Studies on Pyrimidine Derivatives. XXIV.1) Synthesis of 3-Substituted 1,2,4-Triazines by Nucleophilic Substitution

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(Received June 15, 1981)

The potassium permanganate oxidation of 3-methylthio-5,6-diphenyl-as-triazine in the presence of a phase-transfer catalyst afforded 3-methylsulfonyl-5,6-diphenyl-as-triazine. The 3-sulfonyl-as-triazine readily reacted not only with active methylene compounds but also with methyl or methylene ketones under basic conditions, and 5,6-diphenyl-as-triazines containing a functionalized carbon substituent at the 3-position were obtained. Similarly, 2-substituted 4,6-dimethylpyrimidines were synthesized by the nucleophilic substitution of 4,6-dimethyl-2-phenylsulfonylpyrimidine with various ketones.

Keywords—nucleophilic substitution; active methylene compounds; 3-chloro-5,6-diphenyl-1,2,4-triazine; 3-methylsulfonyl-5,6-diphenyl-1,2,4-triazine; 3-acylmethyl-5,6-diphenyl-1,2,4-triazines; 4,6-dimethyl-2-phenylsulfonylpyrimidine; 2-acylmethyl-4,6-dimethylpyrimidines

Investigations on pyrimidine derivatives containing a strongly electronegative group at the 4-position are not well advanced. For example, the synthesis of 4-nitropyrimidines has not yet been achieved, and the 4-cyanopyrimidines readily transform to the corresponding 4-methoxyl derivatives,2) when they are allowed to stand in methanol under basic conditions. 1,2,4-Triazine (as-triazine) is regarded as a model of such pyrimidines owing to the electronic effects of the additional ring nitrogen atom. Furthermore, among various six-membered monocyclic N-heteroaromatics, as-triazines form a relatively less explored family. In particular, useful results were not obtained in the nucleophilic substitution of as-triazine derivatives, although the synthesis of as-triazines by ring-closure reactions is being actively investigated by several groups.3-6)

Our interest was focussed on the chemistry of as-triazine derivatives, from the above points of view. The present paper deals with carbon-carbon bond formation at the 3-position of as-triazine by nucleophilic substitution, in comparison with the same type of reaction at the 2-position of pyrimidine.

Firstly, in order to determine the chemical properties of 3-chloro-5,6-diphenyl-as-triazine (2) unambiguously, some conflicting results in the literature7) were checked as follows. This compound (2) was already obtained by treatment of 3-oxo-5,6-diphenyl-2,3-dihydro-as-triazine (1)8) with phosphoryl chloride in good yield. The chloride (2), mp 158—159°C, was also reported to be convertible into the 3-ethoxy derivative monohydrate (3a'), mp 221—222°C, by heating an ethanolic solution of 2 in the absence of bases. Since the yield of 3a' was unspecified, we reinvestigated the above experiment and obtained the product having the reported melting point in 70% yield. However, after the product had been heated at 100°C for several days under reduced pressure, the resultant compound was identical with 1. In contrast, the reaction of 2 with a calculated amount of sodium ethoxide in hot ethanol gave 3-ethoxy-5,6-diphenyl-as-triazine (3a), C17H12N4O, mp 76—77°C. When excess sodium ethoxide was used, 2 was transformed into 1, and 3a was not obtained. In addition to this, 3a was changed to 1 under the same conditions. Accordingly, it is suggested that alkoxy groups at the 3-position of as-triazine are not very resistant to both acidic and basic conditions and are transformed into the corresponding 3-oxo compounds. In connection with the above, Sasaki et al.9)
obtained the 3-methoxyl and 3-phenoxy derivatives from 2 by the reaction with a limited amount of the corresponding sodium alkoxide.

The compound (2), as well as many N-heteroaromatics containing active halogen atoms, reacted with various amines as shown in Chart 1. In the case of hydrazine hydrate, it was reported\(^7\) that the reaction in pyridine afforded 3-hydradino-5,6-diphenyl-as-triazine (3d), mp 171—173°C, but the reaction conditions were not described in detail. However, the use of an equimolecular amount of hydrazine hydrate in pyridine gave \(N,N'\)-bis(5,6-diphenyl-3-as-triazinyl)hydrazine (5), mp 238°C (dec.), as a sole product. When 2 was treated with excess hydrazine hydrate in methanol, the desired compound (3d) was obtained in 48% yield.

![Chemical structure diagram]

Secondly, the introduction of a functionalized carbon substituent into the 3-position was investigated. Since the reaction of 2 with potassium cyanide or ethyl cyanoacetate failed to give the desired compound, 2 was transformed into 5,6-diphenyl-3-(p-toluenesulfonyl)-as-triazine (4), mp 162.5—163°C, in 74% yield by treatment with sodium \(p\)-toluenesulfinate in \(N,N\)-dimethylformamide. This product (4) seemed to be more reactive than 2. For example, 4 reacted with sodium ethoxide, \(n\)-butylamine, aniline, and hydrazine hydrate to give the corresponding 3-substituted as-triazine (3a—d) in better yields than those from 2. Treatment of 4 with potassium cyanide in \(N,N\)-dimethylformamide afforded 3-cyano-5,6-diphenyl-as-triazine (6), mp 156—157°C, in 75% yield. When 4 was heated with ethyl cyanoacetate in the presence of sodium amide in benzene, ethyl \(\alpha\)-(5,6-diphenyl-3-as-triazinyl)cyanoacetate (7), mp 235°C (dec.), was obtained in 56% yield. In contrast, the reaction of 4 with ethyl acetoacetate or ethyl benzoylecetate under conditions similar to the above
afforded the same product, ethyl 5,6-diphenyl-3-az-triazinylacetate \((8)_{\text{mp 123—124.5°C}}\), which was probably formed from the \(\beta\)-keto-esters \((9\text{a, b})_{\text{with the loss of an acyl group. Since the reaction of 4 with monoketones, such as acetophenone and cyclohexanone, under similar conditions failed, leaving groups other than the \(\beta\)-toluenesulfonyl group were examined, and the methylsulfonyl group was concluded to be better than the \(\beta\)-toluenesulfonyl group. 3-Methylthio-5,6-diphenyl-az-triazine \((10)_{\text{easily obtained by the condensation of benzil and 5-methylthiosemicarbazide, was oxidized with potassium permanganate in the presence of a phase-transfer catalyst, tetra-n-butylammonium bromide, to give 3-methylsulfonyl-5,6-diphenyl-az-triazine \((11)_{\text{mp 139—140°C, in 75% yield. This compound (11) smoothly reacted not only with potassium cyanide, ethyl cyanacetate, and ethyl acetoacetate, but also with acetophenone and cyclohexanone. Namely, the reaction of 11 with cyclohexanone in tetrahydrofuran in the presence of sodium hydride gave 2-(5,6-diphenyl-3-az-triazinyl)cyclohexanone \((12)_{\text{mp 172—173°C, in 53% yield. Although the reaction of 11 with an equimolecular amount of acetophenone in the presence of sodium hydride resulted in the formation of bis-(5,6-diphenyl-3-az-triazinyl)methane \((14)_{\text{mp 175°C (dec.), the use of excess acetophenone gave 5,6-diphenyl-3-az-triazinylmethyl phenyl ketone \((13)_{\text{mp 130—132°C, as expected. The spectral data of all the products are in good agreement with their structures illustrated in Chart 1, except for 12 and 13. In the cases of 12 and 13, the existence of keto-enol tautomerism due to the presence of the carbonyl group is suggested by their nuclear magnetic resonance \((^1\text{H-NMR})_{\text{spectra. However, the tautomerism was not studied in detail in this work, because the same type of tautomerism is already well known in the corresponding quinoline\textsuperscript{11} and pyrimidine derivatives.\textsuperscript{12}\) }}

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{N} & \quad \text{N}^+ \\
\text{CH}_2\text{N}^{+}\text{SO}_2\text{Ph} & \rightarrow \quad \text{CH}_3 \\
15 & \quad 16: R=\text{CH}_2\text{CN} \\
17: R=\text{CH}_2\text{COOEt} & \quad 18: R=\text{CH}_2\text{COOPh} \\
19: R=\text{O} & \\
\end{align*}
\]

Chart 2

Finally, the nucleophilic substitution of 2-phenylsulfonyl-4,6-dimethylpyrimidine \((15)_{\text{was compared with that of 4 and 11. As shown in Chart 2, various 2-substituted pyrimidines \((16—19)_{\text{were synthesized by the reaction of 15 with carbonyl compounds such as ethyl cyanacetate, acetone, acetophenone and cyclohexanone under basic conditions. These products were identical with authentic samples prepared by known methods.\textsuperscript{12,14—16} \)}

Although the reason for the high reactivity of 15 toward the monoketones described above is not clear at present, the use of an appropriate sulfonyl group as a leaving group is concluded to be an effective procedure for the introduction of functionalized carbon side chains into the 3-position of az-triazines and the 2-position of pyrimidines.

**Experimental**

All melting points and boiling points are uncorrected. Infrared (IR) spectra were measured with a JASCO IRA-1 spectrometer. Mass spectra (MS) were taken with a Hitachi M-52G spectrometer. \(^1\text{H-NMR} \) spectra were taken at 60 MHz with Hitachi-Perkin-Elmer R-20 and JEOL JNM-PMX60 spectrometers. Chemical shifts are expressed as ppm downfield from tetramethylsilane (TMS) as an internal standard. The following abbreviations are used: s = singlet, t = triplet, q = quartet, m = multiplet, and b = broad. The analytical data for the products are shown in Table I.

**The Reaction of 3-Chloro-5,6-diphenyl-az-triazine (2) with Ethanol**—A solution of 2 (1.3 g, 5 mmol) in EtOH (100 ml) was heated under reflux for 48 h. The reaction mixture was concentrated under reduced pressure to give 0.9 g (70%) of 3-oxo-5,6-diphenyl-2,3-dihydro-az-triazine \((1)_{\text{mp 221—223°C (lit.\textsuperscript{8} mp}}

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224—225°C), as pale yellow prisms. IR spectral comparison showed this compound to be identical with an authentic sample.9

5,6-Diphenyl-3-(p-toluenesulfonyl)-as-triazine (4) —— A mixture of 2 (5.0 g, 20 mmol) and sodium p-toluenesulfonate (6.0 g, 24 mmol) in DMF (50 ml) was heated at 50—60°C for 1.5 h with stirring. The reaction mixture was poured into water and the precipitate was collected by filtration and washed with H2O. Recrystallization from MeOH gave 5.60 g (74%) of 4, mp 162.5—163°C, as pale yellow needles. IR νmax cm⁻¹: 1155, 1355.

3-Methylsulfonyl-5,6-diphenyl-as-triazine (11) —— A solution of KMnO₄ (4.6 g, 30 mmol) in H₂O (150 ml) was added to a solution of 3-methylthio-5,6-diphenyl-as-triazine (10) (4.2 g, 15 mmol) [prepared according to the procedure of Paudler et al.4], tetra-n-butylammonium bromide (0.5 g), and AcOH (30 ml) in benzene (100 ml). The mixture was stirred at room temperature for 16 h. A sat. NaHSO₃ solution was added to the mixture until the purple color disappeared and the colorless solution was neutralized with solid K₂CO₃. The benzene layer was separated and dried over Na₂SO₄. After removal of the solvent, the residue was recrystallized from AcOEt-hexane to give 3.5 g (75%) of 11, mp 139—140°C, as pale yellow prisms. ¹H-NMR (CDCl₃) 3.50 (3H, s), 7.08—7.75 (10H, m).

3-Ethoxy-5,6-diphenyl-as-triazine (3a) —— i) A solution of NaOEt—EtOH [prepared from metallic sodium (0.345 g, 0.015 g-atom) and abs. EtOH (150 ml)] was added to a solution of 2 (4.02 g, 15 mmol) in abs. EtOH (50 ml), and the mixture was refluxed for 0.5 h. The precipitate (NaCl) was filtered off and the filtrate was concentrated to dryness in vacuo. The residue was neutralized with 3x HCl and extracted with CHCl₃. The CHCl₃ solution was dried over Na₂SO₄ and the solvent was removed. The residue was recrystallized from hexane to give 2.7 g (66%) of 3a, mp 76—77°C, as pale yellow needles. ¹H-NMR (CDCl₃) 1.54 (3H, t, J = 7 Hz), 4.71 (2H, q, J = 7 Hz), 7.20—7.70 (10H, m).

ii) A solution of NaOEt—EtOH [prepared from metallic sodium (0.345 g, 0.015 g-atom) and abs. EtOH (150 ml)] was added to a solution of 4 (5.8 g, 15 mmol) in abs. EtOH (50 ml), and the mixture was stirred at room temperature for 3 h. The reaction mixture was treated according to the procedure used above to give 3.4 g (83%) of 3a, mp 76—77°C, as pale yellow needles. This compound was identical with the sample obtained above.

3-n-Butylamino-5,6-diphenyl-as-triazine (3b) —— i) A mixture of 2 (0.53 g, 2 mmol) and n-butylamine (0.5 g, 7 mmol) in dry benzene (30 ml) was refluxed for 0.5 h. The precipitate was collected by filtration and washed with H₂O. The crude product was recrystallized from EtOH to give 0.43 g of 3b, mp 131—132°C, as yellow needles. The benzene layer was washed with 3x NaOH and H₂O and dried over K₂CO₃. After removal of the solvent, the residue was recrystallized from EtOH to give 0.07 g of 3b, mp 131—132°C. The total yield was 0.5 g (82%). IR νmax cm⁻¹: 3230. ¹H-NMR (CDCl₃) 0.97 (3H, t, J = 6 Hz), 1.20—1.72 (4H, m), 3.60 (2H, q, J = 6 Hz), 5.60—6.10 (1H, b), 7.10—7.70 (10H, m).

ii) A mixture of 4 (0.77 g, 2 mmol) and n-butylamine (0.5 g, 7 mmol) in dry benzene (30 ml) was refluxed for 0.5 h. The reaction mixture was treated according to the procedure used above to give 0.56 g (93%) of 3b, mp 131—132°C, as yellow needles. This compound was identical with the sample obtained above.

3-Anilino-5,6-diphenyl-as-triazine (3c) —— i) A mixture of 2 (0.53 g, 2 mmol) and aniline (0.37 g, 4 mmol) in dry xylene (30 ml) was refluxed for 10 h, then the reaction mixture was concentrated to dryness in vacuo. The residue was chromatographed on an alumina column. The first eluate with benzene gave 0.13 g (21%) of 3c, mp 229—230°C (lit.19 mp 230°C), as pale yellow needles (MeOH). The second elute with benzene gave 0.38 g (68%) of starting material (2).

ii) A mixture of 4 (0.77 g, 2 mmol) and aniline (0.37 g, 4 mmol) in dry benzene (30 ml) was refluxed for 10 h. The reaction mixture was treated according to the procedure used above to give 0.4 g (60%) of 3c, mp 230°C, as pale yellow needles. This compound was identical with the sample obtained above.

3-Hydrazino-5,6-diphenyl-as-triazine (3d) —— i) A mixture of 2 (0.53 g, 2 mmol) and hydrazine hydrate (18 ml) was heated at 80°C for 2 h with stirring. The precipitate was collected by filtration and washed with H₂O. Recrystallization from MeOH gave 0.25 g (48%) of 3d, mp 171—173°C (lit.7 mp 171—173°C), as yellow needles.

ii) A mixture of 4 (1.16 g, 3 mmol) and hydrazine hydrate (0.3 g, 6 mmol) in MeOH (30 ml) was refluxed for 1 h. The reaction mixture was concentrated to dryness in vacuo. H₂O (10 ml) was added to the residue and the solution was made alkaline with K₂CO₃. The precipitate was collected by filtration and recrystallized from EtOH to give 0.5 g (64%) of 3d, mp 172—173°C, as yellow needles. This compound was identical with the sample obtained above.

N,N'-Bis(5,6-diphenyl-3-as-triazinyl)hydrazine (5) —— A mixture of 2 (0.8 g, 3 mmol) and hydrazine hydrate (0.2 g, 4 mmol) in pyridine (5 ml) was refluxed for 1 h. The reaction mixture was poured into H₂O, and the precipitate was collected by filtration. Recrystallization from EtOH gave 0.28 g (38%) of 5, mp 238°C (dec.), as yellow needles. IR νmax cm⁻¹: 3220. ¹H-NMR (DMSO) 7.40 (s), 15.10 (s); the integrated ratio of the former signal and the latter signal was 10:1.

3-Cyano-5,6-diphenyl-as-triazine (6) —— i) A mixture of 4 (1.18 g, 3 mmol) and KCN (0.4 g, 6 mmol) in DMF (30 ml) was stirred at room temperature for 45 min. The reaction mixture was concentrated to dryness in vacuo, and a small amount of H₂O was added to the residue. The aqueous solution was extracted with CHCl₃, and the extract was dried over K₂CO₃. After removal of the solvent, the residue was purified
by passing it through an alumina column with benzene. Recrystallization from Et₂O–hexane gave 0.58 g
(75%) of 6, mp 156—157°C (lit. 16 mp 154—155°C), as pale yellow needles.

ii) Compound 6 was also obtained from 11 (0.62 g, 2 mmol) and KCN (0.15 g, 2.3 mmol) according to
the procedure described above as pale yellow needles, mp 154—155°C. The yield was 0.3 g (58%).
This compound was identical with the sample obtained above.

**Ethyl α-(5,6-Diphenyl-3-az-triazinyl)cyaanoacetate (7) — i)** NaNH₂ (0.35 g, 9 mmol) was added to
a solution of ethyl cyaanoacetate (1.08 g, 9 mmol) in dry benzene (20 ml) and the mixture was stirred at room
temperature for 3 h. Compound (4) (1.16 g, 3 mmol) was added thereto and the mixture was refluxed for
1 h. The reaction mixture was concentrated to dryness in vacuo, and a small amount of H₂O was added to the
residue. The resulting precipitate was collected by filtration and recrystallized from AcOEt to give
0.58 g (56%) of 7, mp 235°C (dec.), as pale yellow needles. IR νmax cm⁻¹: 1660, 2200. H-NMR (CDCl₃): 1.47
(3H, t, J = 7 Hz), 2.40 (1H, s), 4.46 (2H, q, J = 7 Hz), 7.70—7.80 (10H, m).

ii) Compound 7 was obtained from 4 (0.94 g, 3 mmol), ethyl cyaanoacetate (0.46 g, 4 mmol), and NaH
(0.25 g, 5 mmol) using dry THF as a solvent according to the procedure described above, as pale yellow needles,
mp 154—155°C. The yield was 0.85 g (83%). This compound was identical with the sample obtained above.

**Ethyl 5,6-Diphenyl-3-az-triazinylacetate (8) — i)** NaNH₂ (0.35 g, 9 mmol) was added to a solution of
ethyl acetocacetate (1.17 g, 9 mmol) in dry benzene (20 ml), and the mixture was stirred at room temperature
for 3 h. A small amount of H₂O was added to the reaction mixture, and then the benzene phase was separated,
and dried over K₂CO₃. After removal of the solvent, the residue was recrystallized from Et₂O–hexane to give
0.5 g (52%) of 8, mp 123—124.5°C, as pale yellow plates. IR νmax cm⁻¹: 1730. H-NMR (CDCl₃): 1.45
(3H, t, J = 7 Hz), 4.30—4.80 (4H, m), 7.40—8.10 (10H, m).

ii) Compound 8 was obtained from 4 (1.16 g, 3 mmol), ethyl benzoyletacetate (1.73 g, 9 mmol) and
NaNH₂ (0.35 g, 9 mmol) according to the procedure described above, as pale yellow plates, mp 123—124.5°C.
The yield was 0.34 g (34%). This compound was identical with the sample obtained above.

iii) NaH (0.25 g, 5 mmol) was added to a solution of ethyl acetocacetate (0.48 g, 4 mmol) in dry THF
(20 ml) and the mixture was stirred at room temperature for 1 h. Compound (11) (0.94 g, 3 mmol) was
added thereto and the mixture was refluxed for 3 h. The reaction mixture was concentrated to dryness
in vacuo and a small amount of H₂O was added to the residue. The aqueous solution was extracted with
CHCl₃, and the extract was dried over K₂CO₃. After removal of the solvent, the residue was purified by
passing it through a silica gel column with benzene–AcOEt (20:1). Recrystallization from Et₂O–hexane
gave 0.55 g (58%) of 8, mp 124—125.5°C, as pale yellow plates. This compound was identical with
the sample obtained above.

**2-(5,6-Diphenyl-3-az-triazinyl)cyclohexanone (12) —** Following the procedure for the preparation of 8,
treatment of 11 (0.94 g, 3 mmol) in dry THF (30 ml) with NaH (0.84 g, 17 mmol) and cyclohexanone (1.47 g,
15 mmol) gave a crude product which was purified by passing it through a silica gel column with benzene.
Recrystallization from AcOEt gave 0.52 g (53%) of 12, mp 172—173°C, as pale yellow needles. IR νmax
cm⁻¹: 1625, 1715. H-NMR (CDCl₃): 1.20—2.25 (m), 2.25—3.31 (m), 6.87—8.18 (m), the proton ratio, from
low to high field, was 5: 2: 2.

5,6-Diphenyl-3-az-triazinylmethyl Phenyl Ketone (13) — Following the procedure for the preparation
of 8, treatment of 11 (0.94 g, 3 mmol) in dry THF (30 ml) with NaH (0.84 g, 17 mmol) and acetophenone
(1.62 g, 15 mmol) gave a crude product which was purified by passing it through a silica gel column with benzene–
AcOEt (20:1). Recrystallization from AcOEt–hexane gave 0.18 g (17%) of 13, mp 130—132°C, as brown prisms.
IR νmax cm⁻¹: 1630, 1690. H-NMR (CDCl₃): 6.50 (1H, s), 7.05—7.74 (13H, m), 7.75—
8.20 (2H, m), 13.21—14.10 (1H, b).

**Bis(5,6-diphenyl-3-az-triazinyl)methane (14) —** Following the procedure for the preparation of 8,
treatment of 11 (0.94 g, 3 mmol) in dry THF (20 ml) with NaH (0.25 g, 5 mmol) and acetophenone (0.5 g,
4.2 mmol) gave a crude product which was purified by passing it through a silica gel column with benzene–
AcOEt (9:1). Recrystallization from acetone–Et₂O gave 0.2 g (27%) of 14, mp 175°C (dec.), as yellow prisms.
H-NMR (CDCl₃): 5.20 (s), 7.22—7.78 (m), the integrated ratio of the former signal and the latter
signal was 10: 1. MS m/e: 478 (M⁺).

**Ethyl α-(4,6-Dimethyl-2-pyrimidinyl)cyaanoacetate (16) —** NaH (0.17 g, 7 mmol) was added to a solution of
ethyl cyaanoacetate (0.68 g, 6 mmol) in dry THF (20 ml), and the mixture was stirred at room temperature
for 10 min. 4,6-Dimethyl-2-phenylsulfonylpyrimidine (15) (0.5 g, 2 mmol) was added thereto and the
mixture was heated under reflux for 1 h with stirring. A small amount of H₂O was added, and the mixture
was concentrated under reduced pressure to give the residue. The residue was acidified with 10% HCl and
extracted with CHCl₃. After removal of the solvent, this residue was purified by passing it through an
alumina column with AcOEt. Recrystallization from benzene–hexane gave 0.27 g (62%) of 16, mp 187—
189°C (lit. 17 mp 192−193.5°C), as yellow prisms. This compound was identical with the sample prepared by
an alternative route.14

**4,6-Dimethyl-2-pyrimidinylmethyl Methyl Ketone (17) —** A mixture of 15 (0.5 g, 2 mmol), acetone
(2 ml) and NaH (0.1 g, 4 mmol) in dry THF (20 ml) was heated at 40°C for 1 h with stirring, and then 10%
HCl (10 ml) was added thereto. The mixture was concentrated to one-third of its original volume under reduced pressure. The residue was washed with Et₂O, made alkaline with NaHCO₃, and extracted with Et₂O. After removal of the solvent, the residual oil was distilled under reduced pressure to give 0.09 g (25%) of 17, bp 91—93° C (3 mmHg), [lit.¹⁹] bp 95° C (4 mmHg). This compound was identical with the sample prepared by an alternative route.¹⁵

4,6-Dimethyl-2-pyrimidinylmethyl Phenyl Ketone (18) — A mixture of 15 (0.5 g, 2 mmol), acetophenone (0.36 g, 3 mmol), and NaH (0.1 g, 4 mmol) in dry THF (20 ml) was refluxed for 1 h with stirring. The reaction mixture was worked up as in the case of 17 to give 0.145 g (32%) of 18, bp 150—155° C (2 mmHg); mp 76—77° C (lit.,¹⁶) mp 74—75.5° C, as pale yellow prisms. This compound was identical with the sample prepared by an alternative route.¹⁶

2-(4,6-Dimethyl-2-pyrimidinyl)cyclohexanone (19) — A mixture of 15 (0.5 g, 2 mmol), cyclohexanone (0.29 g, 2 mmol), and NaH (0.1 g, 4 mmol) in dry THF (20 ml) was refluxed for 1 h with stirring. The reaction mixture was worked up as in the case of 17 to give 0.125 g (35%) of 19, bp 120° C (2 mmHg); mp 68—69° C (lit.,¹⁶a) mp 68—69° C, as pale yellow prisms. This compound was identical with the sample prepared by an alternative route.¹⁶a

Table 1. Analytical Data for the Products

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Acknowledgement The authors are grateful to the staff of the Central Analysis Room of this Institute for elemental analysis and measurements of ¹H-NMR spectra and MS.

References and Notes

7) P.V. Laakso, R. Robinson, and H.P. Vandrewala, Tetrahedron, 1, 103 (1957).