Rod Porter

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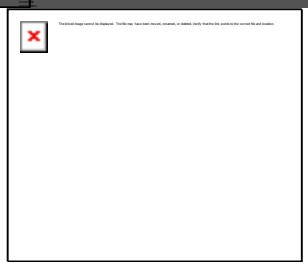
Medicinal Chemistry Newsletter | View Web Version



Medicinal Chemistry News from Rod Porter

December 2014 vol 5. no. 6

Dear Dr Porter,

1. Welcome

The last edition of 2014 for the Medicinal Chemistry newsletter from RodPorterConsultancy - a cliche I know but the year really has blasted by. *As with last time round I have not been able to give as much consideration as I would like to some topics but I hope the referenes will none the less be useful*. Topics featured this month include; .....

Don't forget to have a look at the CompChem Solutions services a range of complementary activities to those of RodPorterConsultancy.

Having just acquired a license for the chemically intelligent Sentira data visualisation software I am looking forward to using this tool to the benefit of my clients during 2015.

Please forward this newsletter to your colleagues – just follow the link at the bottom of this mail. Any comments, criticisms or suggestions for future articles are very welcome please mail Rod Porter.

My next mailing is planned for early February.

WIth the dark days of winter well and truly here, here are a couple of short promotional videos shot, in part, by a film maker for the tour operator while we were in Kyrgyzstan and Uzbekistan in the summer to give you a bit of sunshine. For those of you who know me keep your eyes open and have a good laugh!

Wishing you every success with your research.

In this issue:

Society of Medicines Research- next meeting

The next meeting of the SMR, "SMR Award Meeting: Recent Disclosures of Clinical Candidates" will be on 4th December at the NHLI London. This is always a well attended meeting so please do book early for what promises to be an excellent day of science.

The SMR are pleased to announce that the 2014 SMR Award for Drug Discovery, is to be awarded to Pharmacyclics for the discovery and development of Ibrutinib (ImbruvicaTM), a first in human BTK covalent inhibitor for the treatment of a number of B-cell malignancies.The award will be presented during the the December 2014 SMR meeting "Recent Disclosures of Clinical Candidates".

Together with the SMR award lecture the "Recent Disclosures of Clinical Candidates" meeting features an excellent array of novel molecular therapeutics across several target classes and therapeutic areas, which include oncology (inhibitors of BTK and Mdm2), pain (Nav1.7 modulation), CNS (highly selective M1 agonists and BACE1 inhibitors), bacterial infection (inhibitors of Clostridium difficile) and allergic inflammation (intranasal TLR7 agonists).

For the full programme please visit here.

2. State of the industry

Delivery – not quite as quick as Fedex!

A brief and rather bleak perspective on drug delivery described the few successes that delivery technology has had – most recently the approval of Mannkind's inhaled insulin Afrezza and earlier in the year long-acting versions of glucagon-like peptide, Factor VIII and Factor IX. Short interfering RNA (siRNA) therapeutics have also, finally, notched up success with Alynlam's subcutaneously delivered N-acetylgalactosamine (GalNAc) cluster conjugates have achieved potent gene knockdown in the livers of patients. However, all of these have been real struggles and the prospects for future successes are not bright particularly in areas such as effective delivery to the CNS. The authors propose that moving from the largely empiical past and current approaches there needs to be an increased understanding of the cell biology of uptake of molecules of all shapes and sizes. Difficult to argue with really.

Complementing this nicely was a report of a talk from the newly appointed GSK leader of drug delivery with the brief to pull together all the fragmented drug delivery efforts in the company. A key part of his brief is getting early engagement with research teams – this is a common theme in drug delivery. http://www.nature.com/nbt/journal/v32/n10/full/nbt.3045.html?WT.ec_id=NBT-201410

http://www.fiercedrugdelivery.com/story/gsk-exec-stresses-need-move-away-fragmented-approach-drug-delivery/2014-10-21?utm_medium=nl&utm_source=internal GSK exec stresses need to move away from 'fragmented' approach to drug delivery

3. In Brief

Painful failures - the top ten

It does seem a little previous to be putting out a 2014 hall of shame in October however FierceBiotech have just done that - hopefully it doesn't reflect a lack of big Phase III reports between now and the year end. I am not sure hall of shame is quite the right phrase either it can giuve3 no one any pleasure to see any treatment fail to give patient benefit. Sadly topping it is darapladib a compound from a programme to which I made a minor contribution way back in its early research days. This failure really continues to demonstrate that cardiovascular studies are high cost and high risk although potential gain can be enormous. It was also sad to see the glycine transport inhibitor Bitopertin (Roche) fail in multiple schizophrenia studies a tough area with major unmet medical need. Other lessons were that cancer vaccines in isolation are also high risk although merit in comnbination approachesd may prove better – time (and a lot of money) wiull tell. Other lessons that seem to need relearning every year is that blips of a read out in one study are a high

risk in justifying another costly PhIII study. Of course this also reemphasises how difficult it is to walk away from an advanced asset which has seemed like a good idea for a long time and where risk v. benefit is not an obvious from close up – not fprgetting the truth that hindsight has 20/20 vision. Other failures included Tecemotide (Merck KGaA), MAGE-A3 (GSK again) tabalumab (Liully), Dacomitinib (Pfizerf) amongst oterh major pharma but to show its not only major pharma that has flops add in Cabvozantinib (Exelixis) - that one cost thejobs of 70% of the staff.

Depressing reading

A series of articles in Nature highlight the plight of research on depression and the massive impact depression is having on world health. Depression is by far the biggest contributor to years lost to disability **1** with about 76.4Million YLD with back and neck pain next at 53.9M YLD.- anxiety comes in 5th after anemia and chronic lung conditions with 27.6MYLD. The impact of depression may also be a significant underestimate with likely substantial under or misdiagnosis. It was a shock to see Afghanistan having a 22.5% prevalence of depression with only 0.16 psychiatrists per 100,000 of the population (UK ~3.5% and ~18 respectively) with other troubled countries hovering aroud a 10% prevalence – not a topic that gets reported in the popular media. Despite this cancer is getting over 10 times the funding that depression receives from the American government **2** although while prevalence is lower mortality is higher. Of course there are a range of reasons why research on depression has lagged behind other therapeutic areas – understanding of the fundamentals of the disease – let alone diagnosis or means of patient segmentation being only some of the issues as discussed in. Also raised, however, **3** is the continuing issue of recognising and handling people with depression – someone taking their own life is more "news worthy" than the travails that person went through on a daily and possibly lifelong basis. That may say more about the general population than anything. Attitudes to drug treatment are also contradictory – the wonder cancer cure versus the seemingly poisonous attitude to anti-depressants which sadly tend to only work in a moderate proportion of patients.

Tools are emerging **4** to help with CNS psychiatric research but progress is slow perhaps the US and Europe "Brain" initiatives will help to accelerate progress. There are appeals for more large scale genetic studies as well. There was also an appeal **5** for a more adventurous approach for testing existing drugs for antidepressant behaviour – or at least to gather anecdotal information on mood changes found with drugs not being taken as antidepressants to support new clinical trials

1. K. Smith Nature 2014, 515, 179
2. H. Ledford Nature 2014, 515, 182
3. Editorial Nature 2014, 515, 163
4. S. Hyman Nature 2014, 515, 189
5. D. Nutt Nature 2014, 515, 165

Papers with the most citations

A bit of a curiosity that caught my eye was a report **1** on the most cited articles of all time to mark the 50th anniversary of the Science Citation index. The analysis used Thomson Reuters Web of Science which includes both SCI and databases for social sciences, arts and humanities. 12,119 citations are needed to reach the top one hundred most cited papers but only 14,499 papers have more than 1,000 citations. Also the top three papers achieve over 100,100 citations the 4th a "mere" 65,335. An initial surprise was that few of the "classic" papers in their field which may hae led on to Nobel prizes make the top 100 one example being the first report of carbon nanotubes (36th) but discovery of the first high temperature superconductors or the determination of the DNA double helix do not make the cut. However, on reflection the fact that many of these highly cited papers are for methods is perhaps less surprising. A charming quote written in 1977 from the late lead author of the most cited paper (305,148 citations) US biochemist Oliver Lowry "Although I really know it is not a great paper ……..I secretly get a kick out of the response" His paper, published in 1951 describes an approach to quantify proteins in solution. So if citations matter to you develop a good method!

1. R. V. Noorden, B. Maher and R. Nuzzo Nature 2014, 514, 550

And where the literature goes wrong

While numbers of citations is one measure of achievement another, which is developing a more sinister trait is the importance of the length of ones publication record. The concern raised in an entertaining piece in Chemistry World from the inimitable Derek Lowe highlights the issue of now being able to pay an open access journal to publish stuff that really should not see the light of day.

Clearly manyl open access journals do not follow this cavalier approach to proliferating and despoiling the scientific literature unfortunately some for the sake of making a quick profit are very happy to uncritically publish anything that anyone is prepared to pay to get published. The consequence can be a CV with a long list of worthless (or worse wrong) publications – which look so impressive to an uncritical hiring or evaluating committee. Some conferences are also going down that line. Unfortunately it tends to be academia that gets drawn into this game – industry is rather better at asking if there is any benefit to the company by paying for a publication or to attend a meeting where the merit is deeply suspect.

Derek Lowe Chemistry World Oct 2014

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Winning the script popularity contest

A bit of fun and an interesting perspective on the popularity of drugs – looking at which are prescribed most in the US used rather than most valuable with one or two surprises to me. Crestor topped the list 22M scripts but the surprise to me was Synthroid used for hypothyroidism and the third is Nexium. None of thesse feature in the top ten for value indeed Synthroid is only at 69 with annual sales of $899M. This was based on prescriptions written so the other question to ask is how many prescription days do these represent.

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4. Medicinal Chemistry

Shape changing proteins

A paper from AZ **1** describes an intriguing approach to identify inhibitors of P38α that selectiviely block the phosphorylation (and consequent activation of) MK2 one of many P38α kinase substrates. MK2 has been implicated in the inflammatory responses mediated via the P38 pathway. Effective conventional ATP competitive MK2 inhibitors have proved elusive. The approach adopted was to run an alpha screen inhibition of phosphorylation of inactive non-phosphorylated MK2 by active p38α. The follow-up screening strategy involved a counter screen of actives with the standard P38α synthetic substrate MBP to eliminate those compounds that were active as conventional ATP competitive inhibitors. This left a couple of chemical series (1), (2) that were discussed that showed inhibition of the phosphorylation of MK2 by P38 but no phosphorylation of MSK1 another P38α substrate. Compounds from the series did not show detectable inhibition of the P38α/MBP phosphorylation - IC50 p38α/MBP >10uM. A limited SAR studies were reports the key feature that was observed was the importance of the cyano (1) or sulphonamide (2) group that was essential for selectivity. This was shown by the reported crystallographic studies to form an H-bond to the backbone NH of Asp168 of the DFG loop

Importantly this work was followed up by detailed competition, SPR, 2D NMR and X-ray crystallographic studies. Compounds were shown to be

- • competitive with respect to ATP with Ki's of 0.29, 0.014uM for compounds (1) and (2) respectively.
- • Kd for binding phospho-p38α >> IC50 for p38α/MK2 enzyme assay
- • 2D NMR weak binding to p38α or MK2, strong interaction with p38α/MK2 complex - ATP site
- o Phospho-p38α/MK2 = P38α/MK2
- p38α ATP site binding confirmed by X-ray crystallography

In the p38α/MK2 complex relative to P38α alone changes in the p38α amino acids close to the MK2 surface - Asn114 and Asn115 – ligand binding pocket were seen. The changes in p38α transferred through the protein to Glu71 - 12 Å from the MK2−p38α interface and Phe169 of the DFG loop was in a perpendicular orientation. Finally Asp168 adopted a different conformation in the MK2−p38α complex structure. It would appear that the P38α ATP binding site is allosterically modulated by MK2 in a manner which is somewhat different to any influence other substrates bring to bear on the ATP binding site wich when you think about it further increases ones dilemma in how to interpret

isolated enzyme selectivity data – amongst other consequences and opportunities for that matter. Certainly it seems a strong argument to avoid using synthetic substrates

These are not the first compounds that show selectivity for inhibiting the phosphorylation of MK2 relative to other P38α substrates **2**, as CMPD (3) is reported to have this profile albeit apparently competing with MK2 for binding to P38α rather than action at the ATP binding site.

Finally and following the theme of "the devil is in the detail" for the ATP binding site of kinases is the discussion **3** of the selectivity of Gleevec for cAbl over other tyrosine kinases such as Src. Gleevec apparently adopts virtually identical structures in cAbl and Src but "the origin of Abl's high affinity lies predominantly in a conformational change after binding. An energy landscape providing tight affinity via an induced fit and binding plasticity via a conformational-selection mechanism is likely to be general for many inhibitors." Thus another theme of needng to look beyond apparently well established interactions. A slightly earlier paper **4** also highlights the importance of using as near full length proteins as possible for structural studies as it was shown that cAbl fragment that includes regulatory domains binds Imatinib in an unexpected open conformation that is closed by the addition of an allosteric myristate binding site molecule. Yet more work this year **5** also suggests that conformation selective ATP competitive inhibitors can be designed to modulate domain interactions and post translational modifications removed from the ATP binding site

1. J. G. Cumming et al J. Med. Chem 2014, J. Med. Chem., Article ASAP DOI: 10.1021/jm501038s, Publication Date (Web): September 25, 2014,
2. W. Davidson et al Biochemistry 2004, 43, 11658
3. R. V. Agofonov et al Nature Struct. Mol. Biol 2014, 21, 848
4. L. Skora et al PNAS 2013 110 (47) E4437-E4445
5. S. E. Leonard et al A.C.S. Chem. Biol., 2014, 9, 1894

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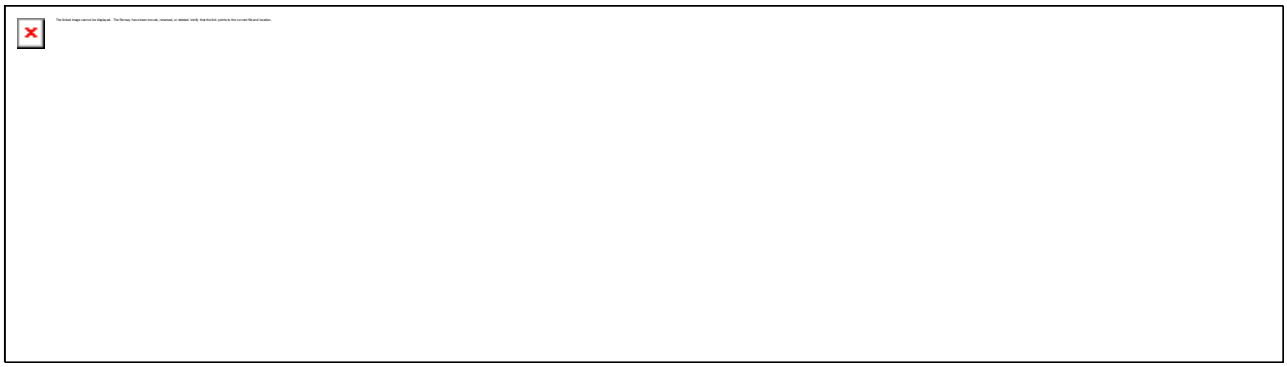

Fragments and PPIs

Papers looking at 3-dimensional descriptors of PPI inhibitors and of the sorts of fragments that appear as hits in PPI fragment screens have appeared. Tying together conclusions from each of these could be worthwhile. Firstly looking at bound conformations of PPI inhibitors 1 it was concluded that four parameters particularly distinguished bound PPI inhibitor conformations . These were EDmin3 (the third lowest local minimum of the interaction energy) and globularity evaluating the resemblance of the molecule to a sphere. These two properties seemed to be more or less universal for a PPI inhibitor independent of the PPI class. Slightly less consistently applicable were the integy moment IW4 (which expresses the imbalance between the centre of mass of the molecule an the barycentre of its hydrophilic regions) and CW2 – the ratio between the surface of the hydrophilic region at -0.5kcal/mol and the total molecular surface. The authors concluded this highlighted how well PPI inhibitors tend to be able to bind to the hydrophobic patch often found at an inhibitory hotspot. This paper also provided an excellent source of PPI databases. Just to highlight the point about hydrophobic interactions is a review on MDM2 inhibitors in the clinic with the three aromatic rings required to mimic three hydrophobic Phe19, Trp23, and Leu26 side chains of the P53 alpha-helix 2.

In the next paper fragments that have been identified as hits for PPI's are analysed and compared with fragments identified as hits for "conventional" targets. The authors concluded that PPI fragments tend to be larger, more lipophlic and contain more polar – as in charged motifs. They did, not in some contradiction to the other paper in this discussion, identify any particular indication of increased 3D shape. This paper also provided a number of useful links to sources for identifying protein "hotspots" . This paper has also featured in a blog discussion in which there are some

disagreements with the idea that PPI inhibitor fragments are much larger than fragments for conventional targets – there is some useful discussion in the comments.

1. M. A. Kuenemann, et al. Chem. Inf. Model., Article ASAP, DOI: 10.1021/ci500487q Publication Date (Web): October 17, 2014 Copyright © 2014, American Chemical Society
2. Y. Zhao, et al . Med. Chem., Article ASAP DOI: 10.1021/jm501092z Publication Date (Web): November 14, 2014 Copyright © 2014, American Chemical Society
3. P. Turnbull et al Research and Reports in Biochemistry 2014:4 13–26

Nitrogen in drugs

Following on from a paper earlier this year 1 looking at rings in approved drugs featured in the March 2014 edition of this newsletter is a paper focused on the structural diversity, substitution patterns and frequency of nitrogen heterocycles in FDA approved drugs. Perhaps a slight surprise that of the 1086 small molecules analysed "only" 59% had at least one nitrogen heterocycle while 84% had at least one nitrogen – average 2.3N/drug. Not surprising was the top three ring systems – piperidine, pyridine and piperazine with cephem next. Tetrazoles are also rather common with 16 incidents though I might have expected benzimidazoles to be ranked higher than 15th. Systems that did surprise me by there frequency were imidazoline, tetrahydroisoquinoline abd imidazoline respectively 19=, 19= and 21st particularly in view of some of the alarms raised around tetrahydroisoquinolines. Quinazolines squeak into the top 25 but quinolines do not. Clearly there are biases with therapeutic class thus cephems, penams and isoquinolinones are particularly common reflecting their antibiotic background. Perhaps the thing that comes out of this are two fold again the lack of diversity of ring systems used and the frequency of what one could consider as reduced aromatics with perceived problems of oxidation state lability

1. R. D Taylor et al J. Med. Chem. 2014, 57, 5845
2. Rod Porter Consultancy Newsletter March 2014 vol 5 no_1 (1)
3. E. Vitaku, D.T. Smith and J. T. Njardarson J. Med. Chem., Article ASAP DOI: 10.1021/jm501100b Publication Date (Web): October 07, 2014 Copyright © 2014, American Chemical Society

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Epigenetics

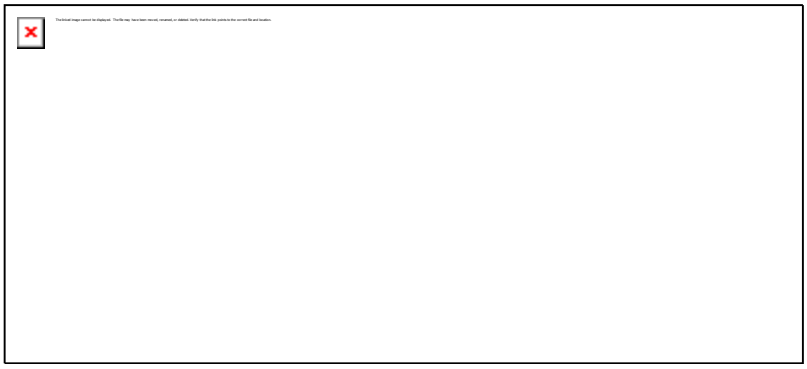
A couple of substantial reviews on histones and epigenetics have appeared **1, 2**. The first 1 a 54 page magnum opus is focused on the contribution of peptide chemistry in, for example, preparing chemically defined post translationally modified histones with application in for example transcription assays or X-ray crystallography studies. A useful compilation diagram (Fig 60!) of post translational modifications and their analogues that have been site specifically incorporated into histones is provided.

More specifically looking at therapeutics rather than biological; tools the second review **2** focuses n the enhancement of neurogenesis and neuroprotection by small molecules that target epigenetic enzymes. The role of histone lysine (de)acetylation and (de)methylation and DNA methylation alongside acetyl lysine readers, neurogenesis and neurodegeneration are briefly reviewed although there is no discussion of methyllysine readers and the lack of understanding of the effect of arginine methylation is highlighted. The reviewers move on to look at the actions of known small molecule epigenetic modulators in neurogenesis. For example valproic acid increases experesion of bHLH pro-neuronal transcription factors such as neurogenin-1 amongst others and also activating the ERK pathway. One point highlighted particularly for the HDAC inhibitors that have been used in neurogenesis experiments is their lack of specific isoform selectivity – at best targeting a class of HDAC's. Thus the description of the p300/CBP specific HAT activator CTPB is conceptually interesting even if the compound itself is structurally less interesting. Perhaps the key message out of this useful review is that we are really scratching the surface in understanding the role of epigenetics in neurodegeneration/genesis and we are just starting to develop the tools both small molecule and peptide/protein reagents cf 1 to help build our understanding of what may be some excellent therapeutic targets of the future. It would help if some of the more recent and reportedly more selective agents were adopted for at least in vitro studies. The concept of HAT activation also falls in line with the discussion of activators of kinase inhibition discussed elsewhere in this newsletter.

Reports continue to emerge of new selective epigenetic modulators – just follow some of the work from the SGC. Also a report of an HDAC6 inhibitor series **3** in which a heterocyclic spacer is proposed to effectively access the wider catalytic channel of HDAC6 compared to other HDAC's.

Finally a review **4** of the progress in discovering acetyllysine reader bromodomain inhibitors by leading proponents of the art and the use of these inhibitors in target validation .

1. M. M. Müller and T. W. Muir Chem. Rev., Article ASAP DOI: 10.1021/cr5003529 Publication Date (Web): October 20, 2014 Copyright © 2014, American Chemical Society
2. A. Swaminathan et al ACS Chem. Neurosci., Article ASAP DOI: 10.1021/cn500117a Publication Date (Web): October 10, 2014 Copyright © 2014, American Chemical Society
3. C. Blackburn et al Bioorg. Med. Chem Lett., 2014, 24, 5450
4. S. Müller and S. Knapp MedChemComm 2014, 5, 288-296



Antibody drug conjugates

The antibody drug conjugate in which a cytotoxic agent is linked to an antibody targeting the tumour cell is a simple, elegant concept in principal but it has proved hard to reduce to practice with the linker often proving the confound. A recent review **1** now discusses the characteristics of clinical proof of concept immunoconjugates bearing calicheamicin, auristatin or maytansine-based cytotoxic payloads and the chemical strategies used to achieve the conjugation.

The issue that particularly arises is ensuring that the toxic payload can be released inside the targeted tumour cells rather than non-selectively and can involve some rather extensive optimisation. For example coupling the chimeric anti-CD30 mAb cAC10, which induces growth arrest of CD30+ tumor cells to monomethylauristatin is accomplished through cysteine residues on the antibody linked to succinimide which is then N-linked (1) via a carbon chain to valine, citrulline and finally a urethane to the cytotoxic agent. The payload is stably linked in plasma but is selectively cleaved by lysosomal enzymes after CD30 receptor mediated internalization. This really emphasised the importance of chemistry to match the biology behind the whole concept of ADC's

In a review from earlier this year **2** similar ground has been covered widening the scope to consider delivery bispecific antibodies, radionuclides and cytokines all of which benefit from targeted delivery.

Finally a report **3** of silyl ethers as acid labile linkers for ADC's (2) with the principal of cleavage in endosomes – the concept is demonstrated using the mAb trastuzumab with the chemotherapeutic, gemcitabine.

1. H. Bouchard et al Bioorg. Med. Chem. Lett., 2014, 24, 5357
2. C. Hess, D. Venetz and D. Neri Med. Chem. Commun., 2014,5, 408-431
3. M. C. Finiss et al Med. Chem. Commun., 2014, 5, 1355

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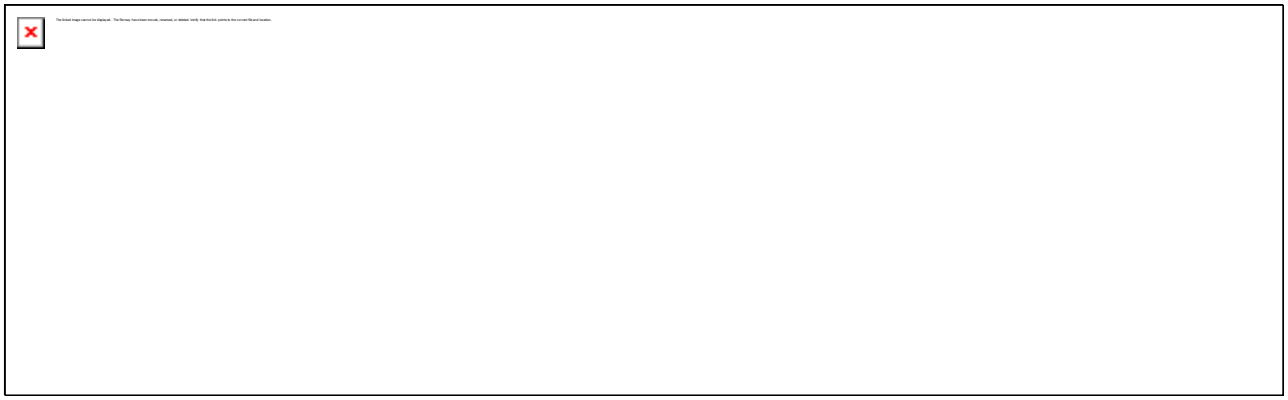

5. Chemistry

SF5 once more

For those of you remembering the discussion of arylpentafluorosulphanyl substitution in drug discovery a review has just appeared 1 on the synthesis and use of this motif in medicinal chemistry.

1. P. R. Savoie and J. T. Welch Chem. Rev, Article ASAP DOI: 10.1021/cr500336u Publication Date (Web): October 24, 2014 Copyright © 2014, American Chemical Society

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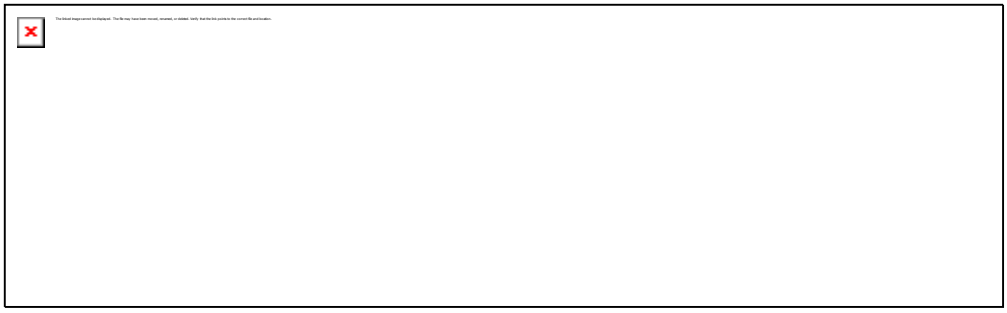

Meta Metallation.

(Hetero)arene ortho-metallation of a directing group substituted aromatic is well documented. However the regiochemical constraint to 1,2-disubstitiution is a limitation. A method is now reported **1** in which a dimetallated complex of an aromatic is generated in a regioselective manner controlled by the template nature of the bases [{KMg(TMP)2(nBu)}6] or [Na4Mg2(TMP)6(nBu)2] giving either a 2,5-dianion or a 3,5-dimetallation depending on the size of the directing group. More bulky groups drive 3,-di,etallation. The nature of the directing group also dictates reaction conditions as might be expected with good directing groups such as urethanes or tertiary amides needing room temperature only while poor directors such as OMe or CF3 require around 100C for a prolonged period of time. Yields are good generally around 90% although onlu I2 or CO2 have been used to quench reactions at this stage. The metal complex is shown to form a cage around the target aromatic ring which may lead to some limitations on reactivity of more highly substituted aromatics. No heteroaromatics were given as examples. It will be interesting to see how this area develops over the next few years

1. A. J. Martinez Martinez et al Science 2014, 346, 834

6. Conferences

Conferences Rod Porter Consultancy will be attending - click on the links for the agenda. This may have happened by the time this mailing goes out. I dont currently have any meetings lined up for

2015 except for the Society of Medicines Research ones planned for the coming year visit this page for more information for forthcoming events

- SMR Award Meeting: Recent Disclosures of Clinical Candidates SMR London, 4th December

Meetings Attended

Three meetings attended since September I have linked the BBB CLub meeting fromt eh 7th Nov to a short slide apck I presented at the meeting looking at a paper (Uchida et al JPET 2014 350: 578-88) looking at pharmacoproteomics reconstruction of in vivo distribution of P-gp substrates in the monkey - a paper I did review when it was first e-published earlier this year. Just before anyone makes a rude comment I am also aware that I am no longer in the Early Career category for the second meeting which I have to say was very good. The young presenters did themselves proud alongside the plenary lectures from John Greenwood and Karl Webster (Medimmune - antibodies in the CNS)

- Blood Brain Barrier Club Kings College London 7th Nov
- Early Career UK and Ireland Blood-Brain Barrier Symposium 21st Nov University College London
- CNS drug discovery symposium SCI 26th Nov Takeda Cambridge

7. Also of interest

Using the web, all sorts of interesting resources appear. If you come across any resources that you would like to share please contact Rod Porter.

Nature has started a digital toolbox available on line or as a monthly print feature looking at seful website compilations of software tools and websites to help more efficient work. Recent examples include looking at "recommendation engines" and future features will look at iPython.

These sites are featured because Rod Porter has found them of interest - featuring these sites does not reflect any endorsement or accountability for their use from Rod Porter Consultancy

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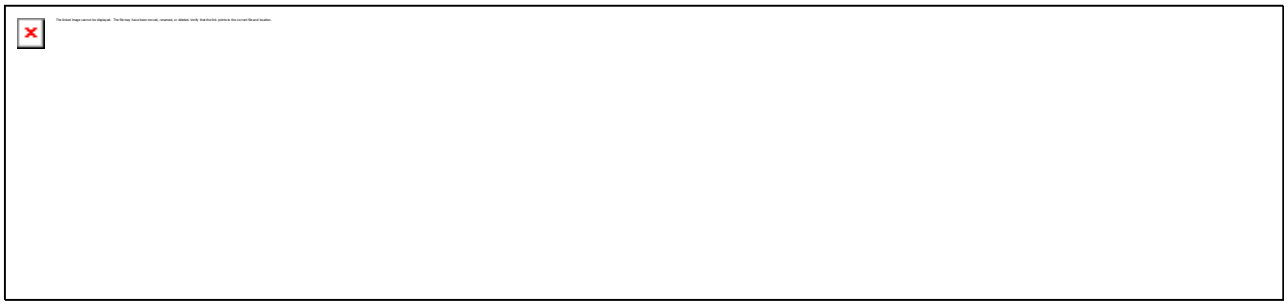

8. About RodPorterConsultancy

Established in 2009 RodPorterConsultancy offers medicinal chemistry consultancy services to a widening client base of small biotechs, academic and charitable bodies. Services offered include assistance with or proposal of medicinal chemistry strategies, with a particular interest in CNS targets, independent, expert review of ongoing programmes and projects, review, critique and refereeing of research proposals, third party due diligence and more. If I can't help you perhaps my informal network of contacts can. Visit the RodPorterConsultancy website, see my linked-in page or contact Rod Porter directly for more information.

Just a reminder that any feedback on the content or suggestions for new content will be gratefully received please e-mail Rod Porter

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CompChem Solutions offers computational chemistry & computational biology services to academic and industrial researchers involved in drug discovery and development. Established in 2004 and based in Cambridge, UK, CompChem Solutions has a wealth of experience across the range of chemoinformatic and computational chemistry disciplines, having worked extensively in many therapeutic areas, particularly oncology, inflammation and pain. Recent publications from CompChem Solutions have exemplified the use of in silico methodology for target validation and identification, particularly within the context of phenotypic screening. Services can be provided in virtual screening, rational ligand design, protein homology modelling, library design, ADMET property prediction, and many other areas.

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