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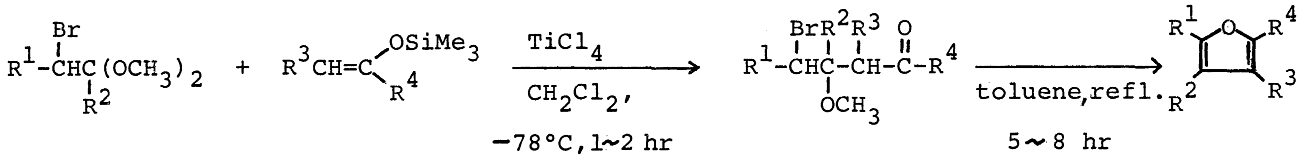
A CONVENIENT METHOD FOR THE SYNTHESIS OF FURAN DERIVATIVES

Teruaki MUKAIYAMA, Hideharu ISHIHARA*, and Katsuhiko INOMATA**
Department of Chemistry, Faculty of Science
The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113

It was found that furan derivatives are synthesized in good yields from β-alkoxy-γ-bromoketones formed by the $TiCl_4$-promoted reaction of α-bromoacetals with silyl enol ethers.

Recently, it was found in our laboratory that trimethylsilyl enol ethers[1)] and enol acetates[2)] react with various acetals in the presence of $TiCl_4$ to give the corresponding β-alkoxyketones in high yields. In the present study, it was established that β-alkoxy-γ-bromoketones(III), formed by the $TiCl_4$-promoted reaction of α-bromoacetals(I) with silyl enol ethers(II), are readily converted to the corresponding furans(IV) on refluxing in toluene.

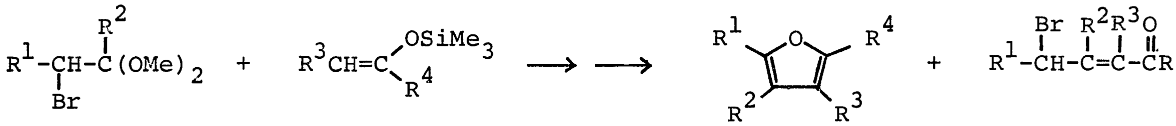


(I) (II) (III) (IV)

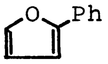
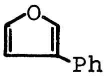
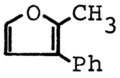
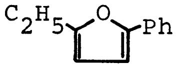
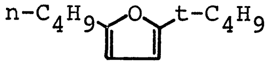
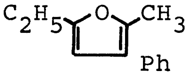
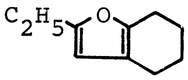
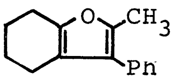
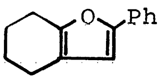
The typical procedure is described for the reaction of 2-trimethylsiloxy-1-phenyl-1-propene with 2-bromobutyraldehyde dimethyl acetal. To a methylene chloride solution(12 ml) of the acetal(197 mg, 1.0 mmol) was added dropwise $TiCl_4$(1.0 mmol) at -78°C under an argon atmosphere. Then a methylene chloride (3 ml) solution of 2-trimethylsiloxy-1-phenyl-1-propene(227 mg, 1.1 mmol) was added drop by drop and the reaction mixture was stirred for additional 2 hours at -78°C. After treating the resulting mixture with a cold buffer solution(pH 6.7; 0.25M KH_2PO_4 + 0.25M Na_2HPO_4), an organic layer was extracted with ether. After removal of the solvent, 10 ml of toluene was added and the solution was refluxed for 8 hours under an argon atmosphere. After removal of toluene under reduced pressure, the residue was separated by tlc. Thus, 5-ethyl-2-methyl-3-phenylfuran[3)] and 5-bromo-3-phenyl-3-hepten-2-one were obtained in 82% and 4% yields, respectively.

In a similar manner, various furan derivatives were prepared in good yields from α-bromoacetals and silyl enol ethers as listed in the following Table.

Table. The Synthesis of Furans

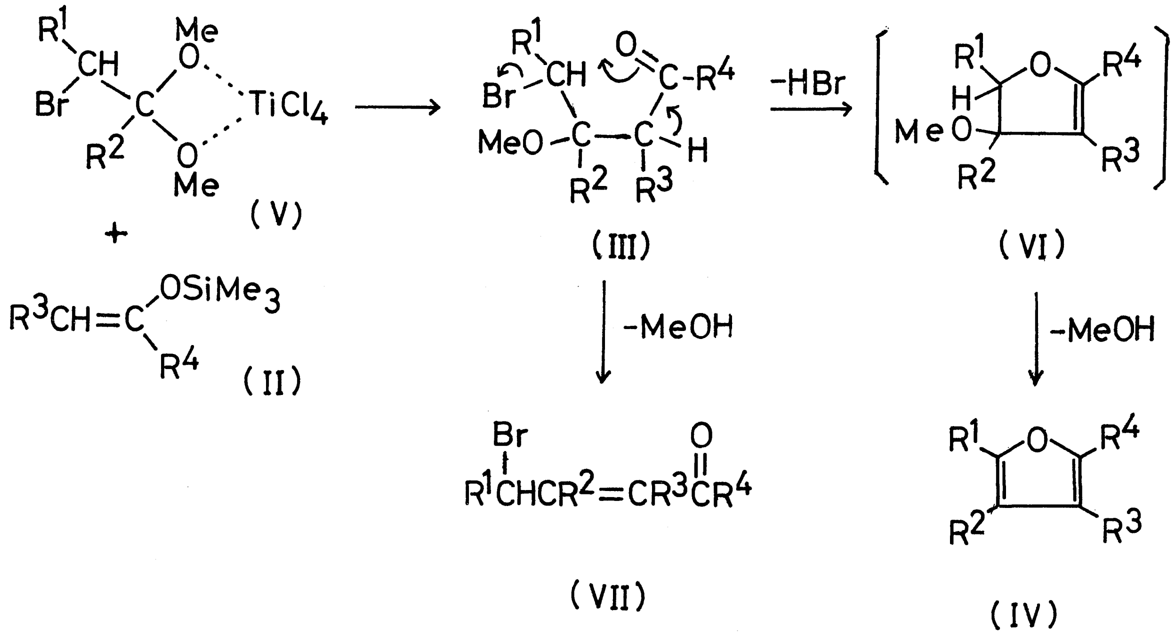


(I) (II) (IV) (VII)

	I		II		Time[*1]	Yield (%)[*3]		
	R^1	R^2	R^3	R^4	hr	IV[*2]		VII
a	H	H	H	Ph	8		45	-
b	H	H	Ph	H	5	 *4	32	21
c	H	H	Ph	CH_3	8		69	-
d	C_2H_5	H	H	Ph	8		70	12
e	n-C_4H_9	H	H	t-C_4H_9	5		71	4
f	C_2H_5	H	Ph	CH_3	8		82	4
g	C_2H_5	H	$-(CH_2)_4-$		5		68	-
h	$-(CH_2)_4-$		H	Ph	15		77	-
i	$-(CH_2)_4-$		H	Ph	5		76	-

[*1] Reaction time in toluene
[*2] All compounds exhibited correct ir and nmr spectral data.
[*3] Yield of isolated product
[*4] mp 99.5-100.5°C

The reaction may be explained by considering an initial formation of highly active acetal-$TiCl_4$ complex(V) produced from acetal and $TiCl_4$. The complex(V) reacts with silyl enol ether(II) to give γ-bromo-β-methoxyketone(III).[4] The ketone(III) is in turn converted to an intermediate(VI) by an intramolecular nucleophilic displacement as sketched below. Then VI is immediately changed to furan with the elimination of methanol. α,β-Unsaturated ketone(VII), by-product, may be formed from III by loss of methanol.



There have been reported a lot of methods for the preparation of furan derivatives. However, in many cases, their preparations consist of multi-steps and the yields are not always good. The present method affords a general procedure for the preparation of substituted furans because of brevity in procedure and of possible choice of substituents involved in the α or β position of furans.

Further development is now in progress.

REFERENCES

* Present address: Fuculty of Engineering, Gifu University, Naka, Kagamihara,
Gifu 504

** Present address: Department of Chemistry, Faculty of Science,
Kanazawa University, 1-1 Marunouchi, Kanazawa, Ishikawa 920

1) T. Mukaiyama and M. Hayashi, Chem. Lett., 15 (1974).

2) T. Mukaiyama, T. Izawa, and K. Saigo, Chem. Lett., 323 (1974).

3) ir(neat) : 3030(=C-H), 1580 cm^{-1}(furan ring): nmr (CCl_4, 60 MHz): δ 7.26(Ph, s, 5H), 6.03(-CH-, s, 1H), 2.63($-\underline{CH_2}CH_3$, q, 2H), 2.05($-CH_3$, s, 3H), 1.24($CH_2\underline{CH_3}$, t, 3H).

4) 5-Bromo-4-methoxy-3-phenyl-2-heptanone obtained by the reaction of 2-bromobutyraldehyde dimethyl acetal with 2-trimethylsiloxy-1-phenyl-1-propene consisted of two diastereoisomers. It was also confirmed that both isomers were converted to the corresponding furans under the above mentioned reaction conditions. Of two isomers, one was readily transformed into the furan at room temperature.

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