Carbon–Carbon Coupling and Alkylation of Furan and Thiophene, involving C–H Bond Activation, with Ruthenium Catalysts in Alcohols

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Reaction of furan and thiophene with an alcohol (R–OH) at 140 °C, using a ruthenium catalyst, affords the R-alkylated dimers (**2**) and R,R-dialkylated trimers (**3**) of furan and of thiophene along with γ-keto esters (**4**).

The C–C coupling reaction involving heterocyclic compounds, such as furan or thiophene, shows potential for the access to dimers or trimers of biological importance.[1,2] These compounds are usually obtained from a 2-halogeno heteroarene and a Grignard reagent with Pd(0) catalysts[2] or from lithiated substrates *via* organoboranes or Cu derivatives.[1] We now report a new ruthenium catalysed reaction involving both C–C coupling and alkylation of furan and thiophene, *via* C–H bond activation, which affords alkylated dimers (**2**) and trimers (**3**) with the parallel formation of the γ-keto-ester (**4**) (Scheme 1).

Treatment of furan (**1a**) (100 mmol) with a catalytic amount

Table 1. Influence of the ratio (**1**) : Ru on the formation of (**2**), (**3**), and (**4**).[a]

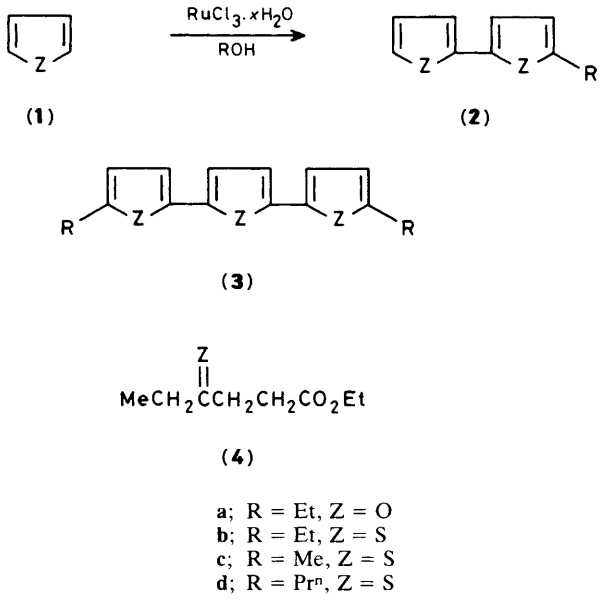
	(**1**) : ($RuCl_3.xH_2O$)		
	50 : 1	150 : 1	500 : 1
(**2a**), (**3a**), (**4a**)	500, 130, 25	150, 45, 0	25, 0, 0
(**2b**), (**3b**), (**4b**)	450, 75, 50	165, 20, 0	30, 0, 0

[a] Percent yields based on $RuCl_3.xH_2O$, determined by gas chromatographic analysis using an internal standard.

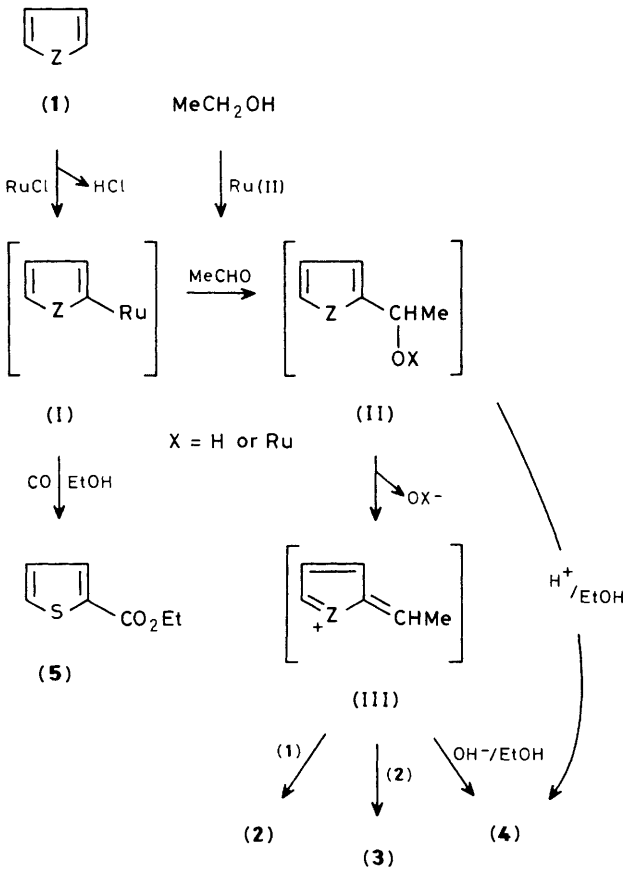
Table 2. Yields[a] of (2), (3), and (4) from (1).[b]

	Catalyst precursor		
	$[RuCl_2(C_6H_6)]_2$	$[RuCl_2(NBD)]_n$[c]	$[RuCl_2(py)_2(NBD)]$[d]
(2a), (3a), (4a)	200, 55, 22	275, 45, 10	175, 80, 0
(2b), (3b), (4b)	310, 180, 24	225, 100, 20	220, 100, 20

[a] Percent yields based on Ru monomer. [b] 100 mmol of Ru monomer; 30 ml of ethanol; 140 °C for 24 h. [c] NBD = Norbornadiene. [d] py = Pyridine.



Scheme 1



Scheme 2

of $RuCl_3.xH_2O$ (2 mmol) in dry ethanol at 140 °C for 24 hours afforded (**2a**) as the major product together with (**3a**) and (**4a**)† (Scheme 1, Table 1). Under similar conditions, thiophene (**1b**) led to the formation of (**2b**), (**3b**), and (**4b**). Analogously, compounds (**2c**), (**3c**), and (**2d**), (**3d**) were obtained as the major products from the reaction of (**1b**) in methanol and n-propanol respectively, at 140 °C. The conversion of (**1**) occurs in the temperature range 85—140 °C. The yields of (**2**), (**3**), and (**4**) decrease rapidly with an increase of the ratio (**1**) : $RuCl_3.xH_2O$ (Table 1). Ru^{II} complexes, such as $[RuCl_2(C_6H_6)]_2$, $[RuCl_2(NBD)]_n$, and $[RuCl_2(py)_2(NBD)]$ also catalyse the transformation of (**1**) into (**2**), (**3**), and (**4**) (Table 2).

The first step of the transformation of (**1**) appears to involve a C–H bond activation process by a Ru^{II} species. The blue colour, typical of the reduction in alcohol of $RuCl_3$ into Ru^{II} species[3] was observed before extraction of products (**2**)—(**4**). When the transformation of (**1b**) was attempted under similar conditions (140 °C, 0.02 equiv. of $RuCl_3$ in ethanol), but under CO (35—40 bar), the ester (**5**) was isolated (15%) along with small amounts of (**2**), (**3**), (**4**), and $Ru_3(CO)_{12}$ (Scheme 2). The formation of (**5**) is expected to arise from the intermediate (I), since aryl–metal complexes produce esters with CO and alcohols. Furthermore, methoxybenzene under similar conditions [*e.g.* PhOMe (10 mmol), $RuCl_3$ (2 mmol), EtOH (2 ml); 140 °C, 48 h] leads to C–C coupling isomers $MeOC_6H_4$–C_6H_4OMe and $MeOC_6H_4$–Cl, obtained respectively in 165 and 45% yields based on Ru. Both compounds are also assumed to result, after C–H bond activation by Ru^{II} species, from aryl–Ru metal intermediates by reductive elimination or substitution with chloride as was observed for a Pd^{II} catalyst.[4]

As no dimer or trimer of (**1a,b**) was observed without an alkyl substituent, it is likely that alkylation of (**1**) takes place before di- and tri-merization. The key intermediate for the formation of (**2**), (**3**), and (**4**) is then expected to be a species of type (II) (Scheme 2) resulting from insertion of aldehyde into the heteroaryl–Ru bond of (I), for the following reasons. (i) The direct alkylation of (**1a**) with toluene-*p*-sulphonate afforded only 2-alkylated monomers[5] therefore (**2**) and (**3**) are not expected to result from direct alkylation of (**1**). (ii) *In situ* formed aldehydes are responsible for the alkylation of amine with alcohol and Ru^{II} catalysts.[6] (iii) Dimerization of thiophene or methylfuran with Pd^{II} catalysts in dimethylformamide does not afford similar alkylated products.[7] It is

† The products were identified by mass spectrometry, n.m.r. and i.r. spectroscopy and gave satisfactory analysis.

noteworthy that $Pd(OAc)_2$ does not lead to compounds (**2**)—(**4**) with (**1a**) in ethanol. (iv) Furfuryl alcohol of type (II) (X = H) in alcohol with strong acids affords a keto ester of type (**4**)[8] *via* the intermediate (III). This proposed intermediate (III)[8] can also account for the formation of (**2**) and (**3**) by alkylation of (**1**) and (**2**) (Scheme 2).

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References

1 J. Kagan and S. K. Arora, *Tetrahedron Lett.*, 1983, **24**, 4043; *Heterocycles*, 1983, **20**, 1937.
2 A. Carpita, R. Rossi, and C. A. Veracini, *Tetrahedron*, 1985, **41**, 1919; A. Carpita and R. Rossi, *Gazz. Chim. Ital.*, 1985, **115**, 575.
3 G. D. Gilbert, D. Rose, and G. Wilkinson, *J. Chem. Soc. (A)*, 1970, 2765.
4 L. M. Stock, K. T. Tse, L. J. Vorvick, and S. A. Walstrum, *J. Org. Chem.*, 1981, **46**, 1757; P. M. Henry, 'Palladium Catalyzed Oxidation of Hydrocarbons,' D. Reidel, Dordrecht, 1980.
5 P. H. Boyle, J. H. Coy, and H. N. Dobbs, *J. Chem. Soc., Perkin Trans. 1*, 1972, 1617.
6 Y. Watanabe, Y. Tsuji, H. Ige, Y. Ohsugi, and T. Ohta, *J. Org. Chem.*, 1984, **49**, 3359; S. I. Murahashi, K. Kondo, and T. Hakata, *Tetrahedron Lett.*, 1982, **23**, 229; A. Arcelli, B. T. Khai, and G. Porzi, *J. Organomet. Chem.*, 1982, **235**, 93.
7 V. E. Tarabanko, I. V. Kozhevnikov, and K. I. Matveev, *React. Kinet. Catal. Lett.*, 1978, **8**, 77.
8 L. Birkofer and R. Dutz, *Liebigs Ann. Chem.*, 1962, **657**, 94; D. W. Chasar and C. C. Hsu, Belg. Pat., 883 067, 1980.