

SYNTHESIS OF 2-METHYL-4, 6-DIARYL -1, 2, 3- TRIAZINONES VIA DIARYLCYCLOPROPENONES

Kiyoshi Matsumoto,^{*a} Akihiro Okada,^a Tomasz Girek,^a Yukio Ikemi,^a
Jong Chul Kim,^a Naoto Hayashi,^a Hiroshi Yoshida,^h and Akiyazu Kakehi^c

^a Graduate School of Human and Environmental Studies, Kyoto University, Kyoto 606-8501,
Japan

^b Faculty of Engineering, Shizuoka University, Hamamatsu 432-8561, Japan

^c Faculty of Engineering, Shinshu University, Nagano 380-8553, Japan

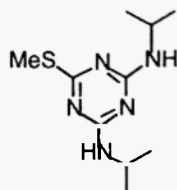
Abstract : 2-Methyl-4,6-bis(4-substituted-phenyl)-1,2,3-triazin-5(2*H*)-ones **9a-d** were prepared from the corresponding cyclopropenones **4a-d** in a similar fashion as described by us previously. One of the the structure of **9b** was established by an X-ray analysis.

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 (i).

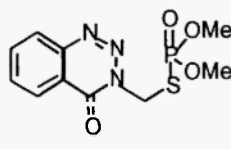
Compounds with triazine skeleton have been rarely seen in those six-membered ring compounds with three nitrogen atoms, i.e. usually, this type of compounds are condensed ones with triazine and benzene ring. These triazine derivatives have rather interesting activities and many of them have been already 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).

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

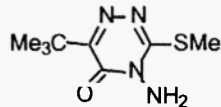
In order to explore further examples of triazines and triazinones having an interesting physiological activity, we have examined on the synthesis of 4,6-diaryl-1,2,3-triazinones via some para-substituted diarylcyclopropenones that were prepared by intramolecular cyclization of the corresponding dibromoketone (Favorskii rearrangement) (Scheme 2 and 3) (3). In the synthesis of the dibenzyl ketone that is the basic skeleton of cyclopropenone synthesis, the easiest way to modify its phenyl group is the introduction of a substituent at the para-position. Of course, this strategy does not hinder the nucleophilic attack in the reaction with sodium azide after preparation of the cyclopropenium cation. Thus, aryl bromides having fluorine, chlorine, bromine or methyl group at the para-position,



Prometryn

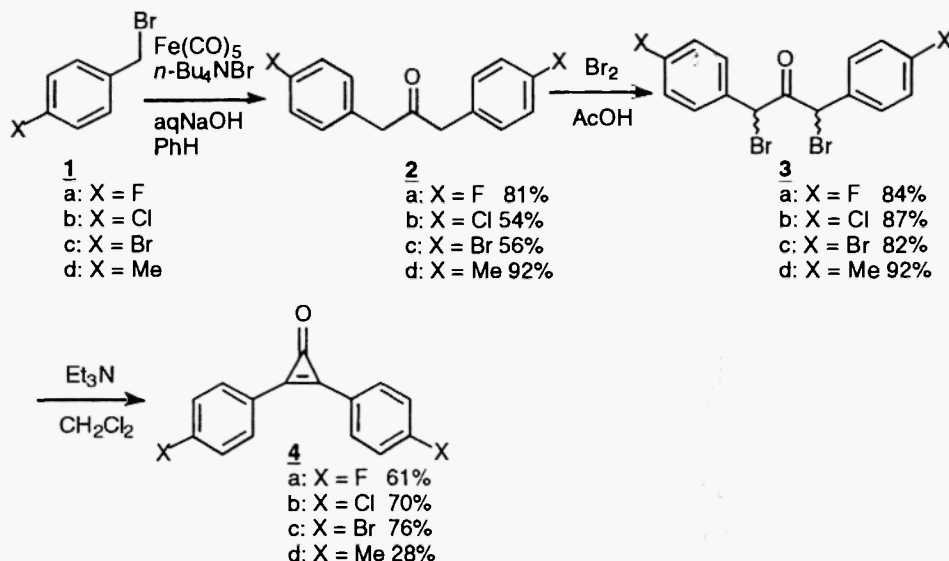


Azinphos-methyl

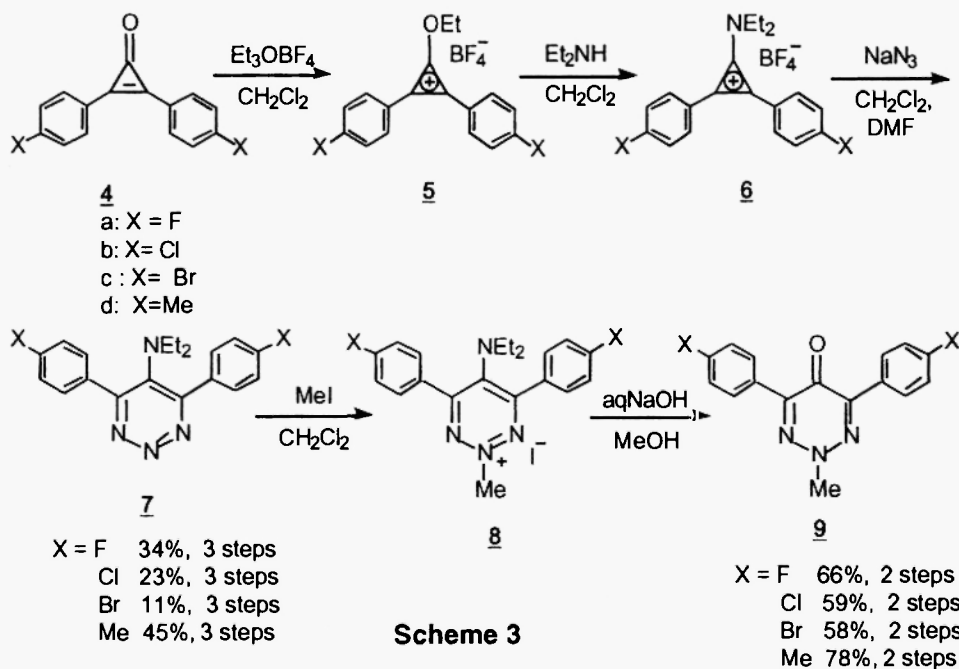


Metribuzin

Scheme 1



Scheme 2



Scheme 3

were used as the starting material that are commercially available. For example, 4-fluorobenzyl bromide **1a** was coupled using pentacarbonyliron according to an established method (4) to produce the corresponding dibenzyl ketone **2** in 81 % yield. The dibenzyl ketone **2a** was reacted with bromine in acetic acid to afford the dibromoketone **3a**, followed by an intramolecular cyclization with triethylamine giving the cyclopropenone **4a** as colorless solids in a 61 % yield (Scheme 2). A characteristic peak of the cyclopropenone appeared around 155 ppm for carbonyl carbon (^{13}C -NMR). The infrared spectrum revealed strong absorbance around at 1850 cm^{-1} and 1640 cm^{-1} .

This cyclopropenone **4a** was converted into the cyclopropenium cation **5a** by reacting with triethyloxonium tetrafluoroborate (Meerwein reagent), because ethyl fluorosulfate which is easier to handle and therefore was used in the previous work, is no more commercially available. The salt **5a** was *in situ* treated with diethylamine, thus the ethoxy group being converted into the diethylamino group. The salt **6a** was further *in situ* reacted with sodium azide in methylene chloride and dimethylformamide to produce the 1, 2, 3-triazine **7a** with a three-step yield of 34 %. The structure **7a** was unambiguously determined by X-ray analyses (5). Finally, the triazinone **9a** could be synthesized from the triazine **7a** by methylating nitrogen at the 2-position to produce triazinium salt **8a**, followed by hydrolysis with aqueous sodium hydroxide in methanol in two-step yield of 66 % (Scheme 3). The triazinone **9a** was a pale yellow solid with a melting point of $198\text{ }^{\circ}\text{C}$, not a single crystal, but fairly stable in air at room temperature.

Similar procedures were followed to synthesize 2-methyl- 4,6-bis(4-chlorophenyl)-1,2,3-triazin-5(2H)-one **9b**, 2-methyl- 4,6-bis(4-bromophenyl)-1,2,3-triazin-5(2H)-one **9c**, and 2-methyl-4,6-bis(4-methylphenyl)-1,2,3-triazin-5(2H)-one **9d**. Fortunately, **9b** formed a single crystal, thus the structure being unambiguously determined by X-ray analyses (6).

Tests for the physiological activity of these triazinones are envisaged to be performed and will be included in a full paper.

ACKNOWLEDGMENTS

This work was supported by Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology, Japan. The authors are also grateful to the Ministry of Education, Culture, Sports, Science, and Technology, Japan for purchasing the high-field NMR instruments (JEOL JNM-A500 and JNM-EX270) by the special fund to K. M. in 1992. Thanks are also

extended to Mr. Shozo Ohnishi (Analytical Application Lab., Shimadzu Corporation, Kyoto, Japan) who kindly performed measurement of mass spectra in this work.

REFERENCES AND NOTES

1. Review on cyclopropanone chemistry: (a) K. T. Potts and J. S. Baum, *Chem. Rev.*, 1974, **74**, 189. (b) T. Elcher and J. L. Weber, *Topics Curr. Chem.*, 1975, **57**, 1. (c) W. E. Billups and A. W. Moorehead, In the Chemistry of the Cyclopropyl Group, Rappoport, Z. Ed; Wiley: New York; 1987; Chapter 24 (d) K. Matsumoto, *Yukiougousei Kagaku Kyoukaishi (J. Synth. Org. Chem. Jpn.)*, 1972, **30**, 1035.
2. H. Yoshida, K. Yagi, T. Tamai, H. Sano, T. Ogata and K. Matsumoto, *Bull. Chem. Soc. Jpn.*, 1985, **58**, 1073.
3. R. Breslow, R. Haynie and J. Mirra, *J. Am. Chem. Soc.*, 1959, **81**, 247.
4. Y. Kimura, Y. Tomita, S. Nakanishi and Y. Otsuji, *Chem. Lett.*, 1979, 321.
5. Data were collected at T=20°C on a Rigaku AFC5S diffractometer; **7a**: C₁₉H₁₈N₄F₂, M=340.37, yellow prism, dimensions 0.320 x 0.640 x 0.860 mm, orthorhombic, space group = Aba2, a=10.558(6)Å, b=18.925(4)Å, c=8.314(5)Å, U=1677(2)Å³, Z=4, Dc=1.348gcm⁻³, F(000)=712. Mo-Kα radiation (λ=0.71069Å), μ=0.92cm⁻¹, ω-2θ scan mode with ω scan width=1.68+0.30tanθ, ω scan speed 16.0 deg min⁻¹ and 1124 reflections were collected in the range 6.0<2θ<55.0. The structure was solved by direct methods using full-matrix least squares on F for all non-hydrogen atoms using Lorenz polarization and absorption corrections to give R=0.037, and Rw=0.043 for 818 independent observed reflections with I>2.00σ(I) and 151 variables for 2θmax=55.0°. The final difference map of maximum and minimum were 0.14 and -0.14 eÅ⁻³, respectively.
6. **9b**: C₁₈H₁₁N₃Cl₂O, M=332.18, yellow prism, dimensions 0.320 x 0.640 x 0.660 mm, monoclinic, space group = P21/n, a=10.472(7)Å, b=15.737(6)Å, c=11.498(5)Å, β=107.03(4)°, U=1812(2)Å³, Z=4, Dc=1.368gcm⁻³, F(000)=776. Mo-Kα radiation (λ=0.71069Å), μ=3.66cm⁻¹, ω-2θ scan mode with ω scan width=1.63+0.30tanθ, ω scan speed 16.0 deg min⁻¹, 4545 reflections were collected in the range 6.0<2θ<55.0 and 4319 unique reflections(Rint=0.053) were used in the refinement. The structure was solved by direct methods using full-matrix least squares on F for all non-hydrogen atoms using Lorenz polarization and absorption corrections to give R=0.064, and Rw=0.065 for 2002 independent observed reflections with I>2.00σ(I) and 226 variables for 2θmax=55.0°. The final difference map of maximum and minimum were 0.54 and -0.43 eÅ⁻³, respectively. The atomic scattering factors for all atoms and the anomalous dispersion correction factors for atoms other than hydrogen were taken from the literature. All calculations were performed using TEXAN crystallographic software package of Molecular Structure Corporation.

Received on February 27, 2002