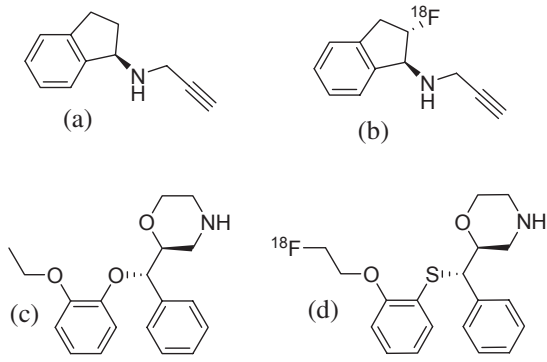

FIGURE 10.5 (a) Azilect® (Rasagiline) (b) [^{18}F] fluororasagiline (c) Edronax® (Reboxetine) (d) [^{18}F] fluororeboxetine.

PET ligand is not a viable option. In order to use Azilect as a radioligand it would be necessary to incorporate a ^{11}C into its structure, but the time required to synthesis ^{11}C labeled material based on the available synthetic chemistry is far too long for practical application (as mentioned above, the $t_{1/2}$ of ^{11}C is only 20 min). As an alternative, the ^{18}F labeled analog, [^{18}F] fluororasagiline (Figure 10.5(b)), was developed. The addition of a fluorine atom to Azilect had minimal impact on its overall properties, allowing it to serve as a surrogate for the clinical agent. New synthetic methods were required in order to prepare the radiolabeled compound, but the longer half-life of ^{18}F increased the time available for synthesis and PET imaging studies. In addition, incorporation of the radioisotope could be accomplished at the end of the synthetic pathway, greatly simplifying the radiochemistry requirements.[35]

In a similar manner, the norepinephrine reuptake inhibitor antidepressant Edronax® (Reboxetine, Figure 10.5(c)) was identified as a potential PET ligand useful for studying the norepinephrine transporter (NET). Edronax's low non-specific binding and high selectivity for NET over the serotonin transporter (SERT) and the dopamine transporter (DAT) provided an opportunity to study the brain distribution of NET. Unfortunately, much like Azilect, the synthesis of Edronax is not conducive to the incorporation of a radioisotope. As an alternative, a new radiolabeled analog of Edronax (Figure 10.5(d)) was identified as a viable alternative. The exchange of an oxygen atom for a sulfur atom had no impact on the NET/SERT/DAT selectivity, and synthetic methods capable of installing an ^{18}F in the final step of the synthetic sequence facilitated the development of this PET ligand. It is worth noting that in this case, alternative radioligands incorporating a ^{11}C were also developed.[36]

The importance of low non-specific binding of Edronax and its radioligand analogs should not be understated. Compounds that are target