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FIRST SYNTHESIS of 4, 6-DIALKYL-1, 2, 3- TRIAZINONES *VIA* DIALKYLCYCLOPROPENONES

Kiyoshi Matsumoto,* Tomasz Girek, Akihiro Okada, and Naoto Hayashi

Graduate School of Human and Environmental Studies, Kyoto University, Kyoto 606-8501, Japan
(E-mail:Kiyoshi.Matsumoto@ma1.seikyou.ne.jp, FAX: +81-75-753-2969)

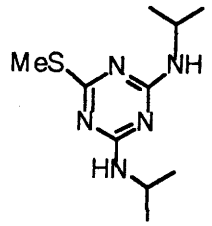
Abstract---2-Methyl-4,6-dialkyl-1,2,3-triazin-5(2*H*)-ones (**12a-e)** were prepared for the first time from the corresponding cyclopropenones that were prepared by Nakamura's method.

Cyclopropenone is an extremely interesting compound that has a relatively stable molecular structure due to the π-electron delocalization while holding a high deformation energy. So far, many investigations have been carried out on the chemical properties of structure and reactions on cyclopropenones.[1]

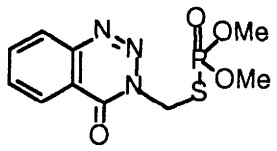
Compounds with monocyclic triazine skeleton have been rarely seen in those six-membered ring compounds with three nitrogen atoms, i.e. usually, this type of compounds are condensed ones with triazine and benzene ring. These triazine derivatives have rather interesting activities and many of them have been already on the market as herbicides or pesticides. Followings are shown some representative examples, that have a basic skeleton of 1,2,3-, 1,2,4- or 1,3,5-triazine (Scheme 1). [2]

Previously, we have reported preparation and conversion of amino-diphenylcyclopropenium salts (**3**) to the 5-amino-4,6-diphenyl-1,2,3-triazines (**4**), followed by methylation and subsequent hydrolysis to give 2-methyl-4,6-diphenyl-

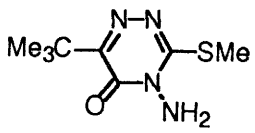
Dedicated to Professor Yuichi Kanaoka for the celebration of his 75th birthday



Prometryn
(Herbicide)

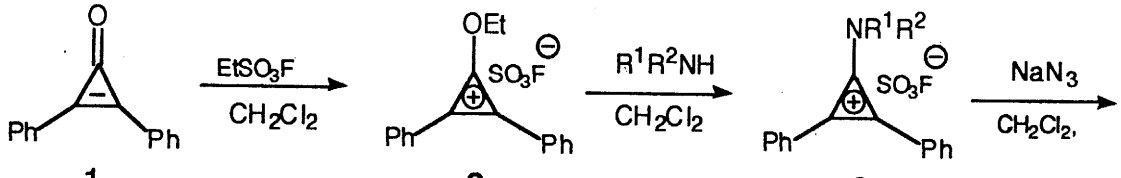


Azinphos-methyl
(Insecticide)

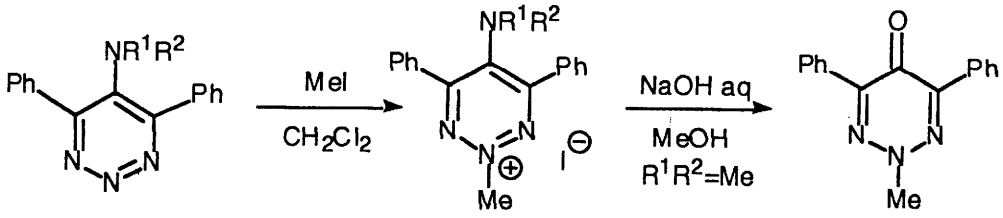


Metribuzin
(Herbicide)

Scheme 1

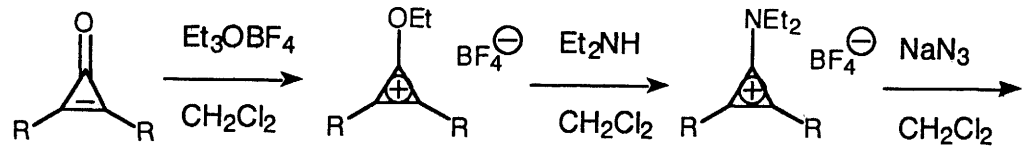


1 **2** **3**



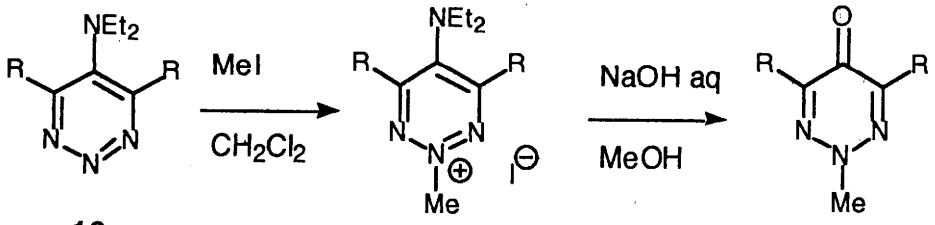
4 **5** **6**

Scheme 2



7

a: R=n-Pr
b: R=n-Bu
c: R=n-C_5H_9
d: R=n-C_6H_{11}
e: R=Cyclohexyl



10 **11** **12**

a: R=n-Pr 38%, 3 steps
b: R=n-Bu 40%, 3 steps
c: R=n-C_5H_9 45%, 3 steps
d: R=n-C_6H_{11} 51%, 3 steps
e: R=Cyclohexyl
43%, 3steps

Scheme 3

a: R=n-Pr 60%, 3 steps
b: R=n-Bu 78%, 2 steps
c: R=n-C_5H_9 75%, 2 steps
d: R=n-C_6H_{11} 80%, 2 steps
e: R=Cyclohexyl
77%, 2 steps

1,2,3-triazin-5(2*H*)-one (**6**) (Scheme 2). [3] In extension of this work, we are interested in preparation of 4, 6-dialkyl-1, 2, 3- triazinones *via* dialkylcyclopropenones since 4, 6-dialkyl-1, 2, 3- triazinones have been never synthesized probably because of severe limitations of the methods.[4] Before invention of Nakamura's method, we have employed a variety of the existing methods, but none of them worked well. Fortunately, Nakamura *et al*. developed highly elegant and general synthesis of cyclopropenones based upon the chemistry of metalated cyclopropenone acetals. [4]

This new synthetic method prompted and encouraged us again to embark to synthesize 4, 6-dialkyl-1, 2, 3- triazinones *via* dialkylcyclopropenones. This is a subject of the present communication. Initially and unfortunately, we have encountered one problem, that is, ethyl fluorosulfate which undergoes reaction with cyclopropenones extremely smoothly and cleanly to give the cyclopropenium salts such as **2** is no more commercially available presumably because of environmental problems. An alternative but less desirable reagent would be Meerwein reagent; indeed, when this reagent was used, all attempts to isolate pure **2** failed in our hands, whereas with ethyl fluorosulfate, the pure salt (**2**) was easily obtained.[3] Therefore, in this event, we have not made any great effort to isolate the salts (**8**) and (**9**). Similarly, in the cases of the dialkyl-substituted salts (**11**), purification was also difficult. Therefore, only 2-ethyl-4,6-dialkyl-1,2,3-triazines (**10**) and 2-methyl-4,6-dialkyl-1,2,3-triazin-5(2*H*)-ones (**12)** were isolated.[5] The representative results are summarized in Scheme 3.

In conclusion, 2-methyl-4,6-*dialkyl*-1,2,3-triazin-5(2*H*)-ones (**12a-e**) were prepared for the first time from the corresponding cyclopropenones. Further work is under way on the scope and limitations of the present method for the formation of compounds such as 4,6-unsymmetrically substituted-1,2,3-triazin-5(2*H*)-ones as well as on their physiological activities.

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5. Typical procedure: **8b**; To 2,3-dibutylcyclopropenone (**7b**, 4.68 g, 28 mmol) was added Meerwein reagent in dichloromethane (1.0 mol/L, 50.0 mL, 50 mmol) at rt under argon and stirred for 1 h. To this mixture, dry ether was added to precipitates which filtered and was washed with dry ether to give **8b** (8.0 g), **8b** was difficult to purify and was unstable. **9b**: To a solution of **8b** (6.0 g, 21.3 mmol) in dichloromethane (20 mL), a solution of diethylamine (2.2 mL, 21.3 mmol) was added dropwise at rt with stirring and stirring was continued for 1.5 h. The mixture was reduced in a vacuum to give the crude **9b** (6.8 g) which was used for next step without further purification. **10b**: To a solution of **9b** (6.8 g) in dichloromethane (20 mL) was added sodium azide (5.0 g, 76.9 mmol) and the mixture was stirred for 24 h. The solution was concentrated in a vacuum. The residue was chromatographed on silica gel (CH_2Cl_2/hexane) to give the pure **10b** (2.22 g, 40 % from **7b**). IR ν max (KBr) cm^{-1} : 2961, 2932, 2872, 1510, 1464, 1408, 1379, 1339, 1296, 1261, 1196, 1130, 1103, 1069.^{1}H NMR ($CDCl_3$) δ : 0.93 (6H, t, J = 7.2 Hz, NEt_2), 1.02 (6H, t, J = 7.2 Hz, C4-Bu, C6-Bu), 1.40 (4H, m, C4-Bu, C6-Bu), 1.81 (4H, m, C4-Bu, C6-Bu), 2.84 (4H, t, J = 7.2 Hz, C4-Bu, C6-Bu), 3.11 (4H, q, J = 7.2 Hz, NEt_2).^{13}C NMR ($CDCl_3$) δ : 13.9 (C5-NEt_2), 14.1, 22.9, 30.3, 31.7 (C4-Bu, C6-Bu), 46.9 (C5-NEt_2), 139.4 (C-5), 161.5 (C-4, C-6). **11b**: To a solution of **10b** (1.14 g, 4.33 mmol) in methanol (40 mL) iodomethane (2.7 mL, 43 mmol) was added at rt, and the mixture was stirred for 2d. The mixture was reduced in a vacuum to give crude **11 b** (2.04 g). **12b**: To a solution of **11b** in methanol (40 mL) aq. sodium hydroxide (1.0 M, 10.0 mL) was added dropwise at rt and the whole was stirred for 50 min. The mixture was extracted with dichloromethane. The organic layer was washed with water and dried over anhydrous $MgSO_4$ and concentrated in a vacuum. The residue was chromatographed on silica gel (CH_2Cl_2/hexane) giving the pure **12b** (0.745 g, 78 % from **10b**). IR ν max (KBr) cm^{-1} : 3001, 2959, 2932, 2874, 1605, 1458, 1427, 1369, 1315, 1215, 1076, 922, 756, 667.^{1}H NMR ($CDCl_3$) δ : 0.88 (6H, t, J = 7.2 Hz, C4-Bu, C6-Bu), 1.33 (4H, m, C4-Bu, C6-Bu), 1.57 (4H, m, C4-Bu, C6-Bu), 2.61 (4H, t, J = 7.2 Hz, C4-Bu, C6-Bu), 4.02 (3H, s, N2-Me).^{13}C NMR ($CDCl_3$) δ : 13.9, 22.6, 28.5, 29.0 (C4-Bu, C6-Bu), 49.9 (N2-Me), 156.3 (C-4, C-6), 162.6 (C-5).