# Rearrangement of Radical *ipso*-Intermediates by 1,2-Shift of a Formyl Group. Reactions of Adamantyl Radicals with Thiophencarbaldehydes

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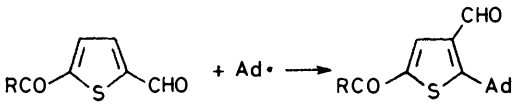
The reaction of 1-adamantyl radicals with some 5-substituted thiophen-2-carbaldehydes gives rise to the products of adamantyldeformylation; this process is a new example of homolytic aromatic *ipso*-substitution. Moreover, the reaction with thiophen-2,5-dicarbaldehyde affords, as the major product, 2-(1-adamantyl)thiophen-3,5-dicarbaldehyde in which a formyl group has migrated from the 2- to the 3-position. This result is explained by assuming that the initially formed radical *ipso*-intermediate rearranges by 1,2-shift of the *ipso*-substituent.

SEVERAL examples of the addition of an alkyl or acyl radical to a substituted position of an aromatic substrate to give an *ipso*-intermediate have been reported; in most cases these radical σ-complexes evolve by elimination of the *ipso*-substituent to give *ipso*-substitution products.[1-3] However, examples have been observed, particularly in the case of furan [4] and thiophen [5] derivatives, in which the *ipso*-intermediates




SCHEME 1

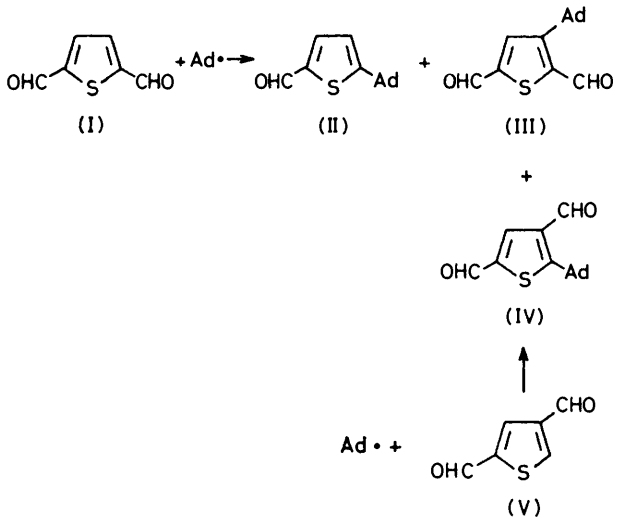
preferentially give rise to other processes rather than that of displacement of the *ipso*-substituent. We report now some reactions of adamantyl radical (Ad•) which demonstrate that in the thiophen series these intermediates can also give rise to rearrangement reactions by migration of an *ipso*-formyl group to a vicinal position (Scheme 1).

## RESULTS AND DISCUSSION

The reaction of 1-adamantyl radical with thiophen-2,5-dicarbaldehyde (I) afforded three products, 5-(1-adamantyl)thiophen-2-carbaldehyde (II) (19%), 3-(1-adamantyl)thiophen-2,5-dicarbaldehyde (III) (10%), and 2-(1-adamantyl)thiophen-3,5-dicarbaldehyde (IV) (56%) (Scheme 2). The structure of the rearrangement product (IV) was also confirmed by independent synthesis. Compound (IV) was obtained (60%) as the sole product from the radical adamantylation of the thiophen-2,4-dicarbaldehyde (V); it has been shown in previous work [5] that radical substitution occurs selectively at the 2-position of thiophen derivatives bearing electron-withdrawing substituents at the 3- and 5-positions.

In compound (II) Ad• has replaced the formyl group; this is therefore a new example of homolytic aromatic *ipso*-substitution, namely alkyldeformylation. In compound (IV) a formyl group has migrated from the 2- to the 3-position. This rearrangement seems to be peculiar to the formyl group; other acyl derivatives of thiophen do not give rearrangement products. Thus, the reaction of Ad• with 2,5-diacetylthiophen (VI) afforded only the product of adamantyldeacylation,[1] 2-(1-adamantyl)-5-acetylthiophen (VII) (33%) and the product of substitution at the β-position, 3-(1-adamantyl)-2,5-diacetylthiophen (VIII) (16%) (Scheme 3). Moreover, from the reaction of Ad• with 2,5-bismethoxycarbonylthiophen (IX) the only product obtained was 3-(1-adamantyl)-2,5-bismethoxycarbonylthiophen (X) (25%); displacement of the $CO_2Me$ group by the adamantyl radical was not observed, confirming previous results obtained for other aromatic systems.[1,3]

The behaviour of the formyl group was also confirmed by the results obtained from the 5-acetylthiophen-2-carbaldehyde (XI) (Scheme 4). A more complicated product mixture was obtained in this case; the products of displacement of the acetyl group (II) (10%) and of the formyl group (VII) (17%) were isolated together with the 3-(1-adamantyl)-5-acetylthiophen-2-carbaldehyde (XII) (11%) and the rearrangement compound 2-(1-

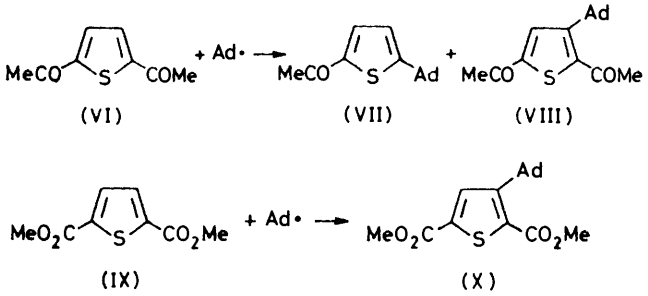



SCHEME 2

adamantyl)-5-acetylthiophen-3-carbaldehyde (XIII) (13%). In this case also the structure of the rearranged compound was confirmed by independent synthesis (56% yield) by radical adamantylation of 2-acetylthiophen-4-carbaldehyde (XIV).

Structural assignments were carried out by n.m.r. spectroscopy. In particular the presence of an *ortho*-

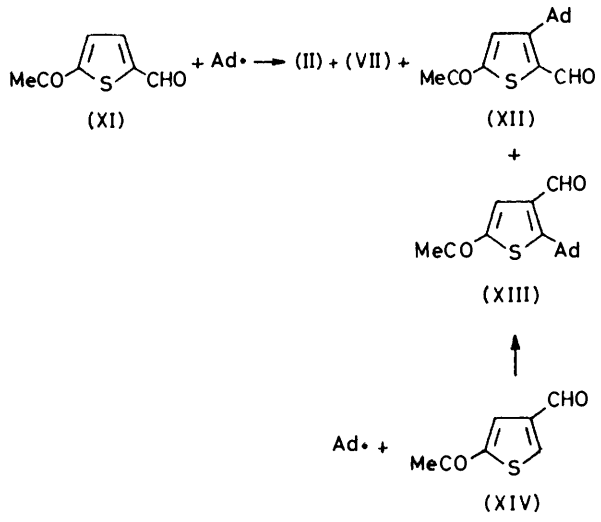
adamantyl group produces a deshielding of the formyl proton which absorbs below δ 10 [see compounds (III), (IV), and (XIII)]. This observation was used to demonstrate that the addition of Ad• to the β-position of (XI) gave (XII); in the alternative structure in which the




SCHEME 3

adamantyl group occupies the 4-position, the CHO absorption should occur in the usual range, δ 9.5—9.8 [as observed in the starting products (I), (V), (XI), (XIV) as well as in (II) and in compounds (III) and (IV) for the formyl group in the 5-position]. In the rearrangement products (IV) and (XIII) the proton in the 4-position is considerably deshielded relative to that in the isomers (III) and (XII) and in compounds (VIII) and (X), confirming that a formyl group is present in the 3-position.

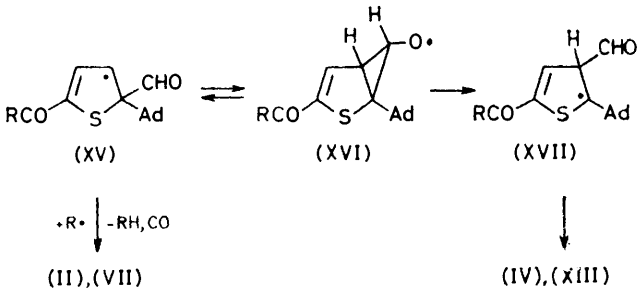
The formation of 5-(1-adamantyl)thiophen-2-carbaldehyde (II) and of 2-(1-adamantyl)thiophen-3,5-dicarbaldehyde (IV) from thiophen-2,5-dicarbaldehyde (I) as well as 2-(1-adamantyl)-5-acetylthiophen (VII) and 2-(1-adamantyl)-5-acetylthiophen-3-carbaldehyde (XIII) from




SCHEME 4

5-acetylthiophen-2-carbaldehyde (XI) can be explained assuming that the products in each case are formed from the same radical *ipso*-intermediate (XV; R = H or Me). Compounds (II) and (VII) are the result of an *ipso*-substitution process. The elimination of the formyl group, however, is probably not a spontaneous process but requires the assistance of another species which effects the abstraction of the formyl hydrogen; hence, the preferred reaction of (XV) is the rearrangement to (XVII; R = H or Me) which can occur through the intermediate radical cyclopropane derivative (XVI; R = H or Me). The σ-complexes (XVII) will then easily re-aromatize to give (IV) or (XIII). The whole process is therefore an example of a radical 1,2-shift of the formyl group.

On the basis of the known behaviour of β-oxoalkyl radicals,[6] of which (XV) represents an example, an alternative interpretation which does not involve the intermediate formation of (XVI) can be suggested. This would imply that (XVII) originates from (XV) through an elimination–addition mechanism. This interpretation, however, seems unlikely because if a formyl radical is formed by elimination its addition to




SCHEME 5

the resulting 5-acyl-2-(1-adamantyl)thiophen should preferentially occur at the 4- rather than at the 3-position, as observed.

The formation of the rearrangement products (IV) and (XIII) thus represents a further interesting example of one of the possible ways through which a radical *ipso*-σ-complex intermediate can evolve, namely a 1,2-shift of the *ipso*-substituent. To our knowledge the only previous convincing example of this process is the formation of 3-bromo-4-chloronitrobenzene from the photo-initiated chlorination of *p*-bromonitrobenzene.[7] Addition of chlorine at the carbon atom bearing the bromine atom affords an *ipso*-intermediate from which bromine migrates to the *ortho*-position to give a σ-complex which is responsible for the formation of the rearrangement product.[7]

## EXPERIMENTAL

Product characterization was accomplished by n.m.r. (JEOL C60HL: $CDCl_3$ solutions) and mass spectrometry (Varian MAT 311A at 70 eV using an all-glass inlet system). M.p.s are uncorrected.

Thiophen-2,5-dicarbaldehyde,[8] thiophen-2,4-dicarbaldehyde,[9] 2,5-diacetylthiophen,[10] 5-acetylthiophen-2-carbaldehyde,[11] 2-acetylthiophen-4-carbaldehyde,[11] and 2,5-bismethoxycarbonylthiophen [12] were prepared as described in the literature.

The radical adamantylation of the thiophen derivatives (I), (V), (VI), (IX), (XI), and (XIV) was carried out by the following general procedure. To a stirred solution of the thiophen derivative (3 mmol), adamantane-1-carboxylic

acid (15 mmol), and $AgNO_3$ (0.3 mmol) in 4 : 1 v/v acetonitrile–water (50 ml), a saturated solution of $(NH_4)_2S_2O_8$ (20 mmol) in water was added dropwise, under reflux, over *ca.* 20 min. Stirring and heating were continued for 30 min and the cooled solution was then poured onto ice and $NH_3$; the mixture was extracted with chloroform and the organic layer was washed with 5% NaOH and with water. The residue was chromatographed through a silica gel column using light petroleum–diethyl ether (7 : 3) as eluant. The separation of the products was monitored by t.l.c. Yields are reported in the Results section: 5-(1-*adamantyl*)-*thiophen*-2-*carbaldehyde* (II), m.p. 131—133° (lit.,[5] 131—133°), δ 9.6 (1 H, s), 7.5 (1 H, d), 6.85 (1 H, d, *J* 4.5 Hz), 2.05br (3 H, s), 1.95br (6 H, s), and 1.75br (6 H, s); 3-(1-*adamantyl*)*thiophen*-2,5-*dicarbaldehyde* (III), m.p. 145—147°, δ 10.2 (1 H, s), 9.75 (1 H, s), 7.65 (1 H, s), 2.2br (9 H, s), and 1.8br (6 H, s), *m/e* 274 (100%, *M*), 256 (3), 245 (47), 217 (5), 203 (9), 167 (8), 149 (11), and 135 (3) (Found: C, 70.5; H, 6.7. $C_{16}H_{18}O_2S$ requires C, 70.0; H, 6.6%); 2-(1-*adamantyl*)*thiophen*-3,5-*dicarbaldehyde* (IV), obtained from (I) and from (V), m.p. 150—152°, δ 10.35 (1 H, s), 9.8 (1 H, s), 8.1 (1 H, s), 2.2br (9 H, s), and 1.8br (6 H, s), *m/e* 274 (100%, *M*), 256 (3), 246 (5), 217 (4), 203 (10), 167 (17), 149 (23), and 135 (4) (Found: C, 70.15; H, 6.6%); 2-(1-*adamantyl*)-5-*acetylthiophen* (VII), obtained from (VI) and from (XI), m.p. 114—115°, δ 7.4 (1 H, d), 6.75 (1 H, d, *J* 4.5 Hz), 2.5 (3 H, s), 2.0br (9 H, s), and 1.8br (6 H, s) (Found: C, 74.0; H, 7.6. $C_{16}H_{20}OS$ requires C, 73.8; H, 7.8%); 3-(1-*adamantyl*)-2,5-*diacetylthiophen* (VIII), m.p. 106—108°, δ 7.6 (1 H, s), 2.6 (3 H, s), 2.55 (3 H, s), 2.2br (9 H, s), and 1.8br (6 H, s) (Found: C, 71.25; H, 7.5. $C_{18}H_{22}O_2S$ requires C, 71.5; N, 7.3%); 3-(1-*adamantyl*)-2,5-*bismethoxycarbonylthiophen* (X), m.p. 131—132°, δ 7.6 (1 H, s), 3.8 (6 H, s), 2.2br (9 H, s), and 1.8br (6 H, s) (Found: C, 64.1; H, 6.7. $C_{18}H_{22}O_4S$ requires C, 64.6; H, 6.6%); 3-(1-*adamantyl*)-5-*acetylthiophen*-2-*carbaldehyde* (XII), m.p. 153—155°, δ 10.3 (1 H, s), 7.5 (1 H, s), 2.5 (3 H, s), 2.2br (9 H, s), and 1.8br (6 H, s) (Found: C, 71.0; H, 7.1. $C_{17}H_{20}O_2S$ requires: C, 70.8; H, 7.0%); 2-(1-*adamantyl*)-5-*acetylthiophen*-3-*carbaldehyde* (XIII), obtained from (XI) and from (XIV), m.p. 151—153°, δ 10.3 (1 H, s), 8.0 (1 H, s), 2.5 (3 H, s), 2.2br (9 H, s), and 1.8br (6 H, s) (Found: C, 70.6; H, 7.15%).

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