(c) R. J. Cvetanović, *Adv. Photochem.*, **1**, 115 (1963); (d) R. J. Cvetanović, *J. Phys. Chem.*, **74**, 2730 (1970); (e) D. L. Singleton and R. J. Cvetanović, *J. Am. Chem. Soc.*, **98**, 6812 (1976); (f) M. D. Scheer and R. Klein, *J. Phys. Chem.*, **74**, 2732 (1970); (g) J. J. Havel, *J. Am. Chem. Soc.*, **96**, 530 (1974); (h) J. J. Havel, W. T. Chamberlain, and P. M. Krautter, *ibid.*, **96**, 632 (1974); (i) J. J. Havel and K. H. Chan, *J. Org. Chem.*, **39**, 2439 (1974); (j) J. J. Havel and K. H. Chan, *J. Am. Chem. Soc.*, **97**, 5800 (1975); (k) J. J. Havel and K. H. Chan, *J. Org. Chem.*, **41**, 513 (1976); (l) J. J. Havel and C. J. Hunt, *J. Phys. Chem.*, **80**, 779 (1976).
(2) (a) G. Boocock and R. J. Cvetanović, *Can. J. Chem.*, **39**, 2436 (1961); (b) G. R. H. Jones and R. J. Cvetanović, *ibid.*, **39**, 2444 (1961); (c) E. Grovenstein, Jr., and A. J. Mosher, *J. Am. Chem. Soc.*, **92**, 3810 (1970).
(3) A "ketenelike" intermediate was suggested to be formed in the gas-phase reaction of $O(^3P)$ atoms with alkynes. Various primary decompositions of the "hot" intermediate are possible at low pressures: (a) D. G. Williamson and K. D. Bayes, *J. Phys. Chem.*, **73**, 1232 (1969); (b) H. E. Avery and S. J. Heath, *Trans. Faraday Soc.*, **68**, 512 (1972).
(4) A. Kato and R. J. Cvetanović, *Can. J. Chem.*, **46**, 235 (1968).
(5) The reaction of $O(^3P)$ atoms with alkenes has been investigated under special conditions in condensed phase: (a) S. Hirokami and R. J. Cvetanović, *Can. J. Chem.*, **51**, 373 (1973); (b) S. Hirokami and R. J. Cvetanović, *J. Am. Chem. Soc.*, **96**, 3738 (1974); (c) A. N. Hughes, M. D. Scheer, and R. Klein, *J. Phys. Chem.*, **70**, 798 (1966); (d) A. N. Ponomarev, *Kinet. Katal.*, **7**, 237 (1966); (e) E. E. Kasimovskaya and A. N. Ponomarev, *ibid.*, **9**, 687 (1968); (f) O. Amichai and A. Treinin, *Chem. Phys. Lett.*, **3**, 611 (1969).
(6) (a) D. L. Baulch, F. S. Dainton, and R. L. S. Willix, *Trans. Faraday Soc.*, **61**, 1146 (1965); (b) A. R. Anderson and D. A. Dominey, *Radiat. Res. Rev.*, **1**, 269 (1968); (c) M. Yoshimura, M. Chosa, Y. Soma, and M. Nishikawa, *J. Chem. Phys.*, **57**, 1626 (1972).
(7) H. Sakurai, K. Akimoto, S. Toki, and S. Takamuku, *Chem. Lett.*, 469 (1975).
(8) A. Hori, S. Takamuku, and H. Sakurai, *J. Chem. Soc., Chem. Commun.*, 686 (1976).
(9) I. Haller and G. C. Pimentel, *J. Am. Chem. Soc.*, **84**, 2855 (1962).
(10) L. Wojnarovits, S. Hirokami, and S. Sato, *Bull. Chem. Soc. Jpn.*, **49**, 2956 (1976).
(11) T. H. Varkony, S. Pass, and Y. Mazur, *J. Chem. Soc., Chem. Commun.*, 457 (1975).
(12) W. B. DeMore and O. F. Raper, *J. Chem. Phys.*, **46**, 2500 (1967).
(13) T. H. Varkony, S. Pass, and Y. Mazur, *J. Chem. Soc., Chem. Commun.*, 437 (1974); 709 (1975).
(14) Cyclohexene oxide was probably generated by the reaction of $O(^3P)$ atoms with cyclohexene which was presumed to be produced by the radiolysis of cyclohexane (see ref 7).
(15) C. Walling and B. B. Jacknow, *J. Am. Chem. Soc.*, **82**, 6108 (1960).
(16) (a) H. Yamazaki and R. J. Cvetanović, *J. Chem. Phys.*, **41**, 3703 (1964); (b) G. Paraskevopoulos and R. J. Cvetanović, *ibid.*, **50**, 590 (1969); (c) P. Michaud, G. Paraskevopoulos, and R. J. Cvetanović, *J. Phys. Chem.*, **78**, 1457 (1974).
(17) W. B. DeMore, *J. Phys. Chem.*, **73**, 391 (1969).
(18) P. Neta and R. H. Schuler, *J. Phys. Chem.*, **79**, 1 (1975).
(19) (a) K. V. Krishnamurty, *J. Chem. Educ.*, **44**, 594 (1967), and references cited therein; (b) E. Weissberger, W. H. Breckenridge, and H. Taube, *J. Chem. Phys.*, **47**, 1764 (1967); (c) D. S. Sethi and H. A. Taylor, *ibid.*, **49**, 3669 (1968); (d) M. Arvis, *J. Chim. Phys. Physicochim. Biol.*, **66**, 517 (1969); (e) W. B. DeMore and C. W. Jacobsen, *J. Phys. Chem.*, **73**, 2935 (1969); (f) W. B. DeMore and C. Dede, *ibid.*, **74**, 2621 (1970); (g) P. R. Jones and H. Taube, *ibid.*, **75**, 2991 (1971); (h) M. E. Jacox and D. E. Milligan, *J. Chem. Phys.*, **54**, 919 (1971).
(20) L. Kaplan in "Free Radicals", Vol. II, J. K. Kochi, Ed., Wiley, New York, N.Y., 1973, pp 407–412, and references cited therein.
(21) H. O. House, "Modern Synthetic Reactions", W. A. Benjamin, Menlo Park, Calif., 1972, Chapter 1.
(22) H. Gilman and W. E. Catlin, "Organic Syntheses", Collect. Vol. I, Wiley, New York, N.Y., 1956, p 188.
(23) F. K. Signaigo and P. L. Cramer, *J. Am. Chem. Soc.*, **55**, 3326 (1933).
(24) J. R. Durland and H. Adkins, *J. Am. Chem. Soc.*, **61**, 429 (1939).
(25) G. Stork, *J. Am. Chem. Soc.*, **69**, 576 (1947).
(26) W. G. Dauben, R. C. Tweit, and C. Mannerskantz, *J. Am. Chem. Soc.*, **76**, 4420 (1954).

Notes

A Facile and General Pyridazine Synthesis from α-Diketone Monohydrazones and β-Keto Esters or β-Diketones

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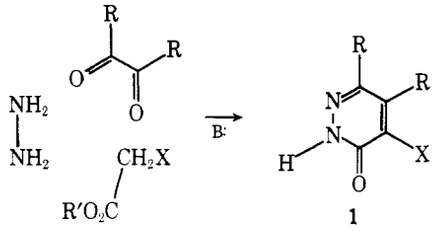
The Schmidt pyridazine synthesis[2] formally involves the base-catalyzed condensation of hydrazine, an α-diketone, and an ester activated methylene compound yielding substituted pyridazinones (**1**). In conjunction with this work, Schmidt and



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X = CO_2R', COR'', CN, etc.

Druey[2] reported that, in the abscence of a basic catalyst, reaction of benzil monohydrazone (**7**) with ethyl acetoacetate (**8a**) yields the "azine" **9a** which could not be converted into a ring-closed product (i.e., **10a**) although no details were given. There are, however, examples in the literature of similar cyclizations. Reaction of α-diketone monohydrazones (**2**) with dimethyl acetylenedicarboxylate (DMAD) yields[3] dicarbomethoxypyridazines **3**, presumably via the azines **4** which are also isolated along with several other products (reaction 1). In addition, we have shown[4] that the stabilized phosphorane **5** yields the pyridazinylmethyltriphenylphosphonium salt **6** on heating (reaction 2).

In the course of another investigation we had occasion to synthesize "azine" **9a**. Azine is actually a misnomer since the molecule exists completely (as determined by NMR and IR spectroscopy) in the enamine tautomer, presumably stabilized by intramolecular hydrogen bonding to the benzoyl carbonyl oxygen. To our knowledge, this represents the first example of preference for the enamine tautomer in an azine, although the intermediacy of the enamine form has been postulated[5] in the α-alkylation of aliphatic ketazines by electron-deficient dienophiles (e.g., maleic anhydride). Throughout this discussion, we will refer to these molecules as azines, although their tautomeric structure should be kept in mind.

Our original intention was to carry out a series of transformations involving the carboethoxy moiety of **9a** beginning with saponification. When **9a** is heated in aqueous ethanol containing potassium hydroxide a deep red color develops which fades to a very pale yellow after 10 min. The single, colorless product formed retains the carboethoxy group and spectral (IR, NMR, mass spectrum) and elemental analyses indicate that the product is the pyridazine carboxylic ester **10a**. The rapidity and efficiency (>90% isolated yield of **10a**) of this reaction stands in marked contrast to the earlier reports of the inertness of **9a** toward ring closure.[2]

It is not necessary to isolate **9a** and, in fact, considerable

losses result during purification. We have adopted a one-pot procedure consisting of initial formation of the azine by heating the reactants in benzene with azeotropic removal of water, removal of benzene in vacuo, and treatment of the crude azine with a catalytic amount of KOH in hot ethanol. The isolated yield of **10a** based on **7** by this method is 93%. Following the same procedure we have prepared 3,4,6-triphenyl-5-carboethoxypyridazine (**10d**) in 55% overall yield from **7** and ethyl benzoylacetate (**8b**).

Further confirmation of the structures of **10a** and **10d** is provided by their transformation into the known 5-unsubstituted pyridazines **10c** and **10f.** Saponification of the esters **10a** and **10d** yields the acids **10b** and **10e** which readily decarboxylate on heating. The physical and spectral parameters for **10c** and **10f** prepared in this manner are identical with those reported in the literature.[6]

In theory, any carbonyl activated methylene compound of the type **8** (X = any carbanion stabilizing group) should be readily convertible to the corresponding pyridazine **13** by

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dehydrative ring closure of its azine with an α-diketone (R'COCOR'). To investigate the generality of the reaction, we have examined the reaction of acetylacetone **8c** with **7.** Complex, tarry reaction mixtures result from the attempted one-pot reaction as outlined above. Thus, we prepared and isolated the azine in an initial step prior to its ring closure. The azine, **11,** can be isolated in sufficient purity for further reaction as an orange solid in 73% yield. As in the case of **9a, 11** is completely in the enamine form. However, it consists of a mixture of two thermally interconvertible isomers (A and B) in approximately a 1.5:1 ratio. The IR and NMR spectra are very similar, suggesting the same gross structure. A reasonable explanation is that A and B are syn and anti isomers about the

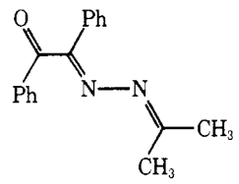
Scheme I

C–N double bond (i.e., **11a** and **11b**). In the anti isomer (**11b**) hydrogen bonding is possible only with the acetyl carbonyl. Similar interactions are possible with either the benzoyl or acetyl carbonyl in the syn isomer **11a;** however, the distinct spectral differences in the methyl, vinyl, and N–H regions of the NMR spectra suggest that the interaction is with the benzoyl carbonyl in this case. We are unable to assign either structure (**11a** or **11b**) unambiguously to either isomer A or B on the basis of the data in hand. Synthetically, the existence of the two isomers presents no difficulty since both yield the same products in the next step.

The ring closure of **11** proves to be more interesting than anticipated. Whereas the cyclizations of **9a** and **9b** to **10a** and **10d** require only a catalytic amount of base, nearly a full equivalent is needed to convert **11** to products. Unlike **9,**

treatment of **11** with hydroxide under a variety of conditions yields a mixture of two products. The expected 3,4-diphenyl-5-acetyl-6-methylpyridazine (**12**) is the minor (10–15%) product. The major (75–80%) product is the 5-unsubstituted pyridazine **10c**. Spectral and analytical data support the acetyl pyridazine structure for **12**. The mass spectrum is particularly useful as a strong peak at m/e 245 $(M - CH_3CO)^+$ is observed. Pyridazine **10c** isolated from this reaction is identical in all respects with **10c** prepared above by decarboxylation of **10b**.

There are several reasonable mechanisms to be considered for the formation of **10c** in this reaction. First, it is possible that it arises from **12** by deacylation, a known reaction in pyridazine *N*-oxide chemistry.[7] However, neither shortening the reaction time nor lowering the temperature leads to an increase in the amount of **12** formed. Also, **12** is recovered unchanged after heating with alcoholic KOH for an extended period of time. Alternatively, **10c** could be the result of "deacylation" of **11** to **14**, but **14** is also inert to the reaction



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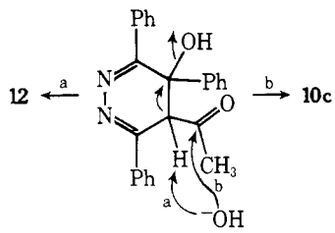
conditions. The evidence suggests a reactive intermediate as the source of **10c**. We believe the probable origin of the mixture of products in this reaction to be competing eliminations from an intermediate dihydropyridazine **15**. Elimination of



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water (path a) gives the expected **12**, while attack of hydroxide at the acetyl carbonyl (path b) yields the "deacylated" product **11a** by elimination of acetic acid and hydroxide. Steric crowding coupled with the increased electrophilicity of the ketone carbonyl carbon compared with that of an ester may be responsible for the favorable competition of the "abnormal" elimination in this system.

We have demonstrated that azines derived from α-diketones and either β-keto esters or β-diketones exist predominantly in the unique enamine tautomeric form and are useful precursors for the pyridazine ring system. The ready availability of active methylene compounds of the type **8** should make this an attractive route to a variety of pyridazine derivatives.

Experimental Section

Benzilacetone azine (**14**) was prepared by heating benzil monohydrazone in acetone containing a catalytic amount of glacial acetic acid, a modification of the method of Taylor et al.[8] All other reagents were commercial (Aldrich) products and used as received. Melting points were determined with a Thomas-Hoover melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 337 instrument referenced to polystyrene film. A Perkin-Elmer R12b nuclear magnetic resonance spectrometer was used to obtain the ^1H NMR data. Spectra were recorded as 5–10% solutions in $CDCl_3$ except as noted and chemical shifts are reported as parts per million (δ) vs. Me_4Si as an internal standard. Mass spectra were recorded on a Du Pont CEC21-110D instrument with a resolution of 1000 (30% valley). Elemental analyses were performed by Micro-Analysis Inc., Wilmington, Del.

Preparation of Benzilethylacetoacetate Azine (9a). To 75 mL of benzene is added 3.5 g (0.027 mol) of ethyl acetoacetate and 5.6 g (0.0246 mol) of benzil monohydrazone and a catalytic amount (10–20 mg) of *p*-toluenesulfonic acid. A Dean-Stark water collector, condenser, and $CaCl_2$ drying tube are attached and the reaction mixture heated at reflux until the theoretical amount of water has collected (~2 h). The benzene is removed in vacuo and the residual golden oil triturated with cold methanol to yield 6.2 g (75%) of a yellow solid, mp 85–100 °C.

The NMR spectrum indicates that this material is essentially pure despite the wide melting point range and it can be converted in high yield to the pyridazine **10a** upon treatment with alcoholic KOH. Repeated crystallization from ethanol yields an analytical sample: mp 110.5–112.5 °C; IR 3190 (br), 1660, 1615, 1565, 1350 cm^{-1}; ^1H NMR δ 1.10 (t, J = 7 Hz, 3 H, $-OCH_2CH_3$), 2.01 [s, 3 H, $CH_3C(NH)=CH-$], 3.89 (q, J = 7 Hz, 2 H, $-OCH_2CH_3$), 4.37 (br s, 1 H, C=CH), 7.3 (br s, 8 H, aromatic), 7.8 (m, 2 H, aromatic ortho to C=O), 11.42 (br s, 1 H, NH). Anal. Calcd for $C_{20}H_{20}N_2O_3$: C, 71.41; H, 5.99. Found: C, 71.12; H, 6.05.

Preparation of 3,4-Diphenyl-5-carboethoxy-6-methylpyridazine (10a). The crude oily azine (above) from 2.7 g (0.021 mol) of ethyl acetoacetate and 4.5 g (0.02 mol) of benzil monohydrazone is dissolved in 75 mL of hot ethanol and 0.2 g of potassium hydroxide is added. A deep red color develops which fades on gentle boiling for 10 min to a pale yellow. The ethanol is removed in vacuo and the residue is partitioned between 50 mL of ether and 10 mL of 5% NaOH. The layers are separated and the ether layer extracted with 10 mL of 5% NaOH, 2 × 10 mL of 5% HCl, and 10 mL of H_2O, dried (Na_2SO_4), and evaporated in vacuo to yield 5.92 g (93%) of **10a**, mp 78–80 °C. Recrystallization from methylene chloride/heptane affords a colorless analytical sample: mp 85.5–86.5 °C; IR (KBr) 1725, 1490, 1440, 1370, 1305, 1225 cm^{-1}; ^1H NMR δ 0.92 (t, J = 7 Hz, 3 H, $-OCH_2CH_3$), 2.74 (s, 3 H, ring CH_3), 4.02 (q, J = 7 Hz, 2 H, $-OCH_2CH_3$), 7.1 (br s, 10 H, aromatic); mass spectrum m/e (% base) 318 (41.6) M^+, 289 (100), 178 (49.2). Anal. Calcd for $C_{20}H_{18}N_2O_2$: C, 75.45; H, 5.70. Found: C, 75.41; H, 5.49.

Saponification of 10a. Preparation of 3,4-Diphenyl-6-methyl-5-pyridazinecarboxylic Acid (10b). Ester **10a** (1.5 g, 4.7 mmol) is heated for 15 h in 40 mL of 50% alcohol containing 0.6 g (~8.9 mmol) of potassium hydroxide. The bulk of the ethanol is removed in vacuo and the residue acidified to pH ≃2 with 5% HCl and thoroughly extracted with methylene chloride. After drying (Na_2SO_4) and removal of the solvent in vacuo, the combined CH_2Cl_2 extracts yield 1.25 g (86%) of **10b** as a white solid. Crystallization from acetonitrile yields an analytical sample: mp 180–181 °C dec (with gas evolution); IR (KBr) 3500 (br), 1720, 1440, 1380 cm^{-1}; ^1H NMR ($CDCl_3$ + Me_2SO-d_6) δ 2.74 (s, 3 H, ring CH_3), 7.16 (br s, 10 H, aromatic), 10.07 (br s, 1 H, $-CO_2H$); mass spectrum m/e (% base) 290 (0.3) M^+, 289 (1.2), 246 (94.4), 245 (100), 178 (93.5). Anal. Calcd for $C_{18}H_{14}N_2O_2$: C, 74.47; H, 4.86. Found: C, 74.27; H, 4.81.

Decarboxylation of 10b. Preparation of 3,4-Diphenyl-6-methylpyridazine (10c). In a 10-mL round-bottom flask fitted with a $CaCl_2$ drying tube is placed 400 mg of acid **10b**. The flask is immersed in an oil bath held at 200 °C for 30 min. As the sample melts it darkens and gas is evolved. The crude tan residue (0.34 g, 99%, mp 119–122 °C) is dissolved in 15 mL of 95% ethanol, treated with Darco G-60 activated carbon, and filtered and the solvent removed. The resulting light yellow solid is recrystallized from methylene chloride/heptane to yield **10c** as an off-white solid: mp 121–123 °C (lit.[5] 122–123 °C); IR (KBr) 1580, 1565, 1400 cm^{-1}; ^1H NMR δ 2.71 (s, 3 H, ring CH_3), 7.16 (m, 11 H, aromatic + pyridazine ring H); mass spectrum m/e (% base) 246 (62.0) M^+, 245 (100), 178 (82.3).

Preparation of 3,4,6-Triphenyl-5-carboethoxypyridazine (10d). The procedure is identical with that described above for the preparation of **10a**, except that 15 h is required to collect the theoretical amount of water in the initial step of the reaction. The crude "azine" thus obtained from 2.25 g (0.01 mol) of benzil monohydrazone and 2.3 g (0.012 mol) of ethyl benzoylacetate is heated in 40 mL of ethanol containing 0.36 g of KOH for 20 min. Again a deep red color which fades as the reaction proceeds is noted. Workup as above and crystallization from ethanol yields 2.08 g (55%) of **10d** as a pale yellow solid, mp 120–124 °C. Recrystallization from ethanol yields a colorless analytical sample: mp 124–125 °C; IR 1730, 1380, 1295 cm^{-1}; ^1H NMR δ 0.78 (t, J = 7 Hz, 3 H, $-OCH_2CH_3$), 3.83 (q, J = 7 Hz, 2 H, $-OCH_2CH_3$), 7.2 (br m, 13 H, aromatic), 7.7 (br m, 2 H, ortho protons in 6-phenyl ring); mass spectrum m/e (% base) 380 (36.5) M^+, 351 (74.6), 178 (100). M^+, calcd for $C_{25}H_{20}N_2O_2$: 380.09. Found: 380.15.

Saponification of 10d. Preparation of 3,4,6-Triphenyl-5-pyr-

idazinecarboxylic Acid (10e). Saponification and workup as above for the hydrolysis of **10a** yields, from 1.0 g (2.64 mmol) of pyridazine ester **10d**, 0.75 g (81%) of acid **10e** as an off-white solid, mp 214–215 °C dec (with gas evolution). Crystallization from ethanol yields a colorless analytical sample: mp 215–215.5 °C dec (with gas evolution); IR ~3500 (br), 1710, 1370, 1280 (br), 1220 cm^{-1}; ^1H NMR ($CDCl_3$ + Me_2SO-d_6) δ 7.3 (m, 13 H, aromatic), 7.8 (m, 2 H, ortho protons, 6-phenyl), 9.09 (br s, 1 H, CO_2H); mass spectrum *m/e* (% base) 352 (12.7) M^+, 308 (90.3), 307 (100), 178 (99.0). M^+, calcd for $C_{23}H_{16}N_2O_2$: 352.12. Found: 352.15.

Decarboxylation of 10e. Preparation of 3,4,6-Triphenylpyridazine (10f). In a 25-mL round-bottom flask fitted with a $CaCl_2$ drying tube is placed 300 mg (0.855 mmol) of pyridazinecarboxylic acid **10e**. The flask is immersed in a 220 °C oil bath for 30 min. As the sample melts, vigorous gas evolution is observed. The yield of slightly yellow solid, mp 170–175 °C, is 0.26 g (99%). Recrystallization from ethanol affords colorless material: mp 170–172 °C (lit.[5] 171–172 °C); IR (KBr) 1580, 1560, 1395 cm^{-1}; ^1H NMR δ 7.2 (br m, 13 H, aromatic), 7.59 (s, 1 H, pyridazine ring H), 7.97 (m, 2 H, ortho protons, 6-phenyl ring); mass spectrum *m/e* (% base) 309 (54.0), 308 (99.6), 307 (100), 178 (99.4).

Preparation of Benzilacetylacetone Azine (11). A mixture of 4.5 g (0.02 mol) of benzil monohydrazone and 4.0 g (0.04 mol) of acetylacetone (**8c**) is heated at reflux in ethanol containing 100 mg of benzoic acid for 60 h. On cooling an orange solid precipitates which is isolated by filtration, yielding 4.48 g (73%) of **11**, mp 122–159 °C. ^1H NMR indicates that this is a 1.5:1 mixture of two isomers, A and B. Careful fractional crystallization from ethanol or carbon tetrachloride allows the isolation of both isomers. Isomer A: light yellow plates, mp 161–162 °C; IR ($CHCl_3$) 3100 (br), 3010, 1635, 1565, 1490 cm^{-1}; ^1H NMR δ 1.90 (s, 3 H, CH_3C=C), 1.99 (s, 3 H, $COCH_3$), 5.11 (s, 1 H, C=CH), 7.3 (m, 8 H, aromatic), 7.8 (m, 2 H, aromatic ortho to C=O), 12.91 (br s, 1 H, NH). Anal. Calcd for $C_{19}H_{18}N_2O_2$: C, 74.49; H, 5.92. Found: C, 74.25; H, 5.90. Isomer B: orange-yellow chunky crystals, mp 146–149 °C; IR ($CHCl_3$) 3100 (br), 3020, 1675, 1620, 1570 cm^{-1}; ^1H NMR δ 1.88 (s, 3 H, CH_3C=C), 2.18 (s, 3 H, CH_3C=O), 5.00 (s, 1 H, C=CH), 7.3 (m, 8 H, aromatic), 7.8 (m, 2 H, aromatic ortho to C=O), 13.47 (br s, 1 H, NH). Either pure isomer is converted to the equilibrium mixture (~1.5:1, A:B) on heating in ethanol for several hours.

Cyclization of 11. Preparation of 3,4-Diphenyl-5-acetyl-6-methylpyridazine (12) and 3,4-Diphenyl-6-methylpyridazine (10c). To a gently boiling solution of 115 mg (~1.78 mmol) of potassium hydroxide in 15 mL of ethanol is added 0.46 g (1.50 mmol) of azine **11** (mixture of isomers). A deep red color develops which fades rapidly. After heating for 5 min, the bulk of the ethanol is removed in vacuo and the residue partitioned between ether and 5% NaOH. The layers are separated, the organic layer thoroughly extracted with 5% HCl, and the acid extracts reserved. The ether layer is dried (Na_2SO_4) and evaporated in vacuo to yield 50 mg (12%) of **12** as a pale yellow solid. Purification by sublimation (140 °C, 1 mm) and recrystallization (CH_2Cl_2/heptane) yields an analytical sample: mp 131.5–132.5 °C; IR (KBr) 1695, 1440, 1375 cm^{-1}; ^1H NMR δ 1.86 (s, 3 H, CH_3C=O), 2.62 (s, 3 H, ring CH_3), 7.2 (br s, 10 H, aromatic); mass spectrum *m/e* (% base) 288 (87.9) M^+, 287 (100), 245 (75.1), 178 (28.3). Anal. Calcd for $C_{19}H_{16}N_2O$: C, 79.14; H, 5.59. Found: C, 79.17; H, 5.86.

Basification of the acid extracts (above) and extraction with methylene chloride yields, after drying (Na_2SO_4) and removal of the CH_2Cl_2 in vacuo, 0.29 g (79%) of **10c**, identical in all respects with the material prepared by decarboxylation of **10b**.

Registry No.—**7**, 5344-88-7; **8a**, 141-97-9; **8b**, 94-02-0; **8c**, 105-45-3; **9a**, 62139-81-5; **10a**, 62139-82-6; **10b**, 62139-83-7; **10c**, 13340-82-4; **10d**, 62139-84-8; **10e**, 62139-85-9; **10f**, 2272-58-4; **11a**, 62139-86-0; **11b**, 62139-87-1; **12**, 62139-88-2.

References and Notes

(1) National Science Foundation Predoctoral Fellow, 1974–1977.
(2) P. Schmidt and J. Druey, *Helv. Chim. Acta*, **37**, 134 (1954).
(3) R. K. Gupta and M. V. George, *Indian J. Chem.*, **10**, 875 (1972); *Chem. Abstr.*, **78**, 97585r (1973).
(4) E. E. Schweizer, C. S. Kim, C. S. Labaw, and W. P. Murray, *J. Chem. Soc., Chem. Commun.*, 7 (1973).
(5) T. Wagner-Jauregg, *Synthesis*, 349 (1976).
(6) N. Obata and I. Moritani, *Bull. Chem. Soc. Jpn.*, **39**, 2250 (1966).
(7) T. Nakagome and R. N. Castle, *J. Heterocycl. Chem.*, **5**, 379 (1968).
(8) T. W. J. Taylor, N. H. Callow, and C. R. W. Francis, *J. Chem. Soc.*, 257 (1939).

2-Phenylthio-2-cyclopentenone, a Useful Synthon for 2,3-Disubstituted Cyclopentanones. Synthesis of *dl*-Methyl Dehydrojasmonate

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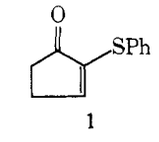
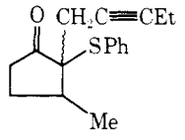
Recently, there has been an increasing amount of research devoted to the development of useful synthetic routes to 2,3-disubstituted cyclopentanones, mainly because of the interest in the pharmacologically important prostaglandins. However, most of the published routes either use as starting material the commercially expensive 2-cyclopentenone[1] or 2-alkylated 2-cyclopentenones,[2] which are not themselves readily available. 2-Phenylthio-2-cyclopentenone (**1**) is expected to be a very useful synthon for the preparation of several 2,3-disubstituted cyclopentanones, since it bears the adequate functionalities for conjugate alkylations,[1,3] or Michael-type additions followed by a regiospecifically directed[4] alkylation at the 2 position ensured by the thioether function. The described[5] syntheses of **1** are too laborious and expensive; therefore, a facile preparation was sought.

Oki[6] described the formation of 2-methylthio-2-cyclohexenone by the reaction of phenylsulfenyl chloride with 2-methylthiocyclohexanone, but did not exploit the preparative aspects of this interesting transformation. We reasoned that, since 2-phenylthiocyclopentanone is expected[7] to be the primary product from the reaction of phenylsulfenyl chloride with cyclopentanone, **1** could be prepared in a single step by reaction of the ketone with an excess of the sulfenyl chloride. Indeed, treatment of cyclopentanone with phenylsulfenyl chloride in dry acetonitrile, followed by chromatography on silica gel, afforded 55–65% yields of the pure unsaturated ketone **1**, based on cyclopentanone. The method[8] is quite economical, since the diphenyl disulfide formed in the reaction can be recovered and reconverted into phenylsulfenyl chloride.

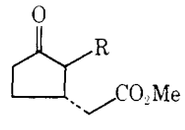
Initial alkylation experiments of **1** with *n*-amylmagnesium

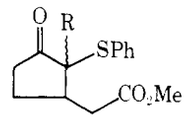


1



2





3, R = CH_2CH=CHEt-*cis*
4, R = CH_2C≡CEt
5, R = H
6, R = CH_2C≡CEt

bromide without copper salt catalysis resulted in about a 45% yield of 1,4-addition, as evidenced by spectroscopic analyses of the reaction products. This large proportion of conjugate addition may be possibly caused by the inductive or steric effects of the 2-phenylthioether group.

On the other hand, alkylation of **1** with lithium dimethylcuprate followed by quenching of the enolate with 2-pentynyl bromide, according to Coates' procedure,[3a] afforded, after preparative TLC, good yields of the ketone **2** as an epimeric mixture. No 5-alkylated ketone could be detected among the minor products, indicating that enolate equilibration[1,4] does not take place under the reaction conditions.

To further test the synthetic potentialities of the ketone **1**,