Termination of radical-polar crossover reactions by intramolecular nucleophiles

John A. Murphy,*†[a] Faiza Rasheed,[a] Stephen J. Roome[a] and Norman Lewis[b]

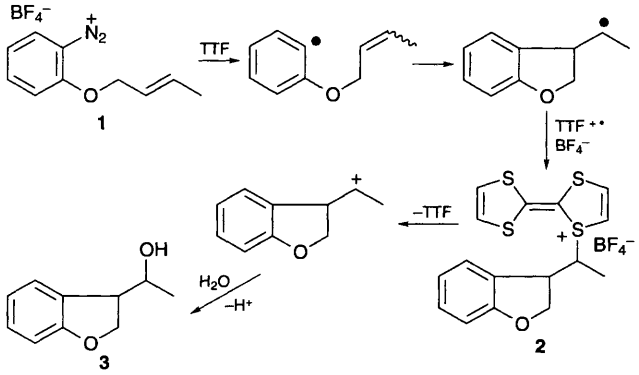
[a] *Department of Chemistry, University of Nottingham, University Park, Nottingham, UK NG7 2RD*
[b] *SmithKline Beecham Pharmaceuticals, Old Powder Mills, Leigh, Tonbridge, Kent, UK TN11 9AN*

Radical-polar crossover reactions featuring intramolecular nucleophilic termination are reported.

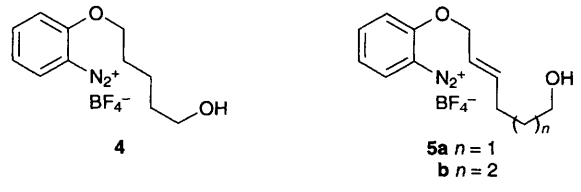
We have previously shown that tetrathiafulvalene (TTF) is an effective catalyst for radical-polar crossover reactions.[1] For example, arenediazonium tetrafluoroborate salt **1** reacts with TTF to give alcohol **3** *via* the alkylsulfonium salt **2**. In this standard reaction, substitution of TTF in **2** occurs *via* S_N1 loss of TTF, followed by trapping of the intermediate carbocation with an external nucleophile (residual moisture in the solvent in the example shown in Scheme 1).

As part of the development of this reaction,[2,3] we were interested in trapping the intermediate carbocation with an internal nucleophile, and hence the reactions of diazonium salts **4** and **5a–b** were initially examined.

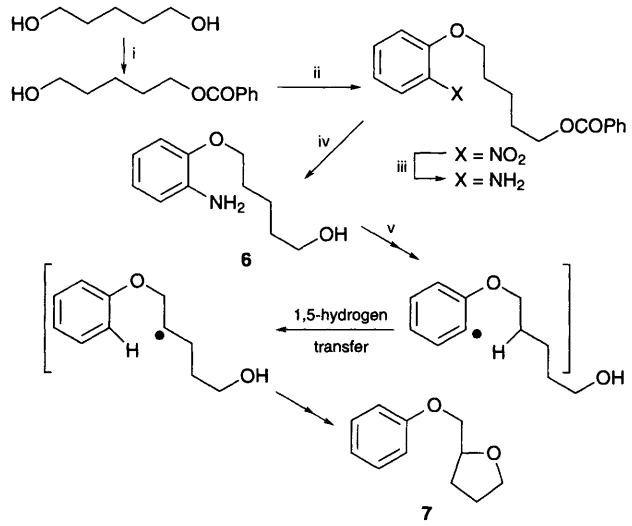
The precursors were conveniently prepared using standard procedures, as outlined in Schemes 2 and 3. Contrary to our previous experience it was found that diazotisation of the aniline precursors of **4** and **5a–b** gave relatively unstable diazonium salts that could not be isolated in solid form. Hence, the diazotisation and TTF reactions were carried out in one pot. Using this procedure, **6** reacted smoothly with nitrosonium tetrafluoroborate in dichloromethane; this was followed by removal of solvent and reaction with TTF in moist acetone to yield the desired cyclic compound **7**. In this case, the diazonium salt is converted into an aryl radical which then undergoes hydrogen atom transfer; coupling with TTF+· only occurs after this step, resulting in the ultimate formation of **7**. Under identical conditions, anilines **8a** and **8b** gave tricyclic compounds **9a** and **9b**. Clearly, the intermediate cation generated in the reaction of all three substrates is trapped by the internal nucleophile.



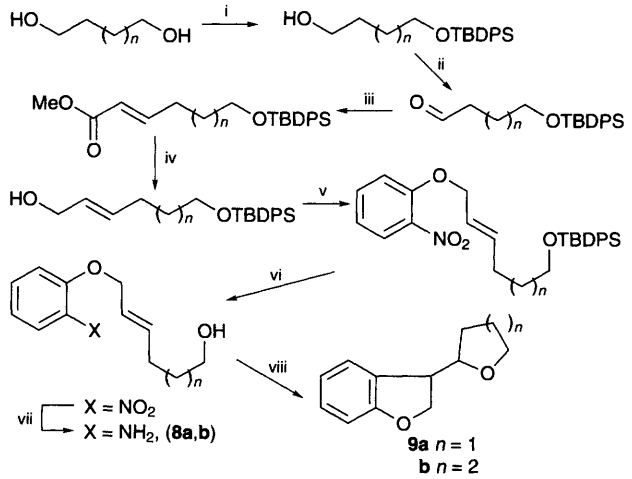
Scheme 1



As a more adventurous demonstration of this process, diazonium salt **10** was prepared; this compound should afford product **11** in which a spirocyclic quaternary centre is formed.

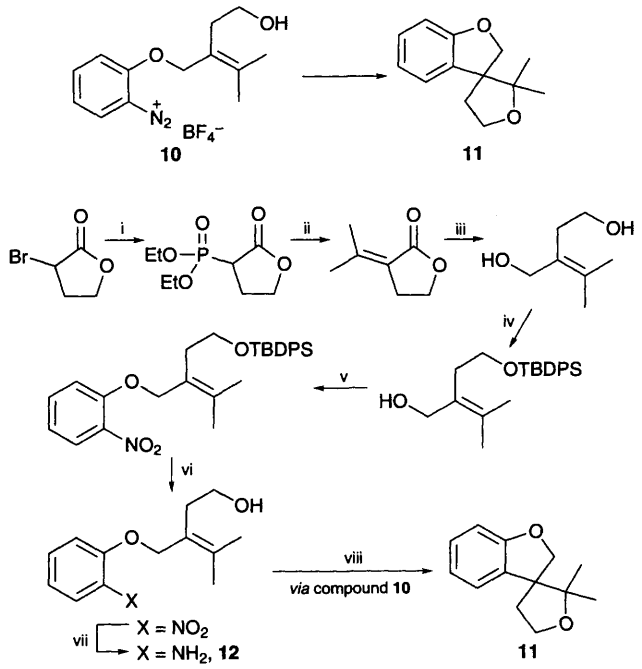


Scheme 2 *Reagents and conditions*: i, PhCOCl, pyridine, THF, 0 °C, 2 h, 98%; ii, 2-$NO_2C_6H_4OH$, Ph_3P, DEAD, THF, 0 °C to room temp., 3 h, 67%; iii, $NaBH_4$, $Cu(acac)_2$, EtOH, 1.5 h, 67%; iv, NaOH, H_2O, EtOH, reflux, 2 h, 94%; v, $NOBF_4$, CH_2Cl_2, 0 °C followed by TTF, moist acetone, 30 min., 38%



Scheme 3 *Reagents and conditions*: i, TBDPSCl, imidazole, DMF, 5 h, **a**, 87%; **b**, 86%; ii, Me_2SO, ClCOCOCl, Et_3N, −78 °C to room temp., 2 h, **a**, 95%; **b**, 85%; iii, NaH, $(MeO)_2P(O)CH_2C(O)OEt$, THF, 0 °C to room temp. 20 h, **a**, 70%; **b**, 92%; iv, DIBAL-H, PhH, −70 °C, 20 min., **a**, 96%; **b**, 89%; v, 2-$NO_2C_6H_4OH$, Ph_3P, DEAD, THF, **a**, 94%; **b**, 94%; vi, TBAF, THF, 1 h, **a** 98%; **b**, 96%; vii, $NaBH_4$, $Cu(acac)_2$, EtOH, 1.5 h, **a**, 96%; **b**, 96%; viii, $NOBF_4$, CH_2Cl_2, 0 °C, followed by TTF, moist acetone, **a**, 42%; **b**, 38%. TBDPSCl = *tert*-butyldiphenylchlorosilane, DEAD = diethyl azodicarboxylate, TBAF = tetrabutylammonium fluoride.

Our approach to diazonium compound **10** is shown in Scheme 4. In a similar manner to the arene diazonium salts described above, we found that diazotisation of amine **12** gave a relatively unstable oil that could not be satisfactorily purified. Hence, **12** was diazotised and subsequently reacted with TTF *in situ*. Using this procedure, the desired spirocyclic compound **11**,‡ the product of attack by an internal nucleophile, was indeed produced. This research hints that radical-polar crossover chemistry may be useful in the construction of more complex molecules; this theme is pursued in the following communication.



Scheme 4 *Reagents and conditions*: i, $(EtO)_3P$, neat, reflux, 4 h, 71%; ii, NaH, MeCOMe, 0 °C to room temp., 37 h, 58%; iii, $LiAlH_4$, Et_2O, reflux, 1 h, 94%; iv, TBDPSCl, imidazole, DMF, 16 h, 69%; v, $NO_2C_6H_4OH$, Ph_3P, DEAD, THF, 0 °C to room temp., 14 h, 71%; vi, TBAF, THF, 4 h, 99%; vii, $NaBH_4$, $Cu(acac)_2$, EtOH, 71%; viii, $NOBF_4$, CH_2Cl_2, 0 °C, 5 min. followed by TTF, moist acetone, room temp., 30 min, 57%

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Footnotes

† Current address: Department of Pure and Applied Chemistry, University of Strathclyde, 295 Cathedral Street, Glasgow, UK G1 1XL

‡ *Selected data* for **11**; δ_H (250 MHz, $CDCl_3$) 1.16 (3 H, s, CH_3), 1.27 (3 H, s, CH_3), 2.31 (1 H, ddd, *J* 12.7, 9.1 and 6.8 Hz, CCH_2CH_2O), 2.53 (1 H, ddd, *J* 12.9, 9.1 and 6.7 Hz, CCH_2CH_2O), 4.00–4.18 (2 H, m, CH_2O), 4.35 (1 H, d, *J* 9.2 Hz, $ArOCH_2$), 4.62 (1 H, d, *J* 9.3 Hz, $ArOCH_2$), 6.88 (1 H, d, *J* 7.9 Hz, ArH), 6.94 (1 H, dd, *J* 7.5 and 7.5 Hz, ArH), 7.22 (1 H, d, *J* 7.6 Hz, ArH) and 7.30 (1 H, dd, *J* 7.9 and 7.9 Hz, ArH); δ_C (67.8 MHz, $CDCl_3$) 23.0 (q), 23.1 (q), 38.5 (t), 57.7 (s), 63.2 (t), 78.2 (t), 109.7 (d), 120.6 (d), 124.9 (d), 128.5 (d), 130.8 (s) and 159.7 (s).

References

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