 65°C
7. ^{1}H nmr (DMSO-d_6) δ 3.15-3.60(m, 2H), 3.95-4.40(m, 2H), 4.53(m, 2H), 5.62(m, 1H), 6.22(m, 1H) : mp 103-105°C
8. a) 2-(2-Carboxyallylthio)-4(1H)-pyrimidinone ; ^{1}H nmr (DMSO-d_6) δ 4.04(s, 2H), 5.94(d, 1H, J=1.5 Hz), 6.16(d, 1H, J=1.5 Hz), 6.13(d, 1H, J=6.5 Hz), 7.92(d, 1H, J=6.5 Hz) : mp 150°C b) 2-(2-carboxyallylthio)pyrimidine ; ^{1}H nmr (DMSO-d_6) δ 4.06(s, 2H), 5.94(d, 1H, J=1.5 Hz), 6.15(d, 1H, J=1.5 Hz), 7.25(t, 1H, J=5 Hz), 8.68(d, 2H, J=5 Hz) ; mp 143-145°C c) 2-amono-5-(2-carboxyallylthio)-1,3,4-thiadiazole ; ^{1}H nmr (DMSO-d_6) δ 3.87(s, 2H), 5.73(d, 1H, J=1.5 Hz), 6.10(d, 1H, J=1.5 Hz), 7.00-7.70(broad s, 2H) ; mp 169-170°C These compounds were prepared in the same way as the reaction for the compounds 3, 10, and 12.
9. R. Gompper and B. Kohl, Tetrahedron Lett., 1980, 21, 907.

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