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UNEQUIVOCAL SYNTHESIS OF PHENACYLIDENEANILINE FROM SILYL ENOL ETHERS AND NITROSOBENZENE AND ONE-POT CYCLOADDITION REACTIONS OF THE RELATED ANILS[1)]

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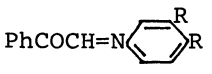
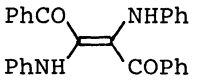
Phenacylideneaniline was formed by Et_3N-catalyzed elimination reaction of the hydroxylamine obtained from silyl enol ether 5a and nitrosobenzene (6). By this method, one-pot procedure was possible for cycloaddition reactions of the related anils. From these reactions, it was revealed that 6 reacted efficiently with a silyl enol ether having a π-donating substituent.

Phenylglyoxal anils had long been known to be prepared easily by means of a conventional condensation reaction.[2a)] In 1952, Yates first reported the reaction of phenylglyoxal with aniline to form an anil 1 (R=H).[2b)] Later, Indian chemists indicated the same reaction to be successful.[2c)] Alternatively, the elimination reaction of *N*-tosylphenacylamine was also attempted under basic conditions.[2d)] However, these efforts were all misleading; the products actually isolated were a dimer 2, an alkoxy-amine 3 and a diamine 4. The unexpected reactivity of the anil caused the further reaction of once formed anil under the conditions employed. It is only very recently that the definite formation of the anil was recognized; Proctor demonstrated that demethanolation of 3 (R=Cl, R'=Me) with Pd on charcoal gave rise to the anil 1 (R=Cl).[2a)] Nevertheless, phenacylideneaniline (1, R=H) itself has not yet been synthesized.



1



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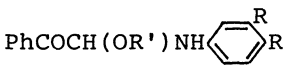

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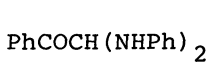

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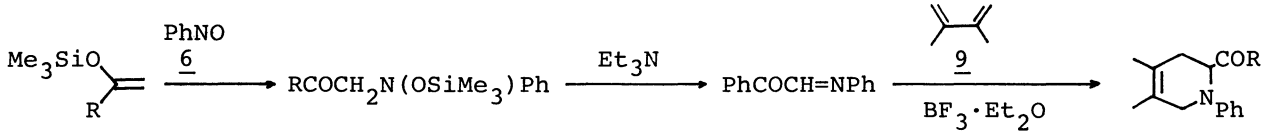
We have recently found that the silyl enol ether 5e of 2-acetylfuran reacted with nitrosobenzene (6) to give a hydroxylamine 7e.[3)] It is reasonable to consider such a hydroxylamine to be a good precursor leading to this interesting class of compounds, possibly through β-elimination. This is indeed the case.

The silyl enol ether 5a of acetophenone readily reacted with 6 at room temperature for 5 h to give 7a in 80% yield.[4)] After several unsuccessful attempts (*i.e.*, $ZnCl_2$ or Pd/C (benzene, reflux), no reaction; HCl, only desilylation; lithium diisopropylamide, formation of the known dimer 2), triethylamine was found to be a mild and effective reagent for the desired elimination reaction. When a solution of 7a in dry $CHCl_3$ was treated with equimolar amount of triethylamine at room

temperature for 1 day, practically pure yellow viscous oil was obtained nearly quantitatively after evaporation of the solvent. The spectral data of this compound were compatible with the monomeric structure of the anil 1 (R=H): the IR spectrum showed absorptions at 1650 and 1580 cm^{-1} due to C=O and C=N respectively and no NH absorptions around 3200-3400 cm^{-1}. The ^1H NMR spectrum showed an aldimine proton at δ 8.10. The mass spectrum revealed rational peaks at m/e 209 (M^+, 17%), 104 (PhN=CH, 100%) and 77 (Ph, 77%). These characteristics are in good agreement with those of the dichloro derivative 1 (R=Cl).[2a] Furthermore, the assigned anil structure was unambiguously affirmed by the chemical reactivity in its cycloaddition reaction with 2,3-dimethylbutadiene (9); treatment of the obtained oil with 9 in the presence of $BF_3 \cdot Et_2O$ at room temperature gave a [4+2] cycloadduct 8a (see Table 1).[5] Thus the present reaction provides a method for the unequivocal synthesis of 1.



5a R=Ph; 5b R=2-furyl

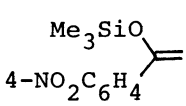
7a R=Ph; 7e R=2-furyl

1 (R=H)

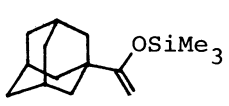
8a R=Ph

As the reagent (Et_3N) and the elimination product (Me_3SiOH) in this experiment are easily removed, a sequence of the above described reaction is possible to carry out in one-pot procedure starting from silyl enol ethers. Firstly, a solution of a silyl enol ether (1 mmol) and 6 (1 mmol) in $CHCl_3$ (2 ml) was stirred at room temperature for 5-8 h, and secondly, Et_3N (1 mmol) was added to this solution and stirring was continued for 1 day. Finally, after evaporation of the volatile materials *in vacuo*, to the residue were added CH_2Cl_2 (2 ml), 9 (1.2 mmol) and $BF_3 \cdot Et_2O$ (0.05 ml) successively, and the solution was stirred at room temperature for 1 h. The usual work up and purification on a silica gel column gave the product. The results are summarized in Table 1.

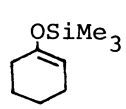
Considering the three steps-conversion, the yields in entries 1-5 seem to be moderate. However, some silyl enol ethers (entry 6 and 7) gave less satisfactory results. This is apparently attributed to the first step to form a hydroxylamine; 6 was observed not to react cleanly with 5f and 5g. Moreover, 6 did not react with 5h-j. These differences in the reactivity suggest the structure dependence of a silyl enol ether to react with 6; the zwitterionic intermediate [A] needs the resonance-stabilization with a π-donating aromatic substituent (cf. 5a-d *vs.* 5h), and formation of [A] may be effected by steric factors (cf. 5g *vs.* 5i). The same reaction of 5a with 1-phenylbutadiene (10) gave a regioisomer 11 as explained by orbital and/or electronic effects (entry 8).



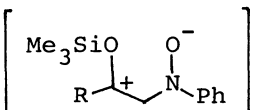
5h



5i

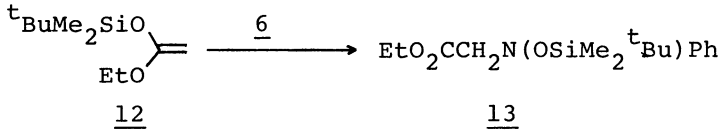


5j



[A]

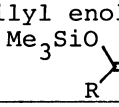
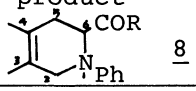
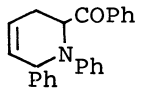
As is expected, the reaction of a ketene silyl acetal 12 with 6 afforded hydroxyamino-ester 13 in 72% yield.[6] However, 13 did not undergo the elimination reaction with triethylamine.



12 13

Because a variety of heterocycles may be available from a glyoxal imine and its precursor,[5] we are now investigating the reaction of a silyl enol ether with nitroso compounds other than 6, and synthetic use of the adduct (*e.g.*, 13).

Table 1. One-pot Cycloaddition Reactions of the Anils from Silyl Enol Ethers and Nitrosobenzene with 2,3-Dimethylbutadiene.

entry	silyl enol ether  5	product[a]  8	yield	mp	IR(KBr); cm^{-1}
1	5a R=C_6H_5	8a	52%[b]	118-112°C	1685
2	5b R=4-$CH_3C_6H_4$	8b	36%	128-130°C	1680
3	5c R=4-$CH_3OC_6H_4$	8c	25%	122-124°C	1660
4	5d R=4=BrC_6H_4	8d	30%	143-145°C	1685
5	5e R=2-furyl	8e	21%	127-129°C	1670
6	5f R=2-pyridyl	8f	7%	110-112°C	1710
7	5g R=CH_3	8g	7%	oil	1715[c]
8[d]	5a R=C_6H_5	 11	25%	141-143°C	1690

a) All new compounds described herein gave satisfactory elemental analyses.

b) Yield based on 7a. c) in neat. d) In this case 10 was used as a diene

e) ^1H NMR(CCl_4 for 8a-f and $CDCl_3$ for 8g and 11); δ

8a: 8.0-6.6 (10H, m, Ph), 5.31 (1H, dd, J=2 and 6 Hz, C_6-H), 3.74 (2H, br s, C_2-H), 2.75 and 2.30 (each 1H, dd, J=6 and 18 Hz and 2 and 18 Hz, respectively, C_5-H), 1.65 (6H, br s, CH_3).

8b: 7.8-6.7 (9H, m, Ph), 5.28 (1H, dd, J=2 and 6 Hz, C_6-H), 3.74 (2H, br s, C_2-H), 2.75 and 2.13 (each 1H, dd, J=6 and 18 Hz and 2 and 18 Hz, respectively, C_5-H), 2.37 (3H, s, Ph-CH_3), 1.65 (6H, br s, C_3- and C_4-CH_3).

8c: 7.8-6.6 (9H, m, Ph), 5.25 (1H, dd, J=2 and 6 Hz, C_6-H), 3.78 (3H, s, OCH_3), 3.75 (2H, br s, C_2-H), 2.70 and 2.30 (each 1H, dd, J=6 and 18 Hz and 2 and 18 Hz, respectively, C_5-H), 1.66 (6H, br s, C_3- and C_4-CH_3).

8d: 7.8-6.5 (9H, m, Ph), 5.20 (1H, dd, J=2 and 6 Hz, C_6-H), 3.68 (2H, br s, C_2-H), 2.62 and 2.27 (each 1H, dd, J=6 and 15 Hz and 2 and 15 Hz, respectively, C_5-H), 1.65 (6H, br s, CH_3).

8e: 7.6-6.4 (8H, m, Ar), 5.21 (1H, dd, J=2 and 7 Hz, C_6-H), 3.82 (2H, br s, C_2-H), 2.77 and 2.36 (each 1H, dd, J=7 and 18 Hz and 2 and 18 Hz, respectively, C_5-H), 1.69 (6H, br s, CH_3).

8f: 8.7-6.4 (9H, m, Ar), 6.09 (1H, dd, J=2 and 7 Hz, C_6-H), 3.88 (2H, br s, C_2-H), 2.84 and 2.31 (each 1H, dd, J=7 and 18 Hz and 2 and 18 Hz, respectively, C_5-H), 1.73 and 1.61 (each 3H, br s, CH_3).

8g: 7.6-6.6 (5H, m, Ph), 4.45 (1H, t, J=4.5 Hz, C_6-H), 3.69 (2H, br s, C_2-H), 2.7-2.3 (2H, m, C_5-H), 1.97 (3H, s, $COCH_3$), 1.69 (6H, br s, C_3- and C_4-CH_3).

11: 7.9-6.7 (15H, m, Ph), 6.07 (2H, br s, C_3- and C_4-H), 5.22 (1H, dd, J=5.5 and 12 Hz, C_6-H), 5.04 (1H, br s, C_2-H), 2.80-2.55 (2H, m, C_5-H).

References

1) Part 42 of "Molecular Design by Cycloaddition Reaction": Part 41; submitted for publication.

2) a) Recent Proctor's report is a good leading reference for the chemistry of phenylglyoxal anil; W. R. McKay and G. R. Proctor, J. Chem. Soc., Perkin Trans. 1, 1981, 2435. b) P. Yates, J. Am. Chem. Soc., 74, 5376 (1952). c) W. U. Malik, D. R. Gupta, and C. L. Taploo, J. Chem. Eng. Data, 1960, 210. d) E. Fraser, W. Paterson, and G. R. Proctor, J. Chem. Soc., 1963, 5107.

3) Part 41 of this series.

4) The hydroxylamine 7a had following physical and spectral data: mp 94-96°C; IR (KBr) 1690, 1605, 1500, 1260, 840 cm^{-1}; ^1H NMR (CCl_4) δ 8.0-7.0 (10H, m, Ph), 4.47 (2H, s, CH_2), 0.03 (9H, s, $SiCH_3$).

5) W. R. McKay and G. R. Proctor, J. Chem. Soc., Perkin Trans. 1, 1981, 2443.

6) The hydroxyamino-ester 13 was obtained as an oil after purification by chromatography on a Florisil column ($CHCl_3$): IR (neat) 1745 cm^{-1}; ^1H NMR (CCl_4) δ 7.4-6.7 (5H, m, Ph), 4.07 (2H, q, J=7 Hz, OCH_2), 3.90 (2H, s, NCH_2), 1.18 (3H, t, J=7 Hz, $OCH_2\underline{CH_3}$), 0.95 (9H, s, ^tBu), 0.06 (6H, s, $SiCH_3$).

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